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UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF IDAHO
SOUTHERN DIVISION

UNITED STATES OF AMERICA, Plaintiff, v. THE STATE OF IDAHO, Defendant.	Case No. 1:22-cv-329-BLW **MOTION FOR A PRELIMINARY INJUNCTION**

THE UNITED STATES'
MOTION FOR A PRELIMINARY INJUNCTION

Plaintiff the United States of America respectfully moves for a preliminary injunction against the State of Idaho—including all of its officers, employees, and agents—prohibiting enforcement of Idaho Code § 18-622(2)-(3) as applied to EMTALA-mandated care. The United States' arguments in support of this motion are fully set forth in the attached memorandum of law and supporting declarations.

Dated: August 8, 2022

Respectfully submitted,

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INTRODUCTION

Federal law requires certain hospitals receiving federal Medicare funds to offer treatment to individuals experiencing medical emergencies. Under the Emergency Medical Treatment and Labor Act (EMTALA), 42 U.S.C. § 1395dd, individual patients must be provided "stabilizing care" when they seek treatment at a covered hospital for an "emergency medical condition." An emergency medical condition exists when a patient's "health" is in "serious jeopardy" or the patient risks "serious impairment to bodily functions" or "serious dysfunction of any bodily organ or part." 42 U.S.C. § 1395dd(e)(1)(A). Some patients who experience these medical emergencies are pregnant, and in some situations the necessary stabilizing treatment for such a pregnant patient involves termination of the pregnancy. In those circumstances, EMTALA requires that hospitals offer that stabilizing treatment to the patient, who can then decide whether to proceed.

In direct conflict with this federal requirement, the State of Idaho has enacted a near-absolute ban on abortion that is scheduled to go into effect on August 25, 2022. *See* Idaho Code § 18-622 (2020). Under Idaho's law, any physician who terminates a pregnancy can be indicted, arrested, and prosecuted on felony charges, regardless of the medical need for the procedure. A physician may avoid criminal liability only by proving a narrow "affirmative defense"—as relevant here, that the abortion was "necessary to prevent the death of the pregnant woman." *Id.* § 18-622(3)(a)(ii). That defense is far narrower than the circumstances in which EMTALA requires providing stabilizing treatment. Where EMTALA's standard is met but the treatment is not strictly "necessary to prevent the death" of the patient, it is impossible for a physician to comply both with the obligations of EMTALA and § 18-622. And even in cases where termination of the pregnancy is necessary to prevent the patient's death, the Idaho law requires a physician to risk arrest and prosecution for each abortion performed because the law affords only an "affirmative defense" that the physician must prove at trial. By threatening physicians with criminal prosecution—even when they provide treatment in emergency, life-

threatening situations as federal law requires—Idaho's law penalizes and discourages such treatment, and thereby conflicts directly with federal law. In these respects, federal law preempts § 18-622.

If allowed to go into effect, the Idaho law will cause significant irreparable harm, including to the public health of patients across Idaho. As the declaration of Dr. Lee A. Fleisher (attached as Ex. A) demonstrates, there are emergency conditions affecting pregnant individuals for which the medically necessary treatment involves termination of the pregnancy. But § 18-622 criminalizes providing such treatment, despite the extremely serious risk that, for example, a patient with an ectopic pregnancy might bleed to death, an infection could turn into sepsis and cause organ failure, or seizures caused by eclampsia might prove uncontrollable. Physicians practicing within Idaho likewise confirm that, if § 18-622 takes effect, pregnant patients experiencing emergency conditions will suffer. *See* Decls. of Dr. Emily Corrigan, Dr. Kylie Cooper, and Dr. Stacy T. Seyb (attached hereto as Exs. B-D). These facts establish clear irreparable harm and a strong public interest in enjoining § 18-622 from going into effect as applied to EMTALA-mandated care. The Court should grant the United States' motion for a preliminary injunction.

BACKGROUND

I. Federal Law

A. Supremacy of Federal Law

The Supremacy Clause of the U.S. Constitution mandates that "[t]his Constitution, and the Laws of the United States which shall be made in Pursuance thereof . . . shall be the supreme Law of the Land . . . any Thing in the Constitution or Laws of any State to the Contrary notwithstanding." U.S. Const. art. VI, cl. 2. Pursuant to that principle, "states have no power . . . to retard, impede, burden, or in any manner control the operations of the Constitutional laws enacted by [C]ongress to carry into effect the powers vested in the national government." *M'Culloch v. Maryland*, 17 U.S. (4 Wheat.) 316, 317 (1819).

When "Congress enacts a law that imposes restrictions or confers rights on private actors," and "a state law confers rights or imposes restrictions that conflict with the federal law," the "federal law takes precedence and the state law is preempted." *Murphy v. NCAA*, 138 S. Ct. 1461, 1480 (2018). If a "statute contains an express pre-emption clause, we do not invoke any presumption against pre-emption but instead focus on the plain wording of the clause, which necessarily contains the best evidence of Congress' pre-emptive intent." *Puerto Rico v. Franklin Calif. Tax-Free Tr.*, 579 U.S. 115, 125 (2016) (citation omitted).

B. The Emergency Medical Treatment and Labor Act (EMTALA)

Medicare is a federally funded program, administered by the Secretary of Health and Human Services (HHS), that generally pays health care providers for health care services under certain circumstances. *See* 42 U.S.C. § 1395 *et seq.* Participation in Medicare is voluntary, and each provider must submit an agreement to the Secretary promising to comply with certain conditions in return for receipt of Medicare funding. *See id.* § 1395cc. Although Medicare generally does not contemplate Federal employees "exercis[ing] any supervision or control over the practice of medicine or the manner in which medical services are provided," 42 U.S.C. § 1395, that does not prevent the Federal Government from establishing and enforcing conditions of participation in Medicare, *see Biden v. Missouri*, 142 S. Ct. 647, 654 (2022), nor does it eliminate Congress's "broad power under the Spending Clause of the Constitution to set the terms on which it disburses federal funds." *Cummings v. Premier Rehab Keller, PLLC*, 142 S. Ct. 1562, 1568 (2022).

Congress enacted EMTALA in 1986, based on "a growing concern about the provision of adequate emergency room medical services to individuals who seek care, particularly as to the indigent and uninsured." H.R. Rep. No. 99-241, Part 3, at 5 (1985); *see also Arrington v. Wong*, 237 F.3d 1066, 1073-74 (9th Cir. 2001) ("The overarching purpose of EMTALA is to ensure that patients, particularly the indigent and underinsured, receive adequate emergency medical care." (alterations and citations

omitted)). EMTALA applies to every hospital that has an emergency department and participates in Medicare, *see* 42 U.S.C. § 1395dd(e)(2), regardless of whether any particular patient qualifies for Medicare. Congress has statutorily required that hospitals participating in Medicare agree to comply with EMTALA as a condition of receiving federal funding. *See id.* § 1395cc(a)(1)(I)(i).

Under EMTALA, when a patient arrives at an emergency department and requests treatment, the hospital must provide an appropriate medical screening examination "to determine whether or not an emergency medical condition" exists. *Id.* § 1395dd(a); *see also* 42 C.F.R. § 489.24(a)(1)(i). Congress defined an "emergency medical condition" as:

> (A) a medical condition manifesting itself by acute symptoms of sufficient severity (including severe pain) such that the absence of immediate medical attention could reasonably be expected to result in-
> (i) placing the health of the individual (or, with respect to a pregnant woman, the health of the woman or her unborn child) in serious jeopardy,
> (ii) serious impairment to bodily functions, or
> (iii) serious dysfunction of any bodily organ or part …
>
> (B) with respect to a pregnant woman who is having contractions-
> (i) that there is inadequate time to effect a safe transfer to another hospital before delivery, or
> (ii) that transfer may pose a threat to the health or safety of the woman or the unborn child.

42 U.S.C. § 1395dd(e)(1). If a hospital determines that an individual has an emergency medical condition, "the hospital must provide either (A) within the staff and facilities available at the hospital, for such further medical examination and such treatment as may be required to stabilize the medical condition, or (B) for transfer of the individual to another medical facility in accordance with" certain requirements. *Id.* § 1395dd(b)(1); *see also* 42 C.F.R. § 489.24(a)(1)(ii). The hospital may also "admit[] th[e] individual as an inpatient in good faith in order to stabilize the emergency medical condition." 42 C.F.R. § 489.24(d)(2)(i). Under EMTALA, "to stabilize" means "to provide such medical treatment of the condition as may be necessary to assure, within reasonable medical probability, that no material deterioration of the condition is likely to result from or occur during the transfer of the individual

from a facility." 42 U.S.C. § 1395dd(e)(3)(A). "[T]ransfer" is defined to include discharge of a patient. *Id.* § 1395dd(e)(4). A hospital satisfies its obligations under EMTALA if, after being informed of the risks and benefits of treatment, the patient (or the patient's representative) does not consent to the treatment. *Id.* § 1395dd(b)(2).

In short, EMTALA requires that hospitals offer stabilizing treatment where "the health" of the patient is "in serious jeopardy," or where a condition could result in a "serious impairment to bodily functions" or a "serious dysfunction of any bodily organ or part." *Id.* § 1395dd(e)(1)(A)(i)-(iii). The hospital may also "transfer" such an individual, but only if the transfer meets certain requirements, *e.g.*, that the medical benefits of the transfer outweigh the risks. *Id.* § 1395dd(c)(1)(A)(ii).

EMTALA contains an express preemption provision, preserving state laws "except to the extent that the requirement directly conflicts with a requirement of this section." *Id.* § 1395dd(f). The intent of this provision was to preserve "stricter state laws," *i.e.*, state laws requiring emergency care *beyond* what EMTALA mandates. H.R. Rep. No. 99-241, Part 1, at 4 (1985); *see also* H.R. Rep. No. 99-241, Part 3, at 5 (1985) (expressing a desire to add "federal sanctions" as a supplement to state law duties "to provide necessary emergency care"); *Harry v. Marchant*, 291 F.3d 767, 773-74 (11th Cir. 2002). For purposes of EMTALA, "[a] state statute 'directly conflicts' with federal law in either of two cases: first, if 'compliance with both federal and state regulations is a physical impossibility,' or second, if the state law is 'an obstacle to the accomplishment and execution of the full purposes and objectives of Congress." *Draper v. Chiapuzio*, 9 F.3d 1391, 1393 (9th Cir. 1993) (citations omitted) (per curiam); *accord Hardy v. N.Y.C. Health & Hosp. Corp.*, 164 F.3d 789, 795 (2d Cir. 1999).

C. Idaho Hospitals' Participation in Medicare and Their Agreements to Comply with EMTALA Obligations

As noted, a hospital participating in Medicare must comply with EMTALA as a condition of receiving federal funds. *See* 42 U.S.C. § 1395cc(a)(1)(I)(i). Additionally, hospitals enter into written agreements with the Secretary confirming they will comply with EMTALA.

Hospitals apply to become certified under Medicare by submitting a Centers for Medicare & Medicaid Services (CMS) Form 855, *see* Decl. of David R. Wright (attached hereto as Ex. E) ¶ 2, in which the provider "agree[s] to abide by the Medicare laws, regulations and program instructions that apply." CMS Form 855, § 15, ¶ A.3 (pg. 48), https://perma.cc/84T6-S2DP. If approved for Medicare certification, the hospital must then sign CMS Form 1561, Wright Decl. ¶ 4, in which the provider likewise "agrees to conform to the provisions of section of 1866 of the Social Security Act [42 U.S.C. § 1395cc] and applicable provisions in 42 CFR." https://perma.cc/5EPE-YLRE. Finally, each fiscal year, a Medicare-participating hospital must submit a cost report, pursuant to which "the Chief Financial Officer or hospital Administrator must certify that he or she is 'familiar with the laws and regulations regarding the provision of health care services, and that the services identified in this cost report were provided in compliance with such laws and regulations,' which include EMTALA." Wright Decl. ¶ 6; *see also* Decl. of Barbara Shadle (attached hereto as Ex. F) ¶¶ 2-5.

Within Idaho, there are 52 Medicare-certified hospitals, at least 39 of which provide emergency services. Wright Decl. ¶ 8. Of the 52 hospitals, 16 are government-owned, and at least 15 of those provide emergency services. *Id.* ¶ 9. These 52 hospitals in Idaho received approximately $3.4 billion in federal Medicare funds during fiscal years 2018-2020; by rough estimate, approximately $74 million was attributable to these hospitals' emergency departments. Shadle Decl. ¶ 6. That funding was conditioned on compliance with EMTALA. Wright Decl. ¶ 14.

II. Idaho's Abortion Law

In 2020, Idaho enacted a law that severely restricts abortion and threatens criminal prosecution against anyone who performs the procedure. The law, codified at Idaho Code § 18-622, is set to take effect August 25, 2022. *See* Idaho Code § 18-622(1)(a).

Under § 18-622, "[e]very person who performs or attempts to perform an abortion . . . commits the crime of criminal abortion," a felony punishable by two to five years imprisonment. *Id.*

§ 18-622(2). The law also requires that "[t]he professional license of any health care professional who performs or attempts to perform an abortion or who assists in performing or attempting to perform an abortion in violation of this subsection shall be suspended by the appropriate licensing board for a minimum of six (6) months upon a first offense and shall be permanently revoked upon a subsequent offense." *Id.* Idaho law defines "[a]bortion" to mean "the use of any means to intentionally terminate the clinically diagnosable pregnancy of a woman with knowledge that the termination by those means will, with reasonable likelihood, cause the death of the unborn child." *Id.* § 18-604(1).[1]

The *prima facie* criminal prohibition and license suspension provisions in Idaho's law do not contain any exceptions, including for when the pregnant patient's health or life is endangered. *See id.* § 18-622(2). Thus, the performance of an abortion—even in an emergency, life-saving scenario—would subject a provider to criminal prosecution and require the provider to assert one of the law's "affirmative defense[s]" at trial. *Id.* § 18-622(3). As relevant here, the accused physician would have to prove to a jury, by a preponderance of the evidence, that "[t]he physician determined, in his good faith medical judgment and based on the facts known to the physician at the time, that the abortion was necessary to prevent the death of the pregnant woman," and that the physician "performed or attempted to perform the abortion in the manner that, in his good faith medical judgment and based on the facts known to the physician at the time, provided the best opportunity for the unborn child to survive, unless, in his good faith medical judgment, termination of the pregnancy in that manner would have posed a greater risk of the death of the pregnant woman." *Id.* § 18-622(3)(a)(ii)-(iii).

STANDARD OF REVIEW

The United States seeks a preliminary injunction against § 18-622's enforcement as applied to

[1] This definition of "abortion" in the Idaho Code is broad and covers some procedures that may not be characterized as an abortion in the medical community, including some circumstances in which a pregnancy is nonviable or termination of pregnancy is necessary to treat a pregnant patient's medical condition. *See* Fleisher Decl. ¶ 32, Ex. A-B. For purposes of this case, the United States uses the term "abortion" as it is defined under the Idaho Code.

EMTALA-mandated care. To obtain such preliminary relief, "a party must show: (1) it will likely succeed on the merits, (2) it will likely suffer irreparable harm in the absence of preliminary relief, (3) the balance of the equities tips in its favor, and (4) the public interest favors an injunction." *AK Futures LLC v. Boyd St. Distro, LLC*, 35 F.4th 682, 688 (9th Cir. 2022) (citation omitted).

ARGUMENT

I. The United States is Likely to Succeed in Demonstrating that EMTALA Preempts Idaho's Abortion Law

The United States has a clear likelihood of success on its claim. EMTALA requires hospitals with emergency departments to provide stabilizing treatment for emergency conditions. Physicians treating emergency conditions will sometimes determine that the medically necessary treatment involves or will result in the termination of a pregnancy. Idaho's law conflicts with EMTALA by subjecting physicians to criminal prosecution for terminating *any* pregnancy, irrespective of the medical circumstances. The law also imposes felony criminal liability on physicians who provide abortions, unless the physician is able to prove through an affirmative defense that (as relevant here) the abortion was "necessary to prevent the death of the pregnant woman"—which is far narrower than the standard EMTALA requires for the provision of medically necessary care. Thus, Idaho's abortion law conflicts directly with EMTALA, and is preempted in the context of EMTALA-mandated care.

A. EMTALA Requires Participating Hospitals to Provide Stabilizing Treatment, Which Includes Abortions for Some Medical Conditions

Under EMTALA, hospitals that receive Medicare funds are generally required (barring an appropriate transfer to another medical facility) to offer and provide "stabilizing treatment" to all patients who arrive at their emergency departments while experiencing an "emergency medical condition." 42 U.S.C. § 1395dd(b)(1). For such patients, hospitals are required to provide "further medical examination and such treatment as may be required to stabilize the medical condition." *Id.*

§ 1395dd(b)(1)(A); *see also* 42 C.F.R. § 489.24(a)(1)(i)-(ii).

Congress explicitly contemplated that pregnant patients would be among those arriving at an emergency department experiencing an "emergency medical condition." *Id.* § 1395dd(e)(1)(A)(i), (B). A number of conditions can arise during, or can be exacerbated by, pregnancy that may constitute "emergency medical conditions." For some patients, a physician will determine that the stabilizing treatment for the patient's emergency condition is termination of the pregnancy. Fleisher Decl. ¶¶ 12-27; Corrigan Decl. ¶¶ 8-30; Cooper Decl. ¶¶ 5-11; Seyb Decl. ¶¶ 6-12. For example, a pregnant patient may arrive at an emergency department with bleeding, pelvic pain, or severe abdominal pain that is being caused by an ectopic pregnancy, a condition in which a nonviable embryo implants outside the uterus, often in a fallopian tube, which can never lead to a live birth. Fleisher Decl. ¶ 13. This is an "emergency medical condition" because it could cause the fallopian tube to rupture, and the patient could bleed to death. *Id.* In most cases, the physician cannot reasonably know when that rupture will occur—rupture can occur within minutes, hours, or days of an ectopic-pregnancy diagnosis—but without immediate treatment it is reasonably probable that the patient's condition will continue to deteriorate. *Id.* Given the "serious risk of unknown imminence," and the inevitability that the patient's condition will deteriorate, the "appropriate stabilizing treatment is nearly always" termination of the pregnancy through surgery or medication. *Id.*

To take another example, a patient may arrive at an emergency room with nausea and shortness of breath, leading to a diagnosis of pre-eclampsia. Fleisher Decl. ¶ 17. Pre-eclampsia can "quickly progress to eclampsia, with the onset of seizures," that can result in a coma, pneumonia, kidney failure, stroke, or cardiac arrest. *Id.* In many cases, pre-eclampsia and eclampsia can be managed with medications that allow the fetus to mature. But in other cases (*e.g.*, situations in which the seizures cannot be controlled), a physician exercising her medical judgment will conclude that termination of the pregnancy is the necessary stabilizing treatment. *Id.* As Dr. Corrigan described, pre-eclampsia for

one patient caused "water on the lungs," which required an immediate termination of the pregnancy. Corrigan Decl. ¶¶ 27-29; Cooper Decl. ¶¶ 6-7 (pre-eclampsia placed patient at risk for stroke, seizure, and pulmonary edema); Seyb Decl. ¶¶ 9-10. A woman may also arrive at the emergency department with an infection after the amniotic sac surrounding the fetus ruptures. Fleisher Decl. ¶ 19. This condition can progress quickly into sepsis, at which point a patient's organs may begin to fail; like the other conditions discussed above, there are some circumstances in which termination of the pregnancy is the medically necessary treatment. *Id.*; Corrigan Decl. ¶¶ 11-17; Seyb Decl ¶¶ 7-8.

As a further example, a patient may arrive at the hospital with chest pain or shortness of breath, at which point a doctor discovers longstanding elevated blood pressure or a blood clot. Fleisher Decl. ¶ 15. Pregnancy can substantially exacerbate these conditions, and for some patients with severe symptoms, termination is the necessary treatment under EMTALA because there is a high probability of severe impairment of the lungs, heart, and kidneys without treatment. *Id.* Similarly, a patient may arrive at the hospital with vaginal bleeding caused by a placental abruption. *Id.* ¶ 20; Corrigan Decl. ¶¶ 21-25; Seyb Decl. ¶¶ 11-12. If the bleeding is uncontrollable, a physician may conclude that the stabilizing treatment includes termination of the pregnancy, in order to prevent the patient from going into shock which can result in organ dysfunction such as kidney failure. Fleisher Decl. ¶¶ 20-21.

These are just some of the emergency conditions that can place a pregnant patient's health in serious jeopardy or threaten bodily functions or organs. *Id.* ¶ 22. Despite these conditions' serious risks, it may not be possible for a physician to know whether treatment for any particular condition is "necessary to prevent the death" of the pregnant patient. *Id.* ¶¶ 13-21. Absent the stabilizing treatment EMTALA requires, however, the risk is extremely serious that, for example, a patient with an ectopic pregnancy might bleed to death, an infection could turn into sepsis and cause organ failure, seizures from eclampsia might prove uncontrollable, or a blood clot could lead to kidney failure. *Id.*

For each of these emergency medical conditions, where a physician determines that abortion

is the stabilizing treatment, EMTALA's plain text requires that treatment be offered and provided upon informed consent. Once a physician identifies that a pregnant individual suffers from an emergency medical condition, that individual must be offered "such treatment as may be required to stabilize the medical condition." 42 U.S.C. § 1395dd(b)(1)(A); *see also* 42 C.F.R. § 489.24(a)(1)(ii) ("If an emergency medical condition is determined to exist," the hospital must "provide any necessary stabilizing treatment[.]"). The only reasonable interpretation of EMTALA's text is that it requires hospitals to offer stabilizing treatment when medically necessary.

Nothing in EMTALA creates a different rule for circumstances in which the treatment results in termination of a pregnancy. The statute's text does not exempt any particular treatment (abortion or otherwise) from the ambit of stabilizing treatment. *See Bostock v. Clayton Cnty.*, 140 S. Ct. 1731, 1747 (2020) ("[W]hen Congress chooses not to include any exceptions to a broad rule, courts apply the broad rule."); *In the Matter of Baby K*, 16 F.3d 590, 596 (4th Cir. 1994) (finding no "statutory language or legislative history [in EMTALA] evincing a Congressional intent to create an exception to the duty to provide stabilizing treatment"). And any contrary interpretation—*i.e.*, that a hospital need not perform an abortion even when medically necessary to stabilize an emergency medical condition—would undermine EMTALA's overall purpose of ensuring "that patients . . . receive adequate medical emergency care." *Arrington*, 237 F.3d at 1073-74 (citation omitted).

Any argument that EMTALA does not encompass abortions is foreclosed by the specific Affordable Care Act (ACA) provision addressing abortion. *See* 42 U.S.C. § 18023. The ACA allows States to prohibit abortion coverage in certain health plans, *id.* § 18023(a)(1), but the same provision contains a cross-reference to EMTALA and makes explicit that "[n]othing in this Act shall be construed to relieve any health care provider from providing emergency services as required by State or Federal law, including section 1867 of the Social Security Act (popularly known as 'EMTALA.')" *Id.* § 18023(d). Congress therefore left no doubt that EMTALA encompasses abortion services and

that a State may not override that requirement.

The Weldon Amendment, which is a frequently enacted appropriations provision that prohibits discrimination against certain entities that do not perform abortions, reflects the same understanding. The Weldon Amendment's sponsor, when confronted with a concern that "women will die because they will not have access to an abortion needed to save the life of the mother," expressly referenced EMTALA as addressing that concern: "Hyde-Weldon does nothing of the sort. It ensures that in situations where a mother's life is in danger a health provider must act to save the mother's life. In fact, Congress passed [EMTALA] forbidding critical-care health facilities to abandon patients in medical emergencies, and requires them to provide treatment to stabilize the medical condition of such patients—particularly pregnant women." 151 Cong. Rec. H177 (Jan. 25, 2005) (statement of Rep. Weldon).

More generally, when Congress creates special rules for abortion—or excludes abortion care from otherwise-applicable rules—it does so expressly.[2] "Had Congress likewise intended" to exempt abortions from EMTALA, "it knew how to say so." *Rubin v. Islamic Republic of Iran*, 138 S. Ct. 816, 826 (2018). Indeed, the very same legislation through which Congress considered EMTALA included a separate program that *did* expressly carve out abortion. *Compare* Consolidated Omnibus Reconciliation Act of 1985, H.R. 3128, 99th Cong., 1st Sess., § 124 (language that became EMTALA), *with id.* § 302(b)(2)(B) (expressly excluding abortion from a different program's authorized activities). Courts have also previously understood EMTALA to require abortion-related services. *See, e.g.*, *New York v. U.S. Dep't of Health & Hum. Servs.*, 414 F. Supp. 3d 475, 538 (S.D.N.Y. 2019); *Morin v. E. Maine Med.*

[2] Examples of these abortion-specific provisions include 10 U.S.C. § 1093; 20 U.S.C. § 1688; 22 U.S.C. §§ 5453(b), 7704(e)(4); 25 U.S.C. § 1676; 42 U.S.C. §§ 238n, 280h-5(a)(3)(C), 300a-6, 300a-7, 300a-8, 300z-10, 1397ee(c)(7), 2996f(b)(8), and 12584a(a)(9). Congress has also routinely enacted a similar provision in appropriations laws, commonly referred to as the "Hyde Amendment." *See, e.g.*, Consolidated Appropriations Act, 2022, Div. H, Tit. V, §§ 506, 507, Pub. L. No. 117-103, 136 Stat. 49, 496 (2022); *cf. Harris v. McRae*, 448 U.S. 297, 302 (1980).

Ctr., 780 F. Supp. 2d 84, 96 (D. Me. 2010); *California v. United States*, No. 05-cv-328, 2008 WL 744840, at *4 (N.D. Cal. Mar. 18, 2008). Thus, both EMTALA's text and the surrounding statutory scheme confirm that EMTALA includes termination of the pregnancy as a potential stabilizing treatment.

To be sure, EMTALA separately provides that a pregnant person may have an "emergency medical condition" in circumstances in which "the health of [the] . . . unborn child . . . [is] in serious jeopardy." 42 U.S.C. § 1395dd(e)(1)(A)(i). That provision ensures that a hospital's EMTALA obligations extend to a scenario where the "unborn child's" health (and not the pregnant patient's health) is threatened. But nothing in the statutory text indicates that Congress intended to limit the EMTALA-mandated care to pregnant patients, or to require a provider to prioritize the fetus's health over the life or health of the pregnant patient. Instead, when a pregnant patient has an emergency medical condition and a physician concludes that stabilizing treatment would require termination of the pregnancy, EMTALA's text leaves that balancing to the pregnant patient—who may decide, after weighing the risks and benefits, whether to accept or refuse the treatment. *See id.* § 1395dd(b)(2) (acknowledging that "the individual" with an emergency medical condition, after being informed "of the risks and benefits" of treatment, may "refuse[] to consent to the . . . treatment"). There is therefore no conflict between EMTALA's provision respecting a pregnant patient and an "unborn child."

The statutory context further refutes any alternative interpretation that EMTALA's reference to "unborn child" *forecloses* abortion as a stabilizing treatment. That interpretation would mean that every time a hospital emergency room terminated a pregnancy to save a pregnant patient's life, the hospital committed an EMTALA violation—contrary to the consistent Congressional understanding reflected above. Moreover, that interpretation would mean that Congress, when enacting EMTALA in 1986, intended to prohibit hospitals from performing abortions, but only those abortions involving a threat to the pregnant patient's life or health. "Congress does not hide elephants in mouseholes," *Cyan, Inc. v. Beaver County Employees Ret. Fund*, 138 S. Ct. 1061, 1071-72 (2018), and the notion that

Congress intended EMTALA to forbid necessary medical care is fundamentally at odds with the statute's aim of guaranteeing—not prohibiting—emergency medical care. *See, e.g.*, 131 Cong. Rec. S13892 ("We cannot stand idly by and watch those Americans who lack the resources be shunted away from immediate and appropriate emergency care whenever and wherever it is needed.") (statement of Sen. Durenberger). In sum, Idaho cannot meaningfully dispute that EMTALA's requirement to offer stabilizing treatment includes abortion when a provider determines that treatment is medically necessary.

B. Idaho's Near-Absolute Abortion Ban Conflicts with EMTALA

Because Idaho's law makes it a crime to perform an abortion even when a physician concludes that such a procedure is the necessary stabilizing treatment under EMTALA, Idaho's law is preempted.

As EMTALA provides, "any State or local law requirement" is preempted "to the extent that the requirement directly conflicts with a requirement of this section." 42 U.S.C. § 1395dd(f). This preemption provision encompasses both impossibility and obstacle preemption. *Draper*, 9 F.3d at 1393. Applying these principles to a state law that entitled physicians to forgo medical treatment that EMTALA would otherwise require, the Fourth Circuit found the analysis to be straightforward: "[T]o the extent that [the state law] exempts treating physicians in participating hospitals from providing care [under specified circumstances], it is preempted—it does not allow the physicians . . . to refuse to provide her with [stabilizing treatment]." *Matter of Baby K*, 16 F.3d at 597. Numerous courts have likewise found state laws preempted when they stood as obstacles to EMTALA's civil liability provisions. *See Root v. New Liberty Hosp. Dist.*, 209 F.3d 1068, 1070 (8th Cir. 2000) (Missouri state law preempted to the extent it sought to shield its state-operated hospitals from EMTALA liability); *Burditt v. HHS*, 934 F.2d 1362, 1373-74 (5th Cir. 1991) (physician could not avoid EMTALA liability by relying on state law contract principles, because "[w]e recognize no reason for conditioning the applicability of EMTALA's civil penalty provision on the vagaries of the several state laws"); *see also,*

e.g., *Cox v. Cabell Huntington Hosp., Inc.*, 863 F. Supp. 2d 568, 572 (S.D. W. Va. 2012); *Merce v. Greenwood*, 348 F. Supp. 2d 1271, 1277 (D. Utah 2004). Consistent with these decisions, Idaho's abortion law conflicts with EMTALA, and therefore is preempted, for three independent reasons.

First, Idaho law flatly prohibits—and attaches criminal penalties and loss of license to—medical care that EMTALA requires. It is thus impossible for Idaho medical providers to comply with both Idaho and federal law. The Idaho law establishes an affirmative defense for abortions "necessary to prevent the death of the pregnant woman," Idaho Code § 18-622(3)(a)(ii), but EMTALA requires necessary stabilizing treatment for any "emergency medical condition," which is broader than just those treatments necessary to prevent death. *See* 42 U.S.C. § 1395dd(e)(1)(A) (defining "emergency medical condition" to include conditions that "plac[e] the health of the individual . . . in serious jeopardy," threaten "serious impairment to bodily functions," or risk "serious dysfunction of any bodily organ or part"). Serious medical conditions exist that meet EMTALA's criteria but for which an abortion might not be necessary to prevent death. *See* Part I.A, *supra*; Fleisher Decl. ¶¶ 12-27. Because Idaho law criminalizes terminating a pregnancy in these circumstances, but federal law requires physicians to offer and provide such stabilizing treatment when medically necessary, it is impossible for physicians to comply with both laws; the Idaho law is therefore preempted. *See, e.g.*, *Chamber of Com. of U.S. v. Bonta*, 13 F.4th 766, 781 (9th Cir. 2021) ("An arbitration agreement cannot simultaneously be 'valid' under federal law and grounds for a criminal conviction under state law"); *Valle del Sol Inc. v. Whiting*, 732 F.3d 1006, 1028 (9th Cir. 2013) (state law was preempted because it allowed "individuals [to] be prosecuted for conduct that Congress specifically sought to protect").

Second, even in circumstances for which Idaho offers an affirmative defense—where the procedure is "necessary to prevent the death of the pregnant woman," Idaho Code § 18-622(3)(a)(ii)—the affirmative defense structure *itself* "is an obstacle to the accomplishment and execution of the full purposes and objectives of Congress." *Draper*, 9 F.3d at 1394. The Idaho law allows physicians to be

prosecuted for performing *any* abortion, regardless of circumstances. Even where the affirmative defense would be satisfied, the Idaho law would still allow for indictment, arrest, and criminal prosecution of physicians each and every time a pregnancy is terminated—including when the physician determined that the procedure was necessary stabilizing treatment under EMTALA. Relegating any exception from criminal liability to an affirmative defense itself poses an obstacle to EMTALA's "overarching purpose of ensuring that patients . . . receive adequate emergency medical care," *Vargas By & Through Gallardo v. Del Puerto Hosp.*, 98 F.3d 1202, 1205 (9th Cir. 1996), because exposure to criminal prosecution will render physicians less inclined or entirely unwilling to risk providing treatment. *See Buckman Co. v. Plaintiffs' Legal Comm.*, 531 U.S. 341, 350-51 (2001) (holding that fear of being "expose[d] . . . to unpredictable civil liability" under state law, for conduct condoned by federal law, was sufficient for preemption); *Arizona v. United States*, 567 U.S. 387, 408 (2012) (preempting a state law authorizing the arrest of aliens, because "[t]he result could be unnecessary harassment of some aliens . . . who federal officials determine should not be removed").

Third, the Idaho law conflicts with EMTALA by threatening the licenses of medical professionals who perform or assist in providing an abortion. Fleisher Decl. ¶ 27; Corrigan Decl. ¶¶ 32-34; Cooper Decl. ¶ 12; Seyb Decl. ¶¶ 13-14. Specifically, beyond the physician who performs the abortion, *see* Idaho Code § 18-604(12), the Idaho law mandates that any "health care professional . . . who assists in performing or attempting to perform an abortion in violation of this subsection shall be suspended by the appropriate licensing board for a minimum of six (6) months upon a first offense and shall be permanently revoked upon a subsequent offense." *Id.* § 18-622(2). This provision could apply to a number of personnel involved in emergency care, including nurses, pharmacists, physicians' assistants, and anesthesiologists. *Cf. id.* §§ 54-1401 (nursing licensure), 54-1718 (pharmacists), 54-1810 (physicians), 54-1810A (physicians' assistants).

Notably, these professionals' licenses can be revoked even for someone else's conduct,

because in any "disciplinary action by an applicable licensing authority," they must likewise prove the elements of the affirmative defense: that the physician appropriately determined the necessity of the abortion and the appropriate manner to perform it. *See* Idaho Code § 18-622(3)(a)(ii)-(iii). The obvious effect will be to discourage medical professionals from participating in *any* abortions. Even if a doctor *tells* a nurse, for example, that an abortion is necessary to prevent death or serious bodily harm, the nurse could still be subject to disciplinary action for assisting in the abortion, and potentially have their license revoked based on the disciplinary board's determination that the *doctor* erred in making a "good faith medical judgment" about how to treat the pregnant patient. *Id.* Thus, the Idaho law penalizes and deters medical professionals from participating in medically necessary abortions, contrary to EMTALA's "overarching purpose of ensuring that patients . . . receive adequate emergency medical care," *Vargas*, 98 F.3d at 1205.

For each of these reasons, § 18-622 conflicts directly with EMTALA, and the United States has demonstrated a likelihood of success on its preemption claim. Section 18-622 is therefore preempted to the extent it allows Idaho to initiate criminal prosecutions against, attempt to revoke the license of, or seek to impose any other form of liability on, medical providers with respect to EMTALA-covered care.

II. The Equitable Balance Supports Entry of a Preliminary Injunction

The remaining factors all support entry of a preliminary injunction, because allowing the Idaho law to take effect would result in irreparable harm to the public and to the United States' sovereign interests. *Cf. Nken v. Holder*, 556 U.S. 418, 435 (2009) (noting that, in suits involving the United States, the balance of equities and "public interest . . . factors merge").

First and most fundamentally, allowing the Idaho law to go into effect would threaten severe harm to pregnant patients in Idaho, who would no longer be guaranteed the critical emergency care to which they are entitled under federal law. *See Valle del Sol*, 732 F.3d at 1029 ("It is clear that it would

not be equitable or in the public's interest to allow the state to violate the requirements of federal law, especially when there are no adequate remedies available." (modifications omitted)). As discussed above, numerous pregnancy-related conditions could require emergency care including abortion, and these conditions have occurred and will inevitably occur again within Idaho. Corrigan Decl. ¶¶ 8, 15, 23, 29; Cooper Decl. ¶¶ 5, 6, 8, 10, 12; Seyb Decl. ¶¶ 6, 7, 9, 11, 13. To take just one example, in Idaho, Medicaid has covered treatment for approximately 100 ectopic pregnancies each year. Fleisher Decl. ¶ 36. Medical literature also confirms that other diagnoses qualifying as "emergency medical conditions" for pregnant individuals also occur frequently. *Id.* ¶¶ 28-38. And Idaho-based physicians have personally treated patients with these types of conditions. Corrigan Decl. ¶ 8 (anticipating that "the number will increase"); Seyb Decl. ¶ 6 (treating "a dozen" per year); Cooper Decl. ¶ 5.

Given that Idaho has approximately 22,000 births per year,[3] and a large number of high-risk pregnancies due to surrogacy, it is virtually guaranteed that these emergency medical conditions will occur for a sizeable number of pregnant patients within Idaho. Corrigan Decl. ¶¶ 8, 19; Fleisher Decl. ¶¶ 36-38. Allowing the law to go fully into effect would discourage physicians from providing necessary care in emergency circumstances, resulting in significant and irreparable harm to numerous pregnant patients within Idaho. Every day that the law is in effect, there is a likelihood that some pregnant persons suffering medical emergencies will face irreversible health consequences, such as strokes and organ failure, and some are likely to die. *See* Fleisher Decl. ¶¶ 36-38; Corrigan Decl. ¶¶ 8, 17, 23-24, 29; Cooper Decl. ¶ 6, 8, 10, 12; Seyb Decl. ¶ 7, 9, 11, 13; *see also Rodde v. Bonta*, 357 F.3d 988, 999 (9th Cir. 2004) (irreparable harm "includes delayed and/or complete lack of necessary treatment, and increased pain and medical complications"); *Beltran v. Myers*, 677 F.2d 1317, 1322 (9th Cir. 1982) ("Plaintiffs have shown a risk of irreparable injury, since enforcement of the California rule may deny

[3] Idaho Dep't of Health & Welfare, *2010-2020 Idaho Resident Births*, *VS Natality – Data Results, 2010-2020*, https://www.gethealthy.dhw.idaho.gov/idaho-births-vital-statistics (attached as Ex. G-C).

them needed medical care.").

Indeed, patients in Idaho are already facing dire situations. Dr. Corrigan treated a patient who, after initially being denied care, arrived at the hospital two weeks later with an infection in her uterus, at risk of sepsis, and termination was necessary to preserve her life. Corrigan Decl. ¶¶ 12-15. And Dr. Seyb recently received a call from a physician whose patient was "clear[ly]" "in danger" due to severe bleeding, but the physician feared the ramifications of providing medically necessary care. Seyb. Decl. ¶ 13. Had § 18-622 been in effect, the life-saving treatment these patients received could have been further delayed or denied. Corrigan Decl. ¶¶ 31-35; Cooper Decl. ¶ 12; Seyb Decl. ¶¶ 13-14.

Moreover, Idaho's law also interferes with the United States' sovereign interest in ensuring the proper administration of federal law and the Medicare program. *See, e.g.*, *United States v. Alabama*, 691 F.3d 1269, 1301 (11th Cir. 2012) ("The United States suffers injury when its valid laws in a domain of federal authority are undermined by impermissible state regulations."); *cf. Vt. Agency of Nat. Res. v. U.S. ex rel. Stevens*, 529 U.S. 765, 771 (2000). The United States has agreed to provide federal Medicare funds to hospitals in Idaho, in return for those hospitals promising (among other things) to comply with EMTALA for all patients, not just for Medicare beneficiaries. *See* 42 U.S.C. § 1395cc(a)(1)(I). But the Idaho law seeks to disrupt the program and deprive the United States of the benefit of its bargain by prohibiting Idaho hospitals from performing EMTALA-mandated services, notwithstanding that hospitals' receipt of Medicare funds is conditioned on them doing so. Thus, the Idaho law threatens "harm to the administration and integrity of Medicare," *United States v. Mackby*, 339 F.3d 1013, 1018 (9th Cir. 2003), because payments to hospitals will no longer guarantee the availability of services that Congress mandated. Wright Decl. ¶¶ 14, 16. This harm is substantial: the United States provided over $3 billion in Medicare funding to hospitals within Idaho over fiscal years 2018-2020, with approximately $74 million attributable to emergency departments. Shadle Decl. ¶¶ 6-8.

The Idaho law also interferes with the written agreements that the United States has entered

into with hospitals pursuant to Medicare. These Spending Clause agreements likewise require hospitals to comply with EMTALA. *See* Background, Part I.C, *supra*. It is well-settled that third parties may not interfere with the terms of Spending Clause legislation, *see Lawrence Cnty. v. Lead-Deadwood Sch. Dist. No. 40-1*, 469 U.S. 256, 270 (1985), but here, the State of Idaho is directly interfering with the agreements between the United States and the 52 hospitals within Idaho that are receiving Medicare funds. Thus, irreparable harm exists on this basis as well.

Finally, on the other side of the ledger, the State of Idaho will suffer no cognizable harm as a result of the requested preliminary relief. Idaho's abortion law is not currently in effect, has never been in effect, and therefore enjoining it from going into effect, as applied to EMTALA-mandated care, would simply preserve the status quo during the short period necessary for further litigation. *See All. for Wild Rockies v. Pierson*, 550 F. Supp. 3d 894, 898 (D. Idaho 2021) ("The purpose of a preliminary injunction is to preserve the status quo and prevent the 'irreparable loss of rights' before a final judgment on the merits[.]"). Given the significant harms that would result if the Idaho law were to go into effect to prohibit EMTALA-mandated care—both for pregnant individuals as well as the United States' sovereign interests—and the corresponding lack of harm to the State of Idaho from a temporary injunction against certain applications of its law, the equitable factors plainly favor entry of preliminary relief against the Idaho law's enforcement.

CONCLUSION

For the foregoing reasons, the Court should enter a preliminary injunction prohibiting the State of Idaho—including all of its officers, employees, and agents—from enforcing Idaho Code § 18-622(2)-(3) as applied to EMTALA-mandated care.

Dated: August 8, 2022

Respectfully submitted,

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UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF IDAHO
SOUTHERN DIVISION

UNITED STATES OF AMERICA, Plaintiff, v. THE STATE OF IDAHO, Defendant.	Case No. 1:22-cv-329-BLW

[PROPOSED] ORDER

Upon consideration of the United States' Motion for a Preliminary Injunction, and the parties' respective submissions in support thereof and in opposition thereto, the Court hereby ORDERS that the United States' motion is GRANTED.

It is FURTHER ORDERED that the State of Idaho, including all of its officers, employees, and agents, are preliminarily enjoined from enforcing Idaho Code § 18-622(2)-(3) as applied to medical care required by the Emergency Medical Treatment and Labor Act (EMTALA), 42 U.S.C. § 1395dd.

It is FURTHER ORDERED that the State of Idaho, including all of its officers, employees, and agents, are specifically prohibited from initiating any criminal prosecution against, attempting to suspend or revoke the professional license of, or seeking to impose any other form of liability on, any medical provider or hospital based on their performance of conduct that is defined as an "abortion" under Idaho Code § 18-604(1), but that is necessary to avoid: (i) "placing the health of" a pregnant patient "in serious jeopardy"; (ii) a "serious impairment to bodily functions" of the pregnant patient; or (iii) a "serious dysfunction of any bodily organ or part" of the pregnant patient, pursuant to 42 U.S.C. § 1395dd(e)(1)(A)(i)-(iii).

SO ORDERED.

//end of text//

Submitted by: Lisa Newman
Counsel for the United States

EXHIBIT A

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF IDAHO
SOUTHERN DIVISION

UNITED STATES OF AMERICA, Plaintiff, v. THE STATE OF IDAHO, Defendant.	Case No. 1:22-cv-329

DECLARATION OF LEE A. FLEISHER, M.D.

I, Lee A. Fleisher, M.D., of the Centers for Medicare & Medicaid Services (CMS), declare that the following statements are true and correct to the best of my knowledge and belief, and that they are based on my personal knowledge as well as information provided to me in the ordinary course of my official duties.

1. I am employed by the United States Department of Health and Human Services (HHS) in CMS. I am the Chief Medical Officer and Director of the Center for Clinical Standards and Quality for CMS. In this capacity, I am responsible for executing all national clinical, quality, and safety standards for all Medicare and Medicaid-certified healthcare facilities and providers, as well as establishing coverage determinations for items and services that improve health outcomes for Medicare beneficiaries.

2. I am also currently a Professor Emeritus of Anesthesiology and Critical Care at the University of Pennsylvania Perelman School of Medicine and continue to provide anesthesia care approximately three times per month at the Hospital of the University of Pennsylvania. From 2004 until 2020, I was the Robert D. Dripps Professor and Chair of Anesthesiology and Critical Care

and Professor of Medicine at the University of Pennsylvania and Chair of the Department of Anesthesiology and Critical at the Hospital of the University of Pennsylvania (HUP) and Penn Presbyterian Medical Center. Prior to joining the University of Pennsylvania, I was an attending anesthesiologist at The Johns Hopkins Hospital (JHH) from 1992-2003, where I provided obstetrical anesthesia and anesthesia for emergency surgical procedures. While at JHH, I was appointed in 1999 as the Clinical Director of Operating Rooms, a position I held until I moved to the University of Pennsylvania in 2004.

3. In addition, I have held a number of other faculty, hospital, and administrative appointments, which are set forth in my curriculum vitae, which is attached hereto as Ex. A. Among other appointments listed on my CV, since 2007 I have served as an elected member of the National Academy of Medicine (NAM) (formerly Institute of Medicine), and between 2016 and 2018, I served as a member of NAM's Committee on Reproductive Health Services for Assessing the Safety and Quality of Abortion Care, and was an author of the 2018 report on The Safety and Quality of Abortion Care in the United States, available at https://www.ncbi.nlm.nih.gov/books/NBK507236/. My work with this committee on safety of abortion services was focused on risks to women both from the abortion procedure itself and from delays in obtaining abortion procedures. I was also the President of the Medical Board of HUP from 2014-16 and a member of the Board of Trustees of HUP from 2012-16, in which capacity I oversaw the review and approval of hospital policies and procedures including those pursuant to EMTALA. Additionally, I was Chair of the Credentials Committee of HUP from 2008-14, in which capacity I oversaw the evaluation and credentialing of all medical providers on the staff.

4. I graduated with a B.A. from the University of Pennsylvania in Molecular Biology in 1981. I earned an M.D. from the State University of New York at Stony Brook in 1986. I

completed an internship in surgery at the University of Minnesota from 1986 to 1987, and a residency in anesthesiology at Yale University from 1987 to 1990.

5. In my thirty-plus years as a medical doctor, I have had extensive experience providing anesthesia for obstetrical care, including through the provision of anesthesia for the treatment of pregnancy-related conditions that threaten the life and/or health of pregnant patients as well as review of complications of care in my role as Chair of the Department. For example, in my practice at JHH from 1992-2003, I provided emergency obstetrical care approximately 3 times per month. In my role as Clinical Director of the Operating Rooms at JHH, I evaluated and determined the urgency of proceeding to surgery for all emergency surgical cases, including ectopic pregnancies, and provided anesthetic care for many pregnant individuals requiring emergent care including vaginal bleeding and preeclampia/eclampsia.

6. In addition, through my official duties at CMS, I am familiar with federal Medicare and Medicaid requirements, as well as data and other information collected by CMS and HHS regarding medical risks related to pregnancy. And based on my role at CMS, my roles as a medical practitioner, and my leadership roles in several hospitals and medical organizations, I am experienced with the requirements of the Emergency Medical Treatment and Labor Act (EMTALA), 42 U.S.C. § 1395dd, including how they arise in the actual practice of medicine.

IDAHO LAW AND EMTALA

7. I understand that, if the Idaho law goes into effect on August 25, 2022, "[e]very person who performs or attempts to perform an abortion . . . commits the crime of criminal abortion" and that the crime of criminal abortion is a felony that is punishable by up to five years in prison and loss of medical license. Idaho Code § 18-622(2). I further understand that Idaho law defines "abortion" as "the use of any means to intentionally terminate the clinically diagnosable

pregnancy of a woman with knowledge that the termination by those means will, with reasonable likelihood, cause the death of the unborn child." Idaho Code § 18-622. This definition of "abortion" in the Idaho Code covers some procedures that would not be characterized as an abortion in the medical community. In some circumstances in which a pregnancy is nonviable and/or termination of pregnancy is necessary to treat a pregnant patient's medical condition, physicians may not consider that treatment to be properly characterized as an abortion.

8. I further understand that Idaho law includes an "affirmative defense" allowing physicians to avoid criminal liability only if they can prove, among other things, that an abortion was "necessary to prevent the death of the pregnant woman." Idaho Code § 18-622(3)(a)(ii).

9. In addition, I am aware of EMTALA's requirements for hospitals participating in Medicare. In particular, EMTALA requires that "[i]f any individual . . . comes to a hospital and the hospital determines that the individual has an emergency medical condition, the hospital must provide either—(A) with the staff and facilities available at the hospital, for such further medical examination and such treatment as may be required to stabilize the medical condition, or (B) for transfer of the individual to another medical facility" in accordance with certain requirements in subsection (c) of the statute. 42 U.S.C. § 1395dd. A hospital may not discharge or otherwise transfer a person with a medical condition who has not been stabilized unless the individual requests a transfer or a physician certifies that the benefits of a transfer to another medical facility outweighs the increased risks to the patient. 42 U.S.C. § 1395dd(c).

10. I am aware that EMTALA defines "emergency medical condition" as: "(A) a medical condition manifesting itself by acute symptoms of sufficient severity (including severe pain) such that the absence of immediate medical attention could reasonably be expected to result in—(i) placing the health of the individual (or, with respect to a pregnant woman, the health of the

woman or her unborn child) in serious jeopardy, (ii) serious impairment to bodily functions, or (iii) serious dysfunction of any bodily organ or part; or (B) with respect to a pregnant woman who is having contractions—(i) that there is inadequate time to effect a safe transfer to another hospital before delivery, or (ii) that transfer may pose a threat to the health or safety of the woman or the unborn child." 42 U.S.C. § 1395dd(1).

11. I am aware that EMTALA defines "to stabilize" to mean "to provide such medical treatment of the condition as may be necessary to assure, within reasonable medical probability, that no material deterioration of the condition is likely to result from or occur during the transfer of the individual from a facility." 42 U.S.C. § 1395dd(e)(3).

EMERGENCY MEDICAL CONDITIONS IMPLICATED BY IDAHO LAW

12. Based on my experience as a medical practitioner and as the Chief Medical Officer at CMS, I know that pregnant patients experience a number of medical conditions that fall within the definition of "emergency medical condition" set forth in EMTALA. This is because for these medical conditions, "in the absence of immediate medical attention," which can include monitoring, treatment, or both, the condition "could reasonably be expected to result in" the patient's health being "plac[ed] . . . in serious jeopardy," "serious impairment to [the patient's] bodily functions," or "serious dysfunction of any bodily organ or part [of the patient]," as described more fully below. I also know that the appropriate stabilizing treatment that is necessary to avoid "serious jeopardy," "serious impairment," and "serious dysfunction," which would otherwise result from those conditions, is very frequently—and in some cases nearly always—a form of treatment that is covered by the definition of "abortion" set forth in the Idaho Code. EMTALA requires providing such care independent of whether doing so is, or well before doing so becomes, necessary to prevent the patient's death. As explained further below, in some cases where the

patient's health is unambiguously threatened, it may be less clear whether there is also a certainty of death without stabilizing treatment—and a physician may not ever be able to confirm whether death would result absent immediate treatment. EMTALA does not allow leaving the patient untreated when doing so would irreparably risk or harm their health, as with the conditions discussed below.

13. For example, a pregnant individual may present to an emergency department with bleeding, pelvic pain or severe abdominal pain that, when evaluated, is determined to be caused by an ectopic pregnancy. An ectopic pregnancy is when an embryo or fetus grows outside of the uterus, frequently in a fallopian tube. An ectopic pregnancy in a fallopian tube is an emergency medical condition that places the patient's life in jeopardy because it will cause the fallopian tube to rupture and in the vast majority of cases cause significant and potentially fatal internal bleeding. In most cases, the physician cannot reasonably know when that rupture will occur—it could happen within minutes, hours or days of the physician's examination—but without immediate treatment it is reasonably probable that the patient's condition will continue to deteriorate. Accordingly, given this serious risk of unknown imminence, where a patient suffers from an ectopic pregnancy, especially in a fallopian tube, the appropriate stabilizing treatment is nearly always emergency surgery and removal of the involved fallopian tube, including the embryo or fetus, or administration of a drug to cause embryonic or fetal demise. One of these two treatments is necessary because of the inevitability that the fallopian tube will rupture absent surgery or intervention with medication that causes embryonic or fetal demise. There is an extremely high risk that such rupture would result in the patient bleeding to death. Because a physician can determine with reasonable certainty that an ectopic pregnancy exists and that, depending upon the location, a rupture will occur as a result, but the physician cannot discern with reasonable certainty

the time at which that rupture will occur, it is necessary that an ectopic pregnancy be treated immediately or else the patient's life and health will likely continue to deteriorate and remain at constant and ongoing risk.

14. Even though a physician at a hospital where EMTALA applies could conclude that this treatment is required for an ectopic pregnancy, particularly one involving a fallopian tube, Idaho law prohibits this treatment. Idaho's definition of abortion would include both the medical and surgical treatment described in ¶ 13, because both cause embryonic or fetal demise in a clinically diagnosable pregnancy. This treatment would be prohibited by Idaho law even though an ectopic pregnancy has no chance of maturing into a viable child. Additionally, despite the extremely serious risks posed by an ectopic pregnancy, particularly in a fallopian tube, and the inevitability of a rupture, which are apparent at the time when treatment is required to address those risks, a physician may not be able to establish or know, with certainty, that termination of the pregnancy is "necessary to prevent the death of the woman." However, that does not change the fact that the patient's condition will very likely deteriorate without the necessary treatment, and that failure to provide the necessary treatment will seriously jeopardize the patient's health and/or life in the process.

15. As another example, a pregnant individual may present to the emergency room with chest pain and severe shortness of breath, requiring supplemental oxygen to keep their blood oxygen levels in reasonable range. The patient may be early in or mid-pregnancy and during the evaluation may be diagnosed with severe heart failure related to long-standing pulmonary hypertension (i.e., elevated blood pressure in the vessels to the lungs), or a massive pulmonary embolism (i.e., a blood clot to the lungs). For some patients, pregnancy can substantially exacerbate the heart failure and initially cause the patient to have difficulty breathing at rest that

can then turn into further complications from a lack of oxygen as well as a drop in blood pressure. Some pregnant patients may present to the emergency room when they are in extremis, and a physician will need to place the patient on a ventilator and prescribe medications to maintain the blood pressure. Severe heart failure, especially from pulmonary hypertension or a pulmonary embolism, can be an emergency medical condition because if left untreated, the patient's condition will continue to deteriorate and cardiac arrest or inability to oxygenate the patient could result, which places the patient's life, health, and bodily organs in jeopardy. In some circumstances, the appropriate stabilizing treatment for a patient suffering from severe heart failure is treatment of the heart and blood vessels through medications. In severe cases, the physician may determine that, despite other medical treatment, the patient continues to have worsening deterioration of blood oxygenation and maintenance of blood pressure. In such circumstances, the physician could conclude that termination of the pregnancy is medically necessary because, by virtue of the severity of the symptoms, there is a high probability of the pregnant patient's death or impairment or severe dysfunction of bodily organs (such as the lungs, heart, and kidneys) absent that termination.

16. Even though a physician at a hospital where EMTALA applies could conclude that this treatment is required for severe heart failure, Idaho law prohibits this treatment because it would cause embryonic or fetal demise. This treatment would be prohibited by Idaho law even though the pregnant individual with this condition would most likely not survive to carry the pregnancy materially further. Additionally, despite the extremely serious risks posed by severe heart failure, which are apparent at the time when treatment is required to address those risks, a physician may not be able to establish or know, with certainty, that termination of pregnancy is "necessary to prevent the death of the woman." However, that does not change the fact that the

patient's condition will very likely deteriorate without the necessary treatment, and that failure to provide the necessary treatment will seriously jeopardize the patient's health and/or life in the process.

17. As a third example, a pregnant individual may present to the emergency department with nausea and shortness of breath, which an initial evaluation may diagnose as resulting from new onset of high blood pressure. Pre-eclampsia is when high blood pressure and high levels of protein in the urine develop in a pregnant individual, usually midway through the pregnancy. Pre-eclampsia can quickly progress to eclampsia with the onset of seizures, and a physician cannot discern when that progression to seizures will occur with reasonable medical certainty in all cases, especially when the blood pressure cannot be controlled. Pre-eclampsia and eclampsia are emergency medical conditions because they place the patient's life in jeopardy or can cause serious impairment to bodily functions. Without treatment for severe pre-eclampsia/eclampsia, the patient's condition is reasonably likely (indeed nearly certain) to deteriorate. Specifically, the seizures that characterize the transition from pre-eclampsia to eclampsia can cause coma, pneumonia from the aspiration of stomach contents, kidney failure, stroke and even cardiac arrest. While the only curative treatment for pre-eclampsia or eclampsia is delivery of the fetus, in most and many cases, the pregnant patient with pre-eclampsia will respond reasonably promptly to medications to control their blood pressure, reduce their chances of seizures, and mature the fetus' lungs to allow delivery as soon as possible. However, in some cases in which high blood pressure and/or the seizures of severe pre-eclampsia/eclampsia cannot be controlled, termination of the pregnancy is medically necessary. In such cases, absent termination of the pregnancy, death or severe bodily dysfunction of the pregnant patient is the reasonably probable outcome.

18. Even though a physician at a hospital where EMTALA applies could conclude that this treatment is required for severe pre-eclampsia or eclampsia, Idaho law prohibits this treatment because the treatment would cause fetal demise. This treatment would be prohibited by Idaho law even though the pregnant individual with this condition would most likely not survive to carry the pregnancy materially further. Additionally, despite the extremely serious risks posed by this severe preeclampsia/eclampsia, which are apparent at the time when treatment is required to address those risks, a physician may not be able to establish or know, with certainty, that termination of pregnancy is "necessary to prevent the death of the woman." However, that does not change the fact that the patient's condition will deteriorate without the necessary treatment, and that failure to provide the necessary treatment will seriously jeopardize the patient's health and/or life in the process.

19. As a fourth example, a pregnant individual may present to the emergency department with a life-threatening infection of the uterine contents. Such an infection may occur when there is premature rupture of the membranes (PROM), which is when the amniotic sac surrounding the embryo or fetus ruptures and the uterus or embryo/fetus can become infected. The infection can progress to sepsis wherein multiple body organs and functions can start failing including the heart, lungs and blood pressure, which could lead to death. Sepsis can progress quickly, and a physician cannot discern with reasonable medical certainty if or when the sepsis will resolve or result in organ failure or death without immediate treatment. Septic infection is an emergency medical condition because it places the patient's life and health in jeopardy or can cause serious impairment to bodily functions; if untreated, it can lead to kidney failure and even cardiac arrest. In many cases, the pregnant patient can respond to treatment with antibiotics and concurrently be administered medications to support their blood pressure. However, if the

antibiotics cannot control the infection, then removal of the source of the infection is necessary—and in circumstances in which the embryo or fetus is infected and is causing the sepsis, that necessary treatment could include removal of the embryo or fetus, which may result in embryonic or fetal demise. Absent this treatment for severe sepsis unresponsive to antibiotics and blood pressure support, the patient's condition will deteriorate, and death or severe bodily dysfunction of the pregnant patient is the reasonably probable outcome.

20. Even though a physician at a hospital where EMTALA applies could conclude that this treatment is required for severe sepsis, Idaho law prohibits this treatment because the treatment would cause embryonic or fetal demise. This treatment would be prohibited by Idaho law even though the pregnant individual with this condition would most likely not survive to carry the pregnancy materially further. Additionally, despite the extremely serious risks posed by severe sepsis, which are apparent at the time when treatment is required to address those risks, a physician may not be able to establish or know, with certainty, that termination of pregnancy is "necessary to prevent the death of the woman." However, that does not change the fact that the patient's condition will deteriorate without the necessary treatment, and that failure to provide the necessary treatment will seriously jeopardize the patient's health and/or life in the process.

21. As a fifth example, a pregnant individual may present to the emergency department with vaginal bleeding. Vaginal bleeding may occur in some of the previously described conditions, but it can also be a result of a placental abruption, which occurs when the placenta partly or completely separates from the inner wall of the uterus. Placental abruption with uncontrolled and catastrophic bleeding is an emergency medical condition that places the patient's life in jeopardy or can cause serious impairment to bodily functions. This is because catastrophic and/or uncontrolled bleeding can lead to shock, which can result in organ dysfunction such as kidney

failure, and even cardiac arrest. The placental abruption can be diagnosed in the emergency department by examination, including ultrasound, to check the location of the bleeding. If bleeding will not stop, then a physician could conclude that the necessary stabilizing treatment for the uncontrolled and catastrophic bleeding includes removal of the fetus or the entire uterus (*i.e.* a hysterectomy, which also results in termination of the pregnancy), which could result in fetal demise. Absent this treatment for placental abruption where indicated, the patient's condition will deteriorate and death or severe bodily dysfunction of the pregnant patient is the reasonably probable outcome.

22. Even though a physician at a hospital where EMTALA applies could conclude that this treatment is required for placental abruption, Idaho law prohibits this treatment because termination would cause fetal demise. This treatment would be prohibited by Idaho law even though the pregnant individual with a placental abruption would most likely not survive to carry the pregnancy materially further. Additionally, despite the extremely serious risks posed by placental abruption with catastrophic or uncontrolled bleeding, which are apparent at the time when treatment is required to address those risks, a physician may not be able to establish or know, with certainty, that termination of pregnancy is "necessary to prevent the death of the woman." However, that does not change the fact that the patient's condition will deteriorate without the necessary treatment, and that failure to provide the necessary treatment will seriously jeopardize the patient's health and/or life in the process.

23. The emergency medical conditions described in paragraphs 13-22 above are just some examples of those that present in pregnant patients, as to which the treating physician could, in the exercise of their professional medical judgment, determine that the stabilizing treatment would include termination of pregnancy. Myriad other medical conditions that present in pregnant

patients may cause acute symptoms that place the health of the pregnant patient in serious jeopardy, or else risk serious impairment to the pregnant patient's bodily functions or dysfunction of a bodily organ or part. How emergency conditions present in a pregnant patient will often vary depending on the patient's specific circumstances, and termination of pregnancy may be a necessary treatment to stabilize the patient based on their physical circumstances.

24. For each of the medical conditions described above (as well as other emergency medical conditions that present in pregnant patients), in some cases, termination of pregnancy would be the only option to ensure that a pregnant patient will not die, or suffer a serious impairment to their bodily functions, or serious dysfunction of any bodily organ or part as a result of their emergency medical condition. In that regard, a physician could conclude that termination of the pregnancy is the only way to stabilize the pregnant patient as required by EMTALA.

25. In other words, pregnancy termination may be necessary to ensure that "no material deterioration of the patient's condition is likely to result from or occur during the transfer [including discharge] from a facility," as is required by EMTALA. 42 U.S.C. § 1395dd(e)(3). Yet, under the Idaho abortion ban, physicians at hospital emergency rooms could be prosecuted for administering necessary stabilizing treatment to patients with these conditions despite knowing that the patients will suffer severe bodily impairment or serious jeopardy to their health without such treatment.

26. Indeed, under the definition of "criminal abortion" in the Idaho law, this is true even in cases in which the physician knows that there is no chance that the pregnancy will result in a live birth. Because the Idaho law prohibits termination of any pregnancy that would "cause the death of the unborn child," a physician would be forbidden from administering treatment even if: (1) a patient presents with an emergency medical condition; (2) which will render it impossible

for the pregnancy to result in a live birth; but (3) embryonic or fetal demise has not yet occurred at the time the patient arrives at the hospital. Under those circumstances, a physician following Idaho law would be required to wait for embryonic or fetal demise before stabilizing the pregnant patient, causing the pregnant patient to suffer through the emergency medical condition, often with great pain and increased risk to their health and/or life.

27. When stabilizing treatment is provided at a hospital that includes termination of the pregnancy (including "abortion" as defined under Idaho law), that procedure may require the participation of numerous personnel—not just the physician performing the procedure, but also frequently nurses, operating room technicians, anesthesiologists or certified registered nurse anesthetists, pharmacists, physician's assistants, or other medical health professionals.

PREVALENCE OF EMERGENCY PREGNANCY CONDITIONS

28. Based on my role at CMS and my experience in public health, I am aware of statistics regarding the prevalence of emergency pregnancy conditions, and I am experienced in identifying reliable data about those conditions. Data relating to health risks associated with pregnancy confirms that a significant percentage of pregnant patients experience emergency health conditions, including conditions as to which termination of pregnancy is the appropriate stabilizing treatment.

29. According to the Centers for Disease Control and Prevention (CDC), the overall maternal mortality rate in the United States in 2020 was 23.8 maternal deaths per 100,000 live births. *See* Donna L. Hoyert, CDC, *Maternal Mortality Rates in the United States*, 2020 (Feb. 23, 2022), https://www.cdc.gov/nchs/data/hestat/maternal-mortality/2020/maternal-mortality-rates-2020.htm. That represents an increase from 17.4 and 20.1 maternal deaths per 100,000 live births

in 2018 and 2019, respectively. *See id.* The maternal mortality rates for Black women are significantly higher and have similarly increased between 2018 and 2020. *See id.*

30. According to CDC, for each maternal death, more than 50 pregnant women suffer significant short- or long-term consequences to their health. *See* CDC, *Severe Maternal Morbidity: Rate per 10,000 Delivery Hospitalizations* (Feb. 10, 2020), https://www.cdc.gov/reproductivehealth/maternalinfanthealth/smm/rates-severe-morbidity-indicator.htm. These consequences include heart attacks, sepsis, eclampsia, and kidney failure. *Id.*

31. Pregnant patients regularly come to hospitals with emergency medical conditions, including the conditions discussed above.

32. I am aware that the American College of Obstetricians and Gynecologists (ACOG) has reported, for instance, that ectopic pregnancies account for approximately two percent of all pregnancies, though the incidence could be significantly higher given the lack of recent national surveillance data. *See* ACOG Practice Bulletin No. 193 (Mar. 2018) (attached as Exhibit B). I am also aware that data from 2011 to 2013 shows that ruptured ectopic pregnancies account for 2.7 percent of all pregnancy-related deaths and are the leading cause of hemorrhage-related maternal deaths. *See id.*

33. I am also aware that CDC estimates that pre-eclampsia happens in 1 in 25 pregnancies. *See* CDC, *High Blood Pressure During Pregnancy* (May 6, 2021), https://www.cdc.gov/bloodpressure/pregnancy.htm I am further aware that ACOG has reported that the rate of pre-eclampsia in the United States increased by 25 percent between 1987 and 2004. *See* ACOG Practice Bulletin No. 222 (June 2020) (attached as Exhibit C).

34. I am also aware that ACOG has reported that cardiovascular disease— including as a result of hypertension—affects approximately one to four percent of pregnancies in the United

States per year and that cardiovascular disease accounts for 26.5 percent of pregnancy-related deaths in the United States. *See* ACOG Practice Bulletin No. 212 (May 2019) (attached as Exhibit D). ACOG additionally reports that hypertensive disorders affect up to ten percent of pregnancies and that, in those affected pregnancies, pregnant persons are eight to thirteen times more likely to suffer a myocardial infarction (heart attack).

35. Further, I am aware that ACOG has reported that premature rupture of membranes (PROM) complicates two to three percent of pregnancies in the United States. *See* ACOG Practice Bulletin No. 217 (Mar. 2020) (attached as Exhibit E). ACOG has also reported that intraamniotic infection occurs in 15 to 25 percent of preterm PROM cases and postpartum infection occurs in 15 to 25 percent of cases, with the risk higher in cases involving earlier gestational ages.

36. As described above, these conditions frequently require emergency care, including abortion, and given these nationwide numbers, it is not surprising that pregnant patients in Idaho are among persons who require treatment for medical conditions that frequently present as medical emergencies. For example, Idaho providers made claims to Medicaid and the Children's Health Insurance Program ("CHIP") for payment for: 98 ectopic pregnancies that were treated with pregnancy termination in 2018; 72 ectopic pregnancies were treated with pregnancy termination in 2019; 103 ectopic pregnancies were treated with pregnancy termination in 2020; and 108 ectopic pregnancies were treated with pregnancy termination in 2021. Notably, these numbers are based only on patients who are Medicaid or CHIP beneficiaries, not all patients in Idaho—which means the number of patients who presented with ectopic pregnancies in Idaho during those years is likely even higher overall.

37. As discussed above, similar treatment for ectopic pregnancy will no longer be available under Idaho's new abortion law. Based on the consistent historical data, it is a near-

certainty that patients with ectopic pregnancies will continue to require emergency medical treatment that qualifies as a prohibited "abortion" under Idaho law—just like the hundreds of patients who have needed that treatment in recent years. Without access to that treatment, the inevitable result for those patients will be substandard care and dire consequences for their health.

38. With respect to other emergency pregnancy conditions, including those described above in paragraphs 15-22, there is not similar readily available Medicaid/CHIP data. This does not reflect an absence of those conditions for patients in Idaho, but rather only the realities of how hospitals and other providers track diagnose/s and treatments, and how the federal government and private insurance companies reimburse for the costs of health care. However, based on my experience practicing medicine for more than 30 years, it is virtually certain that pregnant persons in Idaho present themselves in emergency rooms across the state each year with these emergency conditions and that the proper treatment in at least some cases would be termination of the pregnancy. Under the Idaho law, that treatment would be unavailable, and the consequence of denying that care to those patients will be tragic.

I declare under penalty of perjury that the foregoing is true and correct. Executed this 8th day of August, 2022 in Philadelphia, PA.

Lee A. Fleisher, M.D.

FLEISHER DECLARATION: EXHIBIT A

UNIVERSITY OF PENNSYLVANIA - PERELMAN SCHOOL OF MEDICINE
Curriculum Vitae

Date: 10/16/2021

Lee A. Fleisher, M.D.

Address: Chief Medical Officer
Director, Center for Clinical Standards and Quality
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Baltimore, MD

Professor of Anesthesiology and Critical Care
Professor of Medicine
Perelman School of Medicine of the University of Pennsylvania
Philadelphia, PA 19104 USA

If you are not a U.S. citizen or holder of a permanent visa, please indicate the type of visa you have:
none (U.S. citizen)

Education:

1981	B.A.	University of Pennsylvania (Molecular Biology)
1986	M.D.	State University of New York at Stony Brook (Medicine)
2024	M.Law	University of Pennsylvania Carey School of Law (Law)

Postgraduate Training and Fellowship Appointments:

1986-1987	Intern in Surgery, University of Minnesota
1987-1990	Resident in Anesthesiology, Yale University

Faculty Appointments:

1990-1992	Assistant Professor of Anesthesiology, Yale University School of Medicine
1992-1996	Assistant Professor of Anesthesiology and Critical Care Medicine, Johns Hopkins University School of Medicine
1993-2003	Joint Appointment in Medicine, Johns Hopkins University School of Medicine
1996-2002	Affiliate Faculty, Program for Medical Technology Assessment and Practice, Johns Hopkins University School of Medicine
1996-2002	Associate Professor of Anesthesiology and Critical Care Medicine, Johns Hopkins University School of Medicine
1996-2003	Joint Appointment in Health Sciences Informatics, Johns Hopkins University School of Medicine
1997-2003	Joint Appointment in Health Policy and Management, Johns Hopkins University School of Public Health
1997-2003	Affiliate Faculty, Center for Evidence Based Medicine, Johns Hopkins University School of Medicine

2002-2003	Professor of Anesthesiology and Critical Care Medicine, Johns Hopkins University School of Medicine
2004	Professor of Anesthesiology and Critical Care, University of Pennsylvania School of Medicine
2004-2010	Adjunct Professor of Health Sciences Informatics, Johns Hopkins University
2004-2015	Consulting Professor of Anesthesiology, Duke University
2004-2017	Professor of Medicine, University of Pennsylvania School of Medicine (Secondary)
2004-2020	Robert Dunning Dripps Professor of Anesthesia, University of Pennsylvania School of Medicine
2019-present	Professor of Medicine, University of Pennsylvania School of Medicine (Secondary)
2020-present	Professor of Anesthesiology and Critical Care, University of Pennsylvania School of Medicine

Hospital and/or Administrative Appointments:

1990-1992	Director, Division of Peripheral Vascular Anesthesia, Yale New Haven Hospital
1990-1992	Attending Physician, Critical Care Anesthesia Service, Yale New Haven Hospital
1990-1992	Attending Physician, Liver Transplantation Team, Yale New Haven Hospital
1992-2003	Attending Physician, Department of Anesthesiology and Critical Care Medicine, Johns Hopkins Hospital
1997-2003	Anesthesia Coordinator, General Operating Room, Johns Hopkins Hospital
1998-2001	Director of Manpower and Program Development Department of Anesthesiology and Critical Care Medicine, Johns Hopkins University School of Medicine
1998-2001	Chief, Division of Perioperative Health Services Research Department of Anesthesiology and Critical Care Medicine, Johns Hopkins University School of Medicine
1999-2003	Clinical Director of Operating Rooms Department of Anesthesiology and Critical Care Medicine, Johns Hopkins University School of Medicine
2001-2003	Vice Chair for Clinical Investigation Department of Anesthesiology and Critical Care Medicine, Johns Hopkins University School of Medicine
2002-2003	Director, Program for Medical Technology Assessment and Practice, Johns Hopkins University School of Medicine
2004-present	Chair, Department of Anesthesiology and Critical Care, University of Pennsylvania Health System
2004-present	Member, Medical Board of the Hospital of the University of Pennsylvania (Vice-Chair, 2012-2014; Chair, 2014-2016)
2007	Vice-Chair, Search Committee for Chair of Medicine,

	University of Pennsylvania
2008-2014	Chair, Credentials Committee, Hospital of the University of Pennsylvania
2008-present	Chair, Committee on Professional Liability, Clinical Practices of the University of Pennsylvania
2010-2012	1st Vice-President, Medical Board, Hospital of the University of Pennsylvania
2010-2012	Chair, Bylaws Committee of the Medical Board of the Hospital of the University of Pennsylvania
2011-2014	Member, Advisory Committee for Medical Education (ACME), University of Pennsylvania School of Medicine
2012-2014	President-elect, Medical Board of the Hospital of the University of Pennsylvania
2012-2014	Chair, Committee on Clinical Effectiveness and Quality Improvement, Hospital of the University of Pennsylvania
2012-2016	Member, Board of Trustees, Hospital of the University of Pennsylvania
2012-2015	Co-Chair, Perelman School of Medicine Information Technology Committee
2012-present	Member, Contracting team with Blue Cross, University of Pennsylvania Health System
2014-2016	President, Medical Board, Hospital of the University of Pennsylvania
2015-2016	Member, Leadership and OversightCommittee, Penn Medicine License Committee on Medical Education (LCME) reaccreditation
2016-present	Member, Advisory Council for the Office of Inclusion and Diversity, Penn Medicine
2017-present	Member, IBC/Penn Medicine Delegated Care Mgmt Workgroup, IBC/UPHS Product Deep-Dive Workgroup, IBC/Penn Medicine Episodes Workgroup
2018-present	Clinical Program Lead, Penn Med-Vinmec Alliance

Other Appointments:

2004-present	Senior Fellow, Leonard Davis Institute for Health Economics (Member, Executive Committee)
2011-present	Member, Managed Care Contracting Advisory Committee of the Clinical Practices of the University of Pennsylvania Health System, Vice-Chair (2014-present)
2014-present	Member,, Medical Alumni Advisory Committee(MAAC), Perelman School of Medicine, University of Pennsylvania
2014-present	Affiliated Faculty, Quattrone Center for the Fair Administration of Justice of the University of Pennsylvania Law School
2020-present	CMS Chief Medical Officer and Director, Center for Clinical Standards and Quality, Centers for Medicare and Medicaid

Services

Specialty Certification:

1991	American Board of Anesthesiology

Licensure:

1991-2004	Maryland - D42689
2004-present	Pennsylvania MD423444

Awards, Honors and Membership in Honorary Societies:

1981	Benjamin Franklin Scholar University of Pennsylvania
1981	Magna cum laude with Distinction in Biology University of Pennsylvania
1986	M.D. with Distinction in Research State University of New York at Stony Brook
1989	Burroughs Wellcome Resident Scholar
1990	Young Investigator Award American Society of Critical Care Anesthesiologists
1995-1996	Richard S. Ross Clinician Scientist
2005-present	John Morgan Society
2007	Member, National Academy of Medicine (formerly Institute of Medicine)
2007	John C. Oakley Pioneer in Pain Medicine Award
2009	Foundation for Anesthesia Education and Research Hononary Research Lecturer
2011	2011 Distinguished Alumni Award, State University of New York at Stony Brook School of Medicine
2011	Eliasberg Medal for Anesthesiology Accomplishments from Mt. Sinai Medical School
2011	Foundation for Anesthesia Education and Research Academy of Mentors
2012	Member (Honorary), Chinese Society of Anesthesiologists
2013	C. William Hanson, Jr., M.D. Service Award, Hospital of the University of Pennsylvania
2015	2015 Innovations in Criminal Justice award, Quattrone Center for the Fair Administration of Justice: Using Root Cause Analysis To Instill a Culture of Self-Improvement (, Association of Prosecuting Attorneys
2015	Chinese Society of Anesthesiologists Distinguished Service Award
2016	Christian R. and Mary F. Lindback Award for Distinguished Teaching, University of Pennsylvania
2018	Honorary Fellow, Chinese College of Anesthesiology, Chinese Society of Anesthesiology
2020	Foundation of Anesthesia Education and Research (FAER)

Mentoring Excellence in Research Award

Memberships in Professional and Scientific Societies and Other Professional Activities:

International:

1990-Present	International Anesthesia Research Society
1990-1996	International Society for Ambulatory Monitoring - Founding Fellow
1990-Present	Society of Cardiovascular Anesthesiologists ((Research Committee, Member 1993-1997, 2003-2004, Chair 1997-2003) (Board of Directors, Member 1995-2001) (Taskforce on Practice Guidelines, Chair 2003-2005))
1993-2000	Association of Pharmacoeconomic and Outcome Research (Education Committee, Member 1997)
1995-2003	International Society for Technology Assessment in Health Care
2000-2004	International Society of Pharmacoeconomics and Outcome Research
2005-Present	Society for Perioperative Assessment and Quality Improvement (Member, Board of Directors)

National:

1987-Present	American Society of Anesthesiologists ((Committee on Acute Medicine, Adjunct Member 1992-1994) (Committee on Refresher Courses, Member 1994, 2003-2008) (Committee on Guidelines for Preoperative Evaluation, Consultant 1994-1997, Member 1999) (Subcommittee on Clinical Circulation, Member 1996-2000, 2005, 2006, 2007, Chair 2001-2004) (Committee on Performance and Outcomes Measurement, Member 2005-present; Chair 2008-2011) (Committee on Regional and Metropolitan Refresher Courses, Adjunct Member 1997-1998) (Committee on Outreach Education, Member 1997-1999) (Committee on Scientific Papers, Member 1997, 2001-2004) (Committee on Annual Meeting, Member 1997, 2001-2004) (Committee on Practice Parameters, Member 2003-present) (Representative to the Surgical Care Improvement Project 2003-present) (Committee on Research, Member 2007-2010, 2011-present) (Representative to American Medical Association Physician Consortium for Performance Improvement 2011-Present); Chair, Patient Safety Initiative Perioperative Brain Health Initiative 2015-Present)
1991-1992	American Society of Critical Care Anesthesiologists (Program Committee, Member

	1991)
1992-1993	National Institute of Mental Health (Biological Psychopharmacology Study Section, Ad-hoc Reviewer)
1993-Present	American Heart Association- Fellow (ACC/AHA Task Force for Perioperative Cardiovascular Evaluation for Noncardiac Surgery (Member 1993-2002, Chair 2003-present) Anesthesiology, Radiology and Surgery Study Committee (Member 1996-2001), Fellow 2007; Executive Database Committee (member 2007-2011); Member, Guideline Transformation & Optimization Advisory Group 2016-Present)
1994-Present	American College of Cardiology - Fellow (Member, ACCF/AHA Task Force on Practice Guidelines (2014-2020))
1994	National Heart, Lung, Blood Institute (SCOR Study Section, Ad-hoc Reviewer)
1995-Present	Society for Medical Decision Making
1998-Present	Society of Ambulatory Anesthesia ((Committee on Annual Meeting, Member 1999-2003) (Committee on Research, Member 2003-present, Chair 2005-2008) (Committee on Development, Member 2003-2004) (Task Force on Benchmarking Project, Member 2006))
1999-Present	Association of University Anesthesiologists (Member (1996-present), Councilor-at-Large (1999-2001), President-elect (2011-2012), President (2012-2014), Past President (2014-2016))
1999-Present	Center for Medicare and Medicaid Services (Technical Expert Panel evaluating applications for the Cardiovascular Demonstration Project 1999, Innovation Advisors Program (2012-2013); Hospital-Acquired Condition (HAC) Reduction Program Technical Expert Panel (2014); Member, Care Transformation Forum, an Initiative of the Health Care Payment Learning & Action Network (2019-2020))
1999	Society for Obstetric Anesthesia and Perinatology
2002-present	Association of American Medical Colleges (Council of Faculty and Academic Specialties (Representative from AUA 2013-present, Member, Administrative Council (2013-2016), Council of Academic Specialties (Representative from AUA 2002-present, Ex-officio member of Administrative Board 2011-2013), , CAS Initiative to Highlight Faculty Innovations (Chair 2010-2013), CAS Leadership Development Task Force (2009-2010);)
2003-2010	Surgical Care Improvement Project (sponsored by the Centers for Medicare and Medicaid Services, Agency for Healthcare Policy and Research, Centers for Disease

	Control and 10 other partners) (Member, Steering Committee; Member, Communications Subcommittee, Member, Technical Expert Panels on Surgical Site Infection and Cardiovascular Disease; Chair, Publications Committee)
2004-2008	American Medical Association (Member, AMA Physician Performance Improvement Committee)
2004-2008	Association of Anesthesiology Program Directors (Council member 2005-6)
2005-present	Morton Society (President (2016-2018))
2006-2015	Foundation for Anesthesia Education and Research (Member, Board of Directors; Member 2006-2015, Development Committee; Member 2006, Grant Awards Review Committee; Member, Geriatric Research Council; Member 2006, Cerebral Functioning Monitoring Task Force)
2007-Present	Academy Health (Member, Committee on Advocacy and Public Policy (2018))
2007-Present	National Academy of Medicine (formerly Institute of Medicine) (Member, IOM Priority Assessment Inventory Working Group (2009); Reviewer, Accounting for Social Risk Factors in Medicare Payment: Identifying Social Risk Factors (2016); Member, Committee on Reproductive Health Services: Assessing the Safety and Quality of Abortion Care (2016-Present); Planning Committee and Presenter, Building the Evidence Base for Improving Health Care: Contributions, opportunities and priorities (2017-8))
2007	Rand Corporation/Assistant Secretary of Health for Planning and Evaluation (Member, Technical Expert Panel)
2008-2014	AAAHC Institute for Quality Improvement (Member, Board of Trustees; Member, Measurement Development Task Force 2009-2011)
2008-Present	National Quality Forum (Ex-oficio member (2015-6), Member (2019-2022), Treasurer (2019-21) Board of Directors; Member, Perioperative Care Steering Committee 2008-2009; Co-Chair, Main Patient Outcomes Steering Committee 2009-2011; Member 2012-2018, Vice-Chair 2014-2015, Chair 2015-2016 Consensus Standards Advisory Committee; Member, Measure Evaluation Committee 2013; Co-Chair, Surgery Standing Committee 2014-7; Measurement and Use Advisory Panel 2015-2016; Member, Measures Application Partnership Hospital Workgroup 2016-2019; Member, Measure Feedback Committee 2018-2019)
2012	Physician Quality Reporting System Program (Preoperative Beta-Blocker in Patients with Isolated CABG Surgery Technical Expert Panel (TEP))
2012	Yale New Haven Health Services Corporation/Center for Outcomes Research and Evaluation (YNHHSC/CORE)/ The Society of Thoracic

	Surgeons (STS)/ CMS (Member, Technical Expert Panel (TEP) for the Coronary Artery Bypass Graft (CABG)outcomes measures)
2013-2019	Physicians Consortium for Performance Improvement (Member, Quality Improvement Advisory Council)
2014-2016	American Institutes for Research (Member, Advisory Board, Gordon and Betty Moore Foundation funded project developing a coordinated approach to measuring patient and family engagement in the hospital setting)
2014-Present	Blue Cross Blue Shield Association (Member, Medical Advisory Panel, Technology Evaluation Center)
2016-Present	American Society for Enhanced Recovery (Member, Advisory Board 2016-Present)
2016-Present	Physician Leadership Academy (joint venture of Deloitte Consulting and Wharton School) (Member, Board of Advisors 2016-Present)
2016-Present	Yale/YNHH Center for Outcomes Research and Evaluation (CORE) (Member, Hospital-Wide Mortality Technical Working Group 2016-present; Member, 90-day CABG Mortality Bundled Payment Technical Evaluation Panel 2018-present; member, Star Ratings Provider Leadership Work Group; member, Technical Expert Panel (TEP) for the Reevaluation of Inpatient Claims-Based Outcome Measure 2019-2020)
2017-2023	Accreditation Council for Graduate Medical Education (Member, Standing Panel for Accreditation Appeals in the specialty of Anesthesiology)
2018-Present	Leapfrog Group (Chair, Ambulatory Surgery Expert Panel)
2019-Present	Health Care Payment Learning and Action Network (LAN) (member, Care Transformation Forum (CTF))
2019	Department of Health and Human Services - Value Based Transformation - June Sepsis Planning Meeting

Editorial Positions:

1994-Present	Ad hoc Reviewer, Anesthesia & Analgesia
1995-Present	Ad hoc Reviewer, Journal of Clinical Anesthesia
1995-2000	Ad hoc Reviewer, Journal of Clinical Monitoring
1996-Present	Editorial Board Member, Journal of Cardiothoracic and Vascular Anesthesia
1996-2001	Co-Editor In-Chief, Problems in Anesthesia
1996-1998	Expert Analyst, Vascular Anesthesia, The Cardiovascular and Thoracic Anesthesia Journal Club Journal

1997-Present	Question Writer, In-Training Council, American Board of Anesthesiology
1999-2002	Editorial Board Member, American Journal of Anesthesiology
1999-Present	Editorial Board Member, Anesthesiology News
1999-2000	Section Editor, Practice Management, Economics and Technology Assessment, Current Anesthesiology Reports
2000-2003	Associate Editor, Anesthesiology
2000-Present	Ad hoc Reviewer, Circulation
2000-Present	Ad hoc Reviewer, American Journal of Physiology
2000-Present	Editorial Board Member, Current Opinion in Anesthesiology
2001-Present	Ad hoc Reviewer, New England Journal of Medicine
2001-Present	Ad hoc Reviewer, Chest
2001-Present	Ad hoc Reviewer, Journal of the American College of Cardiology
2001-Present	Ad hoc Reviewer, Medical Care
2001-Present	Ad hoc Reviewer, Journal of Nuclear Cardiology
2001-2002	Executive Committee Member, American Journal of Anesthesiology
2001-Present	Consulting Editor, Anesthesiology Clinics of North America
2001-Present	Ad hoc Reviewer, Journal of the American Medical Association
2002-Present	Section Editor, Pro/Con, Journal of Cardiothoracic and Vascular Anesthesia
2002-Present	Ad hoc Reviewer, Veterans Administration Clinical Trials Study Section
2002-Present	Ad hoc Reviewer, Urology
2005-Present	Ad-hoc reviewer, Medical Care
2011-present	Perioperative Medicine, Co-Editor-in-Chief (2017-present)
2012-present	Annals of Surgery, Member, Editorial Board

Academic and Institutional Committees:

1990-1992	Member, Residency Review Committee Department of Anesthesiology Yale University School of Medicine
1994-1999	Member, Outpatient General Clinical Research Center Protocol Review Subcommittee Johns Hopkins University School of Medicine
1994-2003	Member, Education Committee Department of Anesthesiology and Critical Care Medicine Johns Hopkins University School of Medicine
1994-1995	Member, Patient Satisfaction Task Force Department of Anesthesiology and Critical Care Medicine Johns Hopkins Hospital
1994-1999	Member, Presurgical Work Group Surgical Services Design Team Johns Hopkins Hospital
1995	Member, Ambulatory Surgery Task Force Johns Hopkins Hospital
1998-2003	Member, Service Executive Committee

	Department of Anesthesiology and Critical Care Medicine Johns Hopkins University School of Medicine
1998-2003	Member, Executive Manpower Committee Department of Anesthesiology and Critical Care Medicine Johns Hopkins University School of Medicine
1998-1999	Member, Operating Room Posting Task Force Johns Hopkins Hospital
1999-2003	Member, Vice-Chairman Committee Department of Anesthesiology and Critical Care Medicine Johns Hopkins University School of Medicine
1999-2003	Member, Minimally Invasive Surgery Focus Group Johns Hopkins Hospital
1999-2003	Member, Operating Room Executive Committee Johns Hopkins Hospital
1999-2003	Member, General Operating Room Subcommittee Johns Hopkins Hospital
2000-2001	Participant, Leadership Development Program Johns Hopkins University School of Medicine
2000-2003	Member, Clinical Competence Committee Department of Anesthesiology and Critical Care Medicine Johns Hopkins University School of Medicine
2000-2002	Member, Office of Technology Licensing Advisory Committee Medical School Council Johns Hopkins University School of Medicine
2000-2003	Member, Government Affairs Committee Clinical Practice Association Johns Hopkins University School of Medicine
2000-2003	Member, Innovations in Patient Care - Long Term Strategies Committee Johns Hopkins Medicine
2000-2003	Member, Simulation Center Committee Johns Hopkins Hospital
2000-2003	Member, Outpatient Surgery Operating Room Committee Johns Hopkins Hospital
2002-2003	Member, Ophthalmology Chair Search Committee Johns Hopkins University School of Medicine
2002-2003	Member, Budget and Finance Committee Clinical Practice Association Johns Hopkins University School of Medicine
2002-2003	Member, Board of Advisors for the Johns Hopkins Biostatistics Center Johns Hopkins School of Hygiene and Public Health
2004-2005	Member, Steering Committee of the Standing Committee Department Chairs, University of Pennsylvania School of Medicine
2004-2020	Member, Clinical Practices of the University of Pennsylvania Board of Directors

2004-2006	Member, Clinical Practices of the University of Pennsylvania Executive Committee
2004-2005	Member, Steering Committee of the Standing Committee of Department Chairs, Centers and Institutes
2004-2020	Member, Standing Committee of Department Chairs, Centers and Institutes
2004-2020	Operating Room Executive Committee, Hospital of the University of Pennsylvania
2004-2005	Chair, Internal Review Committee of the Leonard Davis Institute, University of Pennsylvania
2004-2012	Member, Clinical Practices of the University of Pennsylvania Finance Subcommittee
2005-2007	Member, Clinical Practices of the University of Pennsylvania Clinical Effectiveness and Quality Improvement Committee
2005-2006	Member, Clinical Practices of the University of Pennsylvania Finance Committee
2005-2006	Member, Tenure Track Review Committee, University of Pennsylvania School of Medicine
2005-2006	Chair, Review Committee of the Department of Neurosurgery, University of Pennsylvania School of Medicine
2005-2006	Member, Steering Committee, Magnet Designation, Hospital of the University of Pennsylvania
2006	Member, Tia Sophia Review Committee
2006-2007	Member, Committee to Review the Clinical Transplant Institute Proposal
2006-2020	Member, Penn Advisory Board, Robert Wood Johnson Clinical Scholars Program
2006-2008	Member, 2008 LCME Review Steering Committee (Chair, Medical Student Task Force), University of Pennsylvania School of Medicine
2006-2015	Member, Steering Committee, Comprehensive Neurosciences Center
2007	Co-chair, Department of Medicine Chair Search Committee
2007-2020	Chair, Clinical Practice of the University of Pennsylvania Professional Liability Subcommittee
2008-2009	Member, Chair of Surgery Search Committee, University of Pennsylvania
2008-2009	Member, Search Committee for Chair of Ophthamology
2009-2010	Member, Chair of Dermatology Search Committee
2010-2011	Chair, Seach Committee for the Chair of the Department of Medical Ethics and Health Policy
2010-2020	Vice-Chair, Managed Care Contracting Subcommittee, Clinical Practices of the University of Pennsylvania; Physician representative to UPHS Contracting Committee with Independence Blue Cross (2012, 2016)
2012-2013	Member, Search for Chair of Department of Pediatrics, Perelman School of Medicine

2012-2013	Member, Integrating Knowledge Working Group (IKWG) for the Middle States Reaccreditation Self Study, University of Pennsylvania
2013	Chair, Search for Chair of Department of Biostatics and Epidemiology, Perelman School of Medicine
2014	Chair, Distinguished Alumni Award Committee
2014-2015	Chair, Orthopedic Review Committee
2015-2016	Chair, Department of Ophthalmology Review Committee
2016-2017	Chair, Pathology Review Committee
2016-2020	Member, Advisory Council for the Office of Diversity and Inclusion
2017-2018	Chair, Committee to review the Department of Health Policy and Medical Ethics
2017	Member, Search Committee for Senior Vice Dean for Education
2017	Member, Advisory group: search committee training project
2018-2019	Member, Search Committee for Director of Leonard Davis Institute of Healthcare Economics

Major Academic and Clinical Teaching Responsibilities:

1994-1999	Section Leader, Clinical Decision Making Course Medical Student Curriculum 2nd Year Johns Hopkins University School of Medicine
1996-2003	Course Instructor, Medical Technology Assessment Johns Hopkins University School of Public Health
1997-2003	Course Instructor, Decision Analysis, Summer Institute Johns Hopkins University School of Public Health
1997-2003	Director, Anesthesia Case Conference Department of Anesthesiology and Critical Care Medicine Johns Hopkins University School of Medicine
1999-2003	Instructor, Physician in Society Medical Student Curriculum 2nd Year Johns Hopkins University School of Medicine
1999-2003	Course Instructor, Decision Analysis Johns Hopkins University School of Public Health
2005-2008	"Cost-effectiveness and decision analysis" in Epidemiology for 1st year medical students
2006-2016	Preceptor, Doctoring Course
2007-2008	Guest Lecturer, Health Care Management Undergraduate course
2008-2020	Course Director, Frontiers Course for 4th year medical students, "Science of Quality"
2016-2020	Small Group Preceptor, Health Care Systems, Perelman School of Medicine,

Lectures by Invitation:

Jan, 1999	"Preoperative cardiac evaluation" - Department of Anesthesia, Mount Sinai School of Medicine, New York, NY
Jan, 1999	"Risk of anesthesia" - Department of Anesthesia, Jefferson Medical

	College, Philadelphia, PA
Feb, 1999	"Risk of anesthesia" - Department of Anesthesia, University of Michigan, Ann Arbor, MI
Mar, 1999	"Cardiac risk of noncardiac surgery" - Mini-Course, American College of Cardiology 48th Annual Scientific Session, New Orleans, Louisiana
Apr, 1999	"Outcomes evaluation/measurement in cardiac surgery" - Scientific Program Committee, Society of Cardiovascular Anesthesia Annual Meeting, Chicago, IL
Apr, 1999	"Outcome measure for ambulatory anesthesia" - Society for Ambulatory Anesthesia Annual Meeting, Chicago, IL
May, 1999	"Meet the experts: coronary disease and surgical emergencies" - 33a Jornada Paulista de Anestesiologia by the Sociedade de Anestesiologia do Estado de Sao Paulo, Sao Paulo, Brazil
May, 1999	"Preoperative assessment of the patient with cardiovascular disease" - 33a Jornada Paulista de Anestesiologia by the Sociedade de Anestesiologia do Estado de Sao Paulo, Sao Paulo, Brazil
May, 1999	"Preoperative cardiac evaluation" - Department of Anesthesia, Sunnybrook Health Science Center, Toronto, Canada
Jun, 1999	"Perioperative aschemia: is it a bad thing?" - 2nd Annual Cardiothoracic Update, Hilton Head, SC
Sep, 1999	"Risk of anesthesia" - Department of Anesthesia, Emory University, Atlanta, GA
Nov, 1999	"Preoperative assessment" - 1999 Survey of Current Issues in Surgical Anesthesia, Cleveland, OH
Dec, 1999	"Impact of economic pressures on anesthesia training and practice" - Winter College Lecture, Royal College of Anaesthetists, Dublin, Ireland
Jan, 2000	"Evidence based anesthesia care: the high risk cardiac patient" - Department of Anesthesia, New York University, New York, NY
Feb, 2000	"Evidence based anesthesia care: the high risk cardiac patient" - Department of Anesthesia, SUNY at Stony Brook, Stony Brook, NY
Mar, 2000	"Heart rate variability as a measure of system complexity" - Japanese Society of Intensive Care Management, Nagoya, Japan
Mar, 2000	"Anesthetic management of the cardiac patient undergoing noncardiac surgery" - Japanese Society of Intensive Care Management, Nagoya, Japan
May, 2000	"Risk of readmission after ambulatory surgery by location of care: analysis of Medicare claims" - Society of Ambulatory Anesthesia Annual Meeting, Washington, D.C.
Jun, 2000	"Strategies to reduce cardiac risk of noncardiac surgery" - Department of Anesthesia, Duke University, Durham, NC
Jul, 2000	"Does anything reduce cardiac complications of noncardiac surgery" - Georgia Society of Anesthesiology, Amelia Island, FL
Sep, 2000	"Preoperative cardiac evaluation" - Department of Anesthesia, SUNY at Buffalo, Buffalo, NY

Sep, 2000	"Risk of anesthesia" - Yale Anesthesia Alumni Foundation Lecture, New Haven, CT
Sep, 2000	"Preoperative cardiac evaluation" - Department of Anesthesia, Campus University Hospital Gasthuisberg, Leuven, Belgium
Sep, 2000	"Strategies to reduce cardiac risk of noncardiac surgery" - Department of Anesthesia, Yale University, New Haven, CT
Oct, 2000	"Data mining: Medicare and beyond." - Panel for the Foundation for Anesthesia Education and Research, American Society of Anesthesiologists Meeting, San Francisco, CA
Oct, 2000	"Strategies to reduce the risk of anemia" - Symposium on Hemostatis and Transfusion, Graz, Austria
Oct, 2000	"Risk of outpatient surgery: analysis of Medicare claims" - Panel on Risk of Anesthesia, American Society of Anesthesiologists meeting, San Francisco, CA
Nov, 2000	"Strategies to reduce cardiac risk of noncardiac surgery" - Department of Anesthesia, University of Rochester, Rochester, NY
May, 2001	"Patients with CAD" - Panel on Difficult Medical Patients, Society of Ambulatory Anesthesia, Palm Desert, CA
Jun, 2001	"Strategies to reduce cardiac risk of noncardiac surgery" - Department of Anesthesia, Washington University in St. Louis, St. Louis, MO
Sep, 2001	"Strategies to reduce cardiac risk of noncardiac surgery" - Department of Anesthesia, University of Medicine and Dentistry of New Jersey, Newark, NJ
Sep, 2001	"Strategies to reduce cardiac risk of noncardiac surgery" - Department of Medicine, University of Medicine and Dentistry of New Jersey, Newark, NJ
Nov, 2001	"Preoperative cardiac evaluation" - University of Chicago, Department of Anesthesiology and Critical Care Medicine Annual Meeting, Chicago, IL
Nov, 2001	"Risks of outpatient surgery" - University of Chicago, Department of Anesthesiology and Critical Care Medicine Annual Meeting, Chicago, IL
Dec, 2001	"Does preoperative screening improve anesthetic outcome?" - Panel on Preoperative Testing - Are There Any Standards?, Postgraduate Assembly in Anesthesiology, New York, NY
Dec, 2001	"Perioperative management of the high risk patient for non-cardiac surgery" - Panel on How has Research Changed Your Clinical Practice?, Postgraduate Assembly in Anesthesiology, New York, NY
Apr, 2002	"Recent developments in perioperative stress protection in non-cardiac surgery" - Symposium at the 10th ESA Anniversary Meeting, 24th EAA Annual Meeting, Nice, France
Apr, 2002	"Application of the AHA/ACC guidelines to the elderly ambulatory patient" - Society of Ambulatory Anesthesia Annual Meeting, Orlando, FL

Apr, 2002	"The patient with ischemic heart disease undergoing arthroscopic surgery" - PBLD at the Society of Ambulatory Anesthesia Annual Meeting, Orlando, FL
May, 2002	"Strategies to reduce cardiac risk of noncardiac surgery" - Department of Anesthesia, Western Pennsylvania Hospital, Pittsburgh, PA
May, 2002	"Strategies to reduce cardiac risk of noncardiac surgery" - Department of Anesthesia, Northwestern University Medical Center, Chicago, IL
Aug, 2002	"Strategies to reduce cardiac risk of noncardiac surgery" - Department of Anesthesia, University of Illinois at Chicago, Chicago, IL
Aug, 2002	"Strategies to reduce cardiac risk of noncardiac surgery" - Department of Anesthesia, Rush-Presbyterian Medical Center, Chicago, IL
Sep, 2002	"Strategies to reduce cardiac risk of noncardiac surgery" - Department of Anesthesia, University of California at Los Angeles, Los Angeles, CA
Oct, 2002	"Preoperative assessment of the patient with cardiac disease" - American Society of Anesthesiologists Annual Meeting, Orlando, FL
Oct, 2002	"Preoperative testing: how should I apply the update to the AHA/ACC perioperative cardiovascular evaluation guidelines and the ASA advisory on preanesthetic evaluation?" - Panel Moderator, American Society of Anesthesiologists Annual Meeting, Orlando, FL
Oct, 2002	"Risk of anesthesia (and surgery) in the outpatient setting: the importance of patient, surgery and location of care" - Keynote lecture, Society of Ambulatory Anesthesia Annual Meeting, Orlando, FL
Oct, 2002	"Risk of undertransfusion" - American Academy of Blood Bankers, Orlando, FL
Nov, 2002	"The role of searching and evaluating the literature to ensure patient safety in clinical research: practices and protocol" - Panel, AMIA 2002 Symposium, San Antonio, TX
Dec, 2002	"Cost analysis in cardiac surgery" - Panel, New York State Society of Anesthesiologists Postgraduate Assembly, New York, NY
Dec, 2002	"Evidence-based medicine: perioperative beta-blockers" - Robertazzi Memorial Panel, 56th Postgraduate Assembly in Anesthesiology, New York, NY
Dec, 2002	"Evidence-based medicine: perioperative beta blockers" - Rovenstein Panel, New York State Society of Anesthesiologists Postgraduate Assembly, New York, NY
Jan, 2003	"Strategies to reduce cardiac risk of noncardiac surgery" - Department of Medicine, University of Florida, Gainesville, FL
Jan, 2003	"Strategies to reduce cardiac risk of noncardiac surgery" -

	Departments of Surgery and Anesthesia, University of Florida, Gainesville, FL
Mar, 2003	"Optimizing perioperative outcomes" - Refresher Course, IARS 77th Clinical and Scientific Congress, New Orleans, LA
Mar, 2003	"Operating room management" - Panel, IARS 77th Clinical and Scientific Congress, New Orleans, LA
Jun, 2003	"Risk of anesthesia" - Department of Anesthesia, Oxford University, Oxford, UK
Sep, 2003	"Strategies to reduce cardiac risk of noncardiac surgery" - Department of Anesthesia, University of Colorado, Boulder, CO
Sep, 2003	"Risk of Anesthesia: Does location of care matter?" - Department of Anesthesiology, The Geffen School of Medicine at UCLA, Los Angeles, CA
Sep, 2003	"Cardiac patient presenting for aortic aneurysm resection." - Department of Anesthesiology, The Geffen School of Medicine at UCLA, Los Angeles, CA
Sep, 2003	"Risk of anesthesia: Are we still safe in outpatient surgery?", Colorado Society of Anesthesiologists, Denver, CO.
Oct, 2003	"How old is too old? Risk in the geriatric patient" - Society of Ambulatory Anesthesia Mid-Year Meeting, San Francisco, CA
Oct, 2003	"Tailoring the preop to the procedure: the evidence" - SAMBA Breakfast Panel on Whom Do We Invite to Our Party?: How and why the preoperative evaluation of surgical outpatients is different., American Society of Anesthesiologists Annual Meeting, San Francisco, CA
Oct, 2003	"Differences in outcomes from surgery performed in physicians offices and ambulatory surgery centers" - Panel on the Surgeon Anesthesia Supervisor: How much do they need to know, how is it evaluated, and why do we care?, American Society of Anesthesiologists Annual Meeting, San Francisco, CA
Oct, 2003	"Which patients need what coronary evaluation before carotid endarterectomy?" - Panel on Carotid Endarterectomy: What preoperative evaluation?; What anesthetic technique (regional or GA)?; What neurologic monitoring?, American Society of Anesthesiologists Annual Meeting, San Francisco, CA
Oct, 2003	"Evidence based medicine: perioperative interventions" - Panel on Evidence-Based Medicine in Anesthesiology, American Society of Anesthesiologists Annual Meeting, San Francisco, CA
Oct, 2003	"Preoperative assessment of the patient with cardiac disease" - American Society of Anesthesiologists Annual Meeting, San Francisco, CA
Oct, 2003	"What do I do with a positive stress test result" - Panel Moderator on High-Risk Patients Undergoing Noncardiac Surgery: What do I do about the results of preoperative testing, perioperative testing, perioperative beta-blockers and pacemakers?, American Society of Anesthesiologists Annual Meeting, San Francisco, CA

Dec, 2003	"Vascular Surgery" - Focus Session on What should change our clinical practice? Evidence based medicine: Here to stay., 57th Postgraduate Assembly in Anesthesiology, New York, NY
Dec, 2003	"What should change our clinical practice? Evidence based medicine: Here to stay.", Panel Moderator, 57th Postgraduate Assembly in Anesthesiology, New York, NY
Apr, 2004	"Preoperative cardiac risk assessment and risk reduction" - Royal College of Physicians and Surgeons of Canada, Toronto, Canada
Apr, 2004	"Strategies to reduce cardiac risk of noncardiac surgery"- Meet the experts. World Congress of Anesthaesiologists. Paris, Fr.
Apr, 2004	"What is the most appropriate monitoring for perioperative myocardial ischaemia ?"- World Congress of Anaesthesiologists. Paris, Fr
May, 2004	"Strategies to reduce cardiac risk of noncardiac surgery"- British Cardiac Society. Manchester, England
Jun, 2004	"Risk of anesthesia: importance of location of care"- Ali Gharib Lecture. Department of Anesthesia. Case Western Reserve University School of Medicine
Sep, 2004	"Strategies to reduce cardiac risk for vascular surgery" - Vascular Anaesthesia Society of Great Britain and Ireland. Cambridge, England
Sep, 2004	"Strategies to reduce cardiac risk for vascular surgery"- Vascular Anaesthesia Scoiety of Great Britain and Ireland, Oxford, England
Oct, 2004	"When is Preoperative Testing Worth the Money?" for Panel on The Economics of the Preoperative Process- American Society of Anesthesiologists Annual Meeting, Las Vegas, NV
Oct, 2004	"Current State of the Evidence of Beta-Blockers" for Panel on So the Hospital Mandates a Beta-blocker Protocol, but How do I Implement One?- American Society of Anesthesiologists Annual Meeting, Las Vegas, NV
Oct, 2004	"Preoperative Assessment of the Patient with Cardiac Disease" - ASA Refresher Course, American Society of Anesthesiologists Annual Meeting, Las Vegas, NV
Oct, 2004	"Preoperative Cardiac Evaluation of the Endovascular Stent" for Panel on New Fronteirs in Vascular Surgery: Not Office-based ... Yet- American Society of Anesthesiologists Annual Meeting, Las Vegas, NV
Dec, 2004	"Improving perioperative outcomes: what's the role of the government and other specialty societies?" Panel on To Err is Human: are our patients safe? Postgraduate Assembly of the New York State Society of Anesthesiologists. New York, NY
Mar, 2005	"Is outcome research a waste of time?" - 25th Myron B. Laver International Postgraduate Course, Basel, Switzerland
Mar, 2005	"Preoperative patient evaluation" - 25th Myron B. Lavar International Postgraduate Course, Basel, Switzerland
Mar, 2005	"Cardiovascular risk of vascular surgery" - International Anesthesia

	Research Society Annual Meeting, Honolulu, HI
Apr, 2005	"Cardiac Risk and Beta-Blockade" - Controversies in Adult and Pediatric Anesthesia, HUP/CHOP Symosium, Philadelphia, PA
Apr, 2005	"Strategies to Reduce Cardaic Risk of Noncardiac Surgery"- Lancaster General Hospital, Lancaster, PA
Apr, 2005	"Is Outcomes Research a Waste of Time? Debunking dogma with data"- SUNY at Downstate, Brooklyn, NY
May, 2005	"Surgical Risk Reduction" at Society of Ambulatory Anesthesia Annual Meeting, Scottsdale, AZ
May, 2005	"Academic Practice" on Panel for Resident Component - Society of Ambulatory Anesthesia Annual Meeting, Scottsdale, AZ
May, 2005	"Strategies to Reduce Cardiac Risk of Noncardiac Surgery"- Reading Hospital, Reading, PA
Oct, 2005	"Clinical Forum on cards consult? Revascularization or just beta blockers"- American Society of Anesthesiologists Annual Meeting, Atlanta, GA
Oct, 2005	Preoperative evaluation, Panel on Diabetes Update: The Inpatient, the Outpatient and the Non-Patient"- American Society of Anesthesiologists Annual Meeting, Atlanta, GA
Oct, 2005	"Perioperative beta-blockade- Panel on Strategies to reduce cardiac risk of noncardiac surgery- but I thought we knew the answers!"- American Society of Anesthesiologists Annual Meeting, Atlanta, GA
Oct, 2005	"Preoperative Cardiac Assessment"- American Society of Anesthesiologists Annual Meeting, Atlanta, GA
Oct, 2005	Preoperative evaluation, Panel on Diabetes Update: The Inpatient, the Outpatient and the Non-Patient"- American Society of Anesthesiologists Annual Meeting, Atlanta, GA
Oct, 2005	"Is outcomes research a waste of time?" Orkin Memorial Lecture, Montefiore Hospital, Bronx, NY
Dec, 2005	"Strategies to reduce cardiac risk of noncardiac surgery"- Department of Anesthesiology, University of Virginia, Charlottesville, VA
Dec, 2005	"Risk of anesthesia: importance of location of care"- Department of Anesthesiology, University of Virginia, Charlottesville, VA
Dec, 2005	"Wading through the American Colleg of Cardiology/American Heart Association Algorithm", Panel of Using practice guidelines to improve outcome: what the clinician needs to know. Postgraduate Assembly of Anesthesiology. New York, NY
Dec, 2005	"How can I imporve organ protection during surgery?: Protecting the heart" Postgraduate Assembly in Anesthesiology, New York, NY
Feb, 2006	"Preoperative cardiac evaluation and management" Neurosurgical Grand Rounds, University of Pennsylvania
Apr, 2006	"Strategies to reduce cardiac risk of noncardiac surgery" Pennsylvania Association of Nurse Anesthetists Annual Meeting.

	Hershey, PA
Apr, 2006	"Risk of anesthesia in the outpatient setting" Pennsylvania Association of Nurse Anesthetists Annual Meeting. Hershey, PA
May, 2006	"Pharmacologic management to reduce perioperative myocardial infarction" Panel on Best practices in cardiac surgery. Society of Cardiovascular Anesthesiologists Annual Meeting. San Diego, CA
May, 2006	"From student to mentor and chair: _my journey to return to the University of Pennsylvania" Duke Anesthesiology Academic Evening. Duke University. Durham, NC
May, 2006	"Strategies to reduce cardiac risk of noncardiac surgery"- Department of Anesthesiology, Duke University, Durham, NC
May, 2006	"Strategies to reduce cardiac risk of noncardiac surgery" Departments of Anesthesiology, Surgery and Cardiology. University of Cincinnati. Cincinnati, OH
May, 2006	Guidelines, P4P, and Improving Care. University of Cincinnati Department of Anesthesiology, Cincinnati, OH
Jun, 2006	"Multicenter trials to improve care- noncardiac surgery" European Society of Anesthesiologists, Madrid, Spain
Jun, 2006	"Guidelines, P4P, and improving care". Department of Anesthesia and Perioperative Care, University of California San Francisco, San Francisco, CA
Sep, 2006	"Cardiac Risk Stratification and Risk Reduction for Non-Cardiac Surgery in 2006", 2nd Annual Perioperative Medicine Summit, Cleveland, OH
Sep, 2006	"Strategies to reduce cardiac risk of noncardiac surgery", Department of Medicine Grand Rounds, University of Pennsylvania School of Medicine, Philadelphia, PA
Oct, 2006	"Preoperative cardiac evaluation"- American Society of Anesthesiologists, Chicago, IL
Nov, 2006	"Strategies to reduce cardiac risk of noncardiac surgery"- University of California at San Diego, San Diego, CA
Feb, 2007	"Strategies to reduce cardiac risk of noncardiac surgery"- Department of Anesthesiology and Critical Care, University of Miami, Miami, FL
Feb, 2007	"Guidelines, P4P and Improving Perioperative Care"- Department of Anesthesiology and Critical Care, University of Miami, Miami, FL
Feb, 2007	"Strategies to reduce cardiac risk of noncardiac surgery"- Englewood Hospital, Englewood, NJ
Mar, 2007	"Analyzing retrospective data: the clinical implications of statistical methods"- International Anesthesia Research Society Annual Meeting, Orlando, FL
Apr, 2007	"The new AHA/ACC Guidelines on Beta-Blockade" Society of Cardiovascular Annesthesiologists Annual Meeting. Montreal
May, 2007	"Guidelines, P4P and improving perioperative outcome" Beth-Israel Deaconess Medical Center, Boston, MA
Jun, 2007	"Pharmacologic reduction in perioperative myocardial infarction",

	European Society of Anesthesiologists Annual Meeting, Munich, Germany
Jun, 2007	"Strategies to reduce cardiac risk for noncardiac surgery", Department of Anesthesiology and Perioperative Medicine, Oregon Health Sciences University
Jun, 2007	"How will clinical trials influence practice guidelines and pay for performance", European Society of Anesthesiologists, Munich, Germany
Jun, 2007	"The cardiac risk patient-what is new?" European Society of Anesthesiologists, Munich, Germany
Nov, 2007	"Strategies to reduce cardiac risk for noncardiac surgery" Department of Anesthesiology, Washington University in St. Louis, St. Louis, MO
Nov, 2007	"Risk of outpatient surgery: analysis of medicare claims" Department of Anesthesiology, Washington University in St. Louis, St. Louis, MO
Nov, 2007	"Strategies to reduce cardiac risk of noncardiac surgery" Departments of Anesthesiology and Surgery, Atlantic City Regional Medical Center, Atlantic City, NJ
Nov, 2007	"Did the AHA/ACC Guidelines really say that?" EM Papper Annual Lecture. Columbia University School of Medicine Department of Anesthesiology, New York, NY
Nov, 2007	"Risk of anesthesia in the outpatient setting: Using of claims data" Columbia University School of Medicine Department of Anesthesiology, New York, NY
Dec, 2007	"Outcome-Measures" Focus session on How do we demonstrate quality?. Postgraduate Assembly in Anesthesiology, New York, NY
Dec, 2007	"Outcomes" in Panel on Practice management issues: P4P and other things I better know about. Postgraduate Assembly in Anesthesiology, New York, NY
Jan, 2008	"Strategies to reduce cardiac risk of noncardiac surgery", Detroit Medical Center Department of Anesthesiology
Feb, 2008	"Strategies to reduce cardiac risk of noncardiac surgery", Yale University School of Medicine Department of Anesthesiology, New Haven, CT
Feb, 2008	"Guidelines, P4P, and Improving Perioperative Care", Yale University School of Medicine Department of Anesthesiology, New Haven, CT
Mar, 2008	"Perioperative beta-blockade", Panel of Guidelines on Perioperative Cardiovacular Evaluation, American College of Cardiology Annual Meeting, Chicago, IL
Mar, 2008	"Rolling the Dice: the wise use of statistics", Panel on Publication Roulette, IARS Annual Meeting, San Francisco, CA
Mar, 2008	"Did the AHA/ACC Guidelines really say that?" IARS Annual Meeting, San Francisco, CA

Apr, 2008	"Perioperative cardiovascular evaluation guidelines"
Apr, 2008	"Perioperative Cardiac Guidelines", Society of Hospital Medicine Annual Meeting, San Diego, CA
May, 2008	"Have we pushed office-based surgery too far?", Society of Ambulalatory Anesthesia Annuall Meeting, Miami, FL
Jun, 2008	"Strategies to reduce cardiac risk of noncardiac surgery", Seoul National Hospital 50th Department of Anesthesiology and Pain Medicine Anniversary Meeting, Seoul, Korea
Jun, 2008	"Strategies to reduce cardiac risk of noncardiac surgery" Departments of Anesthesiology and Surgery Grand Rounds, Medical University of South Carolina, Charleson, SC
Jul, 2008	"ACC/AHA Guidelines on Perioperative Cardiovascular Evaluation", Evidence Based Perioperative Medicine Meeting 2008, London, England
Jul, 2008	"Pay-4-Performance, the US perspective", Evidence Based Perioperative Medicine Meeting 2008, London, England
Oct, 2008	"Preoperative assessment of the patient with cardiac disease", American Society of Anestheisologists Annual Meeting, Orlando, FL
Oct, 2008	"Who gets revascularization and how? Update on the Guidelines for preoperative evaluation of the noncardiac surgical patient" American Society of Anestheisologists Annual Meeting, Orlando, FL
Oct, 2008	"The diabetic patient undergoing noncardiac surgery: what should we do from a cardiac evaluation standpoint?" Panel on Management of the diabetic patient. American Society of Anestheisologists Annual Meeting, Orlando, FL
Oct, 2008	"Can we really improve performance?" Panel on Avoiding performance anxiety. American Society of Anestheisologists Annual Meeting, Orlando, FL
Oct, 2008	"From student to mentor and chair: _my journey to return to the University of Pennsylvania" Foundation for Anesthesia Education and Research Scholar Presentation
Nov, 2008	"Postoperative care for the bariatric surgery patient" Panel on The Morbidly Obese Patient. American Heart Association Annual Meeting, New Orleans, LA
Nov, 2008	"Heart disease in the cardiac patient before noncardiac surgery." Panel on Clinical Challenges in Daily Practice and Case-Based Applications of Recent Guidelines I, American Heart Association Annual Meeting, New Orleans, LA
Nov, 2008	"Strategies to reduce cardiac risk for noncardiac surgery", St. Joseph Medical Center, Towson, MD
Jan, 2009	"Strategies to reduce cardiac risk of noncardiac surgery" University of Maryland, Baltimore, MD
Jan, 2009	"Guidelines, P4P and improving perioperative care" University of Maryland, Baltimore, MD

Jan, 2009	"Strategies to reduce cardiac risk of noncardiac surgery: Update on the AHA/ACC Guidelines", Department of Anesthesiology, University of Miami School of Medicine, Miami, FL
Feb, 2009	"Strategies to reduce cardiac risk of noncardiac surgery: Update on the AHA/ACC Guidelines", 4th Annual Perioperative Medicine Summitt, Miami Beach, FL
Mar, 2009	"How do different forms of anesthesia play a role", Panel on Preoperative Cardiac Evaluation, American College of Cardiology Annual Meeting, Orlando, FL
Mar, 2009	"Choice of Anesthesia and Outcome", Panel on perioperative cardiovascular care for noncardiac surgery, American College of Cardiology Annual Meeting, Orlando, FL
Mar, 2009	"Improving perioperative care: Guidelines, P4P, and Quality Measures", Department of Anesthesiology, University of Michigan School of Medicine, Ann Arbor, MI
Mar, 2009	"Strategies to reduce cardiac risk of noncardiac surgery", Department of Anesthesiology, Cardiovascular Medicine Institute, University of Michigan School of Medicine, Ann Arbor, MI
Apr, 2009	"Perioperative cardiovascular evaluation before noncardiac surgery", Cardiology Update 2009, University of Pennsylvania School of Medicine, Absecon, NJ
Apr, 2009	"Evidence based medical management of the patient undergoing noncardiac surgery", Society of Cardiovascular Anesthesiologists Annual Meeting, San Antonio, TX
Apr, 2009	"Surgical Care Improvement Project: Target for the CT anesthesiologist", Society of Cardiovascular Anesthesiologists Annual Meeting, San Antonio, TX
May, 2009	"Strategies to reduce cardiac risk of noncardiac surgery" Stengart Lecture, University of California at Davis, Sacramento, CA
Jun, 2009	"Strategies to reduce cardiac risk of noncardiac surgery", Canadian Anesthesiologists' Society Annual Meeting, Vancouver, Canada
Jul, 2009	"Improving Perioperative outcomes: risk assessment, patient preferences and performance measures", Evidence Based Perioperative Outcomes Meeting, London, England
Jul, 2009	"Improving Perioperative outcomes: risk assessment, patient preferences and performance measures", Massachussets General Hospital, Boston, MA
Jul, 2009	"Strategies to reduce cardiac risk of noncardiac surgery: An update to the AHA/ACC Guidelines" Massachussetts General Hospital, Boston, MA
Aug, 2009	"Strategies to reduce cardiac risk of noncardiac surgery", University of Alabama Department of Anesthesiology, Birmingham, AL
Oct, 2009	Preoperative cardiac assessment for noncardiac surgery" American Society of Anesthesiologists Annual Meeting. New Orleans, LA
Oct, 2009	"Preoperative cardiac evaluation for noncardiac surgery" in Panel on Preparing the cardiac patient for noncardiac surgery. American

	College of Surgeons Annual Meeting, Chicago, IL
Oct, 2009	"Improving perioperative outcomes: my journey into Risk Assessment, Patient Preferences and Performance Measures" Foundation for Anesthesia Education and Research Honorary Research Lecture. American Society of Anesthesiologists Annual Meeting. New Orleans
Nov, 2009	"How to deal with sudden death in your department", Society of Academic Anesthesiology Assocations Annual Meeting, Boston, MA
Dec, 2009	"Anesthesiologist: Measure thyself", Rovenstine Honorary Lecture at the PGA, New York, NY
Apr, 2010	"New insights: the latest data on perioperative outcome and anesthesiology practice". Society of Cardiovascular Anesthesiologists Annual Meeting. New Orleans, LA
Apr, 2010	"Strategies to reduce cardiac risk for noncardiac surgery." Australia and New Zealand College of Anaesthetists Annaul Meeting. Christchurch, NZ
Apr, 2010	"Risks of outpatient surgery". Day Surgery Conference, Australian and New Zealand College of Anaesthetists, Christchurch, NZ
Apr, 2010	"The Institute of Medicine Evidence for limiting resident duty hours". Association of University Anesthesiologists Annual Meeting. Denver, CO
May, 2010	"Improving perioperative outcomes". Day Surgery Conference, Australian and New Zealand College of Anaesthetists, Christchurch, NZ
Jul, 2010	"Risks of Outpatient Surgery", Evidence Based Perioperative Outcomes Meeting, London, England
Sep, 2010	"Strategies to reduce cardiac risk for noncardiac surgery." Walters Visiting Professor, University of Wisconsin, Madison, WI
Sep, 2010	"Development of EB Guideline into Practice: AHA/ACC Guideline" International Congress of Cardiovascular and Vascular Anesthesia, Beijing, CN
Oct, 2010	"Preoperative cardiac evaluation for noncardiac surgery" American Society of Anesthesiologists Annual Meeting, San Diego, CA
Oct, 2010	"Evidence supporting performance measurement and outcome". IN Panel on Performance Anxiety. American Society of Anesthesiologists Annual Meeting, San Diego, CA
Nov, 2010	"Clinical research in anesthesiology" Beijing, Shanghai, Guongzhou, Chonquin, CN
Nov, 2010	"Preoperative cardiac evaluation" University of Florida, Gainseville, FL
Mar, 2011	"Preoperative Cardiac Risk Assessment: Implementing the Guidelines into Practice" Perioperative Medicine Summitt 2011, Miami, FL
Mar, 2011	Panel on "Faculty leaders: how we were prepared for the leadership challenges we face; the leadership skills our successors will need"

	Council of Academic Specialties Annual meeting, American Association of Medical Colleges, Providence, RI
Mar, 2011	"Optimizing perioperative outcomes: my journey into guidelines, patient preferences and measurement", Crawford Long Lecture, Emory University
Apr, 2011	"Evidence-based medicine: how it should inform research and care",International Anesthesia Research Forum, Xi'An, CH
Apr, 2011	"How to look at data", "Is my paper important", "What reviewer and editors are looking for", Workshop on how to write a clinical paper, Xi'an, CH
Apr, 2011	"Strategies to reduce cardiac risk of noncardiac surgery", Anesthesiology and Critical Care Forum, Xi'An, CH
May, 2011	"Optimizing Perioperative Outcomes: Risk Assessment, Patient Preferences and Performance Measures", Shields Lecture, University of Toronto, Toronto, CA
May, 2011	"Cardiac risk stratification for non cardiac surgery: an update", Simposio Mostra Anestesia Rianimazion E Terapia Intensiva, Milan, IT
May, 2011	"Cardiac risk stratification for non cardiac surgery: an update", Simposio Mostra Anestesia Rianimazion E Terapia Intensiva, Milan, IT
May, 2011	"Cardiac risk stratification for non cardiac surgery: an update", Simposio Mostra Anestesia Rianimazion E Terapia Intensiva, Milan, IT
May, 2011	"Perioperative medicine and perioperative outcomes: a personal overview ", Simposio Mostra Anestesia Rianimazion E Terapia Intensiva, Milan, IT
May, 2011	"Perioperative strokes and beta-blockade ", Simposio Mostra Anestesia Rianimazion E Terapia Intensiva, Milan, IT
Jul, 2011	"Biomarkers", Evidence Based Perioperative Medicine Annual Meeting, London, England
Jul, 2011	"Improving Perioperative Outcomes", Evidence Based Perioperative Medicine Annual Meeting, London, England
Oct, 2011	"Improving Perioperative Outcomes", University of California, Irvine, CA
Oct, 2011	"Preoperative cardiac evaluation for noncardiac surgery" American Society of Anesthesiologists Annual Meeting, Chicago, IL
Oct, 2011	"The future of perioperative quality measurement in the landscape of health reform" in Panel on Quality mesurement and reporting in anesthesiology and perioperative care: current controversies and future directions. American Society of Anesthesiologists Annual Meeting, Chicago
Mar, 2012	"Care in the era of Healthcare reform: our role in the value proposition" Eliasberg Lecture, Department of Anesthesiology, Mount Sinai School of Medicine, New York, NY
Mar, 2012	"Strategies to reduce cardiac risk of noncardiac surgery: an update"

	Perioperative Medicine Summit, Miami, FL
Apr, 2012	"Academia and HCR: What does it mean for all 3 missions?" in Panel on Practice Management: From Private to Academics: Advice from the Top in Healthcare Reform Climate. Society of Cardiovascular Anesthesiologists, Boston, MA
May, 2012	"A personal journey into improving outcome" Keynote lecture at Cardiac Disease and Anaesthesia Symposium, Royal College of Anaesthetists, London, England
May, 2012	"Strategies to reduce cardiac risk of noncardiac surgery" Kampine Honoary Lecture, Medical College of Wisconsin, Milwaukee, WI
May, 2012	"Care in the era of Healthcare reform: _our role in the value proposition", Medical College of Wisconsin, Milwaukee, WI
Jun, 2012	"Preoperative Cardiac Evaluation for Noncardiac Surgery" Brigham & Women's Hospital, Boston, MA
Jul, 2012	"Care in the era of Healthcare reform: _our role in the value proposition", Massachusetts General Hospital, Boston MA
Aug, 2012	"Care in the era of U.S. Healthcare reform: _what will drive anesthesia staffing?" in University of Pennsylvania-Chinese Society of Anesthesiologists Communication Forum, Chongqing, China
Sep, 2012	"Guidelines and performance measures: How do you apply the evidence?". UCSF The Changing Practice Of Anesthesia 2012. San Francisco, CA
Sep, 2012	"Value from anesthesia care: where do we influence the outcome/cost equation in medicine?: UCSF The Changing Practice Of Anesthesia 2012. San Francisco, CA
Oct, 2012	"How we improve quality" on FAER Panel on The Science of Quality Improvement: What Leads to Improvement. American Society of Anesthesiologists Annual Meeting. Washington, DC
Oct, 2012	"AHA/ACC Guideline Update for Preoperative Evaluation and Testing in Non-cardiac Surgery" on Panel on Cardiovascular Guidelines: Update for the Patient with Cardiac Disease. American Society of Anesthesiologists Annual Meeting. Washington, DC
Oct, 2012	"Preoperative Cardiac Evaluation for Noncardiac Surgery". American Society of Anesthesiologists Annual Meeting. Washington, DC
Oct, 2012	"Pro: Beta-blockers P4P" on Pro/Con for Does Preoperative Beta-blockade help and should be a P4P Measure. American Society of Anesthesiologists Annual Meeting. Washington, DC
Apr, 2013	"PRO: PERFORMANCE MEASUREMENT: DOES IT MATTER?", Association of University Anesthesiologists, Miami, FL
Apr, 2013	"Bundled care and cardiac surgery:_what does it mean?", Society of Cardiovascular Anesthesiologists, Miami, FL
May, 2013	"Preoperative cardiac evaluation-should we bother?", Keynote lecture, Irish Congress of Anaesthesia 2013, Dublin
May, 2013	"Perioperative beta-blockers and statins- what do we really know?",

	Irish Congress of Anaesthesia 2013, Dublin
Jul, 2013	"Learning valuable lessons from large datasets!", Evidence-Based Perioperative Medicine (EBPOM), London
Jul, 2013	"Preoperative cardiac risk evaluation-where do we stand now?", Evidence-Based Perioperative Medicine (EBPOM), London
Oct, 2013	"Aspirin" on Panel on Perioperative cardiovascular and anti platelet agents: which to take, which to stop? an update. American Society of Anesthesiologists, San Francisco, CA
Oct, 2013	"Perioperative cardiac arrests: what is the evidence". Journal Symposium: cardiac arrest and resuscitation. American Society of Anesthesiologists, San Francisco, CA
Oct, 2013	"Implementation science" on FAER Panel: clinical research in anesthesia. American Society of Anesthesiologists, San Francisco, CA
Oct, 2013	"The Economic Imperative for perioperative medicine" in Panel on Perioperative medicine as the future of anesthesiology: why, who and how. American Society of Anesthesiologists, San Francisco, CA
Oct, 2013	"One chair's perspective: using measures for departmental reporting to CMS and other quality entities: leveraging the process to facilitate resident's and faculty's understanding and involvement in quality" in Panel on Performance measures, academic anesthesiology departments and MOCA: Is there a way to synergize the impact? American Society of Anesthesiologists, San Francisco, CA
Oct, 2013	"PRO: Raising both the stakes and the bar: anesthesiologists and surgeons sharing joint accountability for patient outcomes", American Society of Anesthesiologists, San Francisco, CA
Nov, 2013	"Preparing Felllows to be Faculty", Association of Anesthesiology Specialty Program Directors, Philadelphia, PA
Nov, 2013	"Importance of Health Policy Research to Academic Departments", Society of Academic Anesthesiology Associations, Philadelphia, PA
Feb, 2014	"Value in anesthesia: _when do we make a difference?", Asian Australasian Congress of Anesthesiologists, Aukland, NZ
Feb, 2014	"Evaluation of the cardiac patient for non-cardiac surgery", Asian Australasian Congress of Anesthesiologists, Aukland, NZ
Feb, 2014	"Beta-blockers and statin", Asian Australasian Congress of Anesthesiologists, Aukland, NZ
Apr, 2014	"The new guidelines on perioperative management of patients with heart disease undergoing non cardiac surgery", Oxford University, Oxford, England
Apr, 2014	"The new guidelines on perioperative management of patients with heart disease undergoing non cardiac surgery", Royal College of Anaesthetists, London, England
Jul, 2014	"Cardiac risk for non cardiac surgery", University of New Mexico, Albuquerque, NM
Oct, 2014	"Preoperative Cardiac Evaluation for Noncardiac Surgery",

	American Society of Anesthesiologists, New Orleans, LA
Oct, 2014	"Why Are Process Measures Fading into the Night?", American Society of Anesthesiologists Annual Meeting, New Orleans, LA
Oct, 2014	"PRO: Performance Metrics are an Efficient Way to Promote Enhanced Recovery", ERAS meeting at the ASA Annual Meeting, New Orleans, LA
Jan, 2015	"Improving perioperative outcomes: _Do we just need to apply the evidence?", University of California at Los Angeles, Los Angeles, CA
Mar, 2015	"Improving Medical Care: The Importance of Measuring Outcomes", Penn Wharton China Center Opening Symposium, Beijing, China
Mar, 2015	"The New AHA Guidelines", International Anesthesia Research Society, Honolulu, Hawaii
Mar, 2015	"The Economic Imperative for the Perioperative Surgical Home", International Anesthesia Research Society, Honolulu, Hawaii
Mar, 2015	"Performance_Measurement and new models of determining quality" University of Utah Biomedical Informatics, Salt Lake City, UT
Mar, 2015	"Preoperative cardiac evaluation for non cardiac surgery", Perioperative Medicine Summit 2015, Phoenix, AZ
May, 2015	"Preoperative cardiac evaluation for non cardiac surgery", World Congress of Enhanced Recovery After Surgery and Perioperative Medicine, Washington D.C.
Jul, 2015	"Measuring outcomes in perioperative care: new approaches and paradigms", EBPOM, London
Jul, 2015	"The impact of the ACC/AHA guidelines on reducing perioperative harm", EBPOM, London
Sep, 2015	"Measuring Perioperative Outcomes" Brigham and Women's Hospital, Boston, MA
Sep, 2015	"Strategies to reduce Cardiac Risk of Noncardiac Surgery" Brigham and Women's Hospital, Boston, MA
Sep, 2015	"The future of academic anesthesiology: leading change", Chinese Society of Anesthesiology Annual Meeting, Xi'An, China
Oct, 2015	"Strategies to Reduce Cardiac Risk for Noncardiac Surgery", Japanese Society of Cardiovascular Anesthesia, Fukuoka, Japan
Jan, 2016	"Performance measurement and new ways to measure performance", Penn State Hershey Anesthesiology and Perioperative Medicine, Hershey, PA
Jan, 2016	"Strategies to reduce cardiac risk of non cardiac surgery", Penn State Hershey Anesthesiology and Perioperative Medicine, Hershey, PA
Apr, 2016	"Impact of respiratory compromise in US Healthcare", Becker's Healthcare, Chicago, IL
Apr, 2016	"Does the use of Regional Anesthesia Impact Outcome in Patients with Cardiac Disease Undergoing Non-cardiac Surgery?" Indian Society of Anesthesiologists Delhi Chapter, Delhi, India

Apr, 2016	"Root cause analysis in anaesthesia: Why?" Indian Society of Anesthesiologists Delphi Chapter, Delphi, India
Apr, 2016	"Assessing the patient with CAD for non-cardiac surgery: what's new?", Indian Society of Anesthesiologists Delhi Chapter, Delphi, India
Apr, 2016	"Measuring Outcomes in Perioperative Care: New Approaches and Paradigms", American Society of Enhanced Recovery, Washington, DC
May, 2016	"Health Policy Research: University of Pennsylvania Health System", Association of University Anesthesiologists, San Francisco, CA
May, 2016	"Strategies to reduce cardiac risk of non cardiac surgery", Yale University Department of Anesthesiology, New Haven, CT
May, 2016	"Measuring Outcomes in the Era of Healthcare Reform", Yale University Department of Anesthesiology, New Haven, CT
May, 2016	"Preoperative Exercise Testing and Prehabilitation", International Anesthesia Research Society, San Francisco, CA
Jul, 2016	"Choosing wisely", Evidence based Perioperative Medicine Annual Meeting, London, England
Jul, 2016	"General Anaesthesia - A well tried solution", Evidence based Perioperative Medicine Annual Meeting, London, England
Aug, 2016	"Cost and quality containment", World Congress of Anaesthesiologists, Hong Kong
Aug, 2016	"Achieving value of perioperative care in the elderly", World Congress of Anaesthesiologists, Hong Kong
Aug, 2016	"Anesthesiologists in the value equation: beyond preventing anesthesia related complications", Chinese Society of Anesthesiologists Annual Meeting, Guangzhou, China
Aug, 2016	"Strategies to reduce cardiac risk of non cardiac surgery", Chinese Society of Anesthesiologists Annual Meeting, Guangzhou, China
Aug, 2016	"Improving health and transforming care through measurement: science and policy", Massachusetts General Hospital Department of Anesthesia, Boston, MA
Oct, 2016	"The Brain Health Initiative: What does the patient want to know and what do we want them to know", American Society of Anesthesiologists Annual Meeting, Chicago, IL
Oct, 2016	"Is the Perioperative Surgical Home a viable option for anesthesiology?: Con", American Society of Anesthesiologists Annual Meeting, Chicago IL
Oct, 2016	"Risk stratification tools from the preoperative to the postoperative period", American Society of Anesthesiologists Annual Meeting, Chicago, IL
Nov, 2016	"Panel on Why health is no one's business: economic incentive barriers to improving health" Global Action Summit, Nashville, TN
Mar, 2017	"The place for PhDs in the Medical Schools of Tomorrow: Clinical Department Perspective" Council for Faculty and Academic

	Societies, AAMC, Orlando, FL
Mar, 2017	"Aspirin should be continued preoperatively" in Debate on Perioperative Aspirin Therapy, Perioperative Medicine Summit, Fort Lauderdale, FL
Mar, 2017	"Evaluation Prior to Noncardiac Surgery: ACC/AHA Update", Perioperative Medicine Summit, Fort Lauderdale, FL
Sep, 2017	"Perioperative Brain Health Initiative: Anesthesiologist leadership in improving population health". Chinese Society of Anesthesiologists, Zhengzhou, CN
Sep, 2017	"Leading An Academic Departmentï¼šThe US Perspective On Demonstrating Value". Chinese Society of Anesthesiologists. Zhengzhou, China
Sep, 2017	"Strategies to reduce cardiac risk for non cardiac surgery". Polish Society of Anesthesiology and Intensive Care. Bydgoszcz, Poland
Sep, 2017	"Guidelines and Performance Measures: How do you apply the evidence?" Polish Society of Anesthesiology and Intensive Care. Bydgoszcz, Poland
Oct, 2017	"Strategies to reduce cardiac risk for non cardiac surgery", Boston, MA
Oct, 2017	"Quality Anesthesia: Medicine Measures, Patients Decide", Rovenstine Lecture, American Society of Anesthesiologists, Boston, MA
Oct, 2017	"Brain Health- A Global Safety Challenge", International Forum on Perioperative Safety and Quality, Boston, MA
Oct, 2017	"Quality Anesthesia: Medicine measures, patients decide", University of Kentucky, Lexington, KY
Nov, 2017	"The American perspective: The perioperative surgical home", Perioperative Medicine Special Interest Group of the Australian Society of Anesthesiologists, 6th Annual Australasian Symposium of Perioperative Medicine, Manly, Australia
Nov, 2017	"Value based care: A system overhaul", Perioperative Medicine Special Interest Group of the Australian Society of Anesthesiologists, 6th Annual Australasian Symposium of Perioperative Medicine, Manly, Australia
Nov, 2017	"Research Directions in Perioperative Medicine", Perioperative Medicine Special Interest Group of the Australian Society of Anesthesiologists, 6th Annual Australasian Symposium of Perioperative Medicine, Manly, Australia
Nov, 2017	"Quality Anesthesia: Medicine Measures, Patients Decide", Henry Ford Hospital, Detroit, MI
Dec, 2017	"The Cardiac Patient Presenting for Non-Cardiac Surgery Sub-Topic: Is there Any Value to Cardiology Consults During the Perioperative Period?", Postgraduate Assembly in Anesthesiology, New York, NY
Feb, 2018	"Strategies to reduce cardia risk of noncardiac surgery", University of Pittsburgh, Pittsburgh, PA

Mar, 2018	"Auditing, Reporting to the C-Suite", American Society of Enhanced Recovery, Ft. Lauderdale, FL
Mar, 2018	"Brain Health Initiative", Perioperative Medicine Summit, Ft. Lauderdale, FL
Mar, 2018	"CV Risk Assessment", Perioperative Medicine Summit, Ft. Lauderdale, FL
Mar, 2018	"Postoperative Care has to be Delivered by the Surgeon", American Society of Enhanced Recovery, Ft. Lauderdale, FL
Apr, 2018	"Payment reform, MACRA, Physician-Focused Payment Model update", EBPOM-USA Masters Course. A Perioperative Care Practicum; Atlanta, GA
Jul, 2018	"Perioperative brain health initiative: A population health safety initiative", Evidence Based Perioperative Medicine Symposium, London, England
Oct, 2018	"Perioperative Brain Health", Uniformed Services Society of Anesthesiologists (USSA)/Association of Veterans' Affairs Anesthesiologists (AVAA) Academic Meeting, San Francisco, CA
Oct, 2018	"Preparation of the elderly patient undergoing surgery: when do we need a preoperative consultation as opposed to skipping a clinic visit?", ICAA-CSA symposium, San Francisco, CA
Nov, 2018	"Quality of Perioperative care: using measurement to improve outcome", Asian Australasian Congress of Anaesthesiologists/Chinese Society of Anesthesiology Annual Meeting, Beijing, CN
Apr, 2019	"Patient decision making and engagement: How can we measure and improve it?", American Society of Enhanced Recovery Annual Meeting, Fort Lauderdale, FL
Apr, 2019	"Auditing, Reporting to the C-Suite", American Society of Enhanced Recovery Annual Meeting, Fort Lauderdale, FL
May, 2019	"Findings from the Perioperative Brain Health Initiative and Their Impact on Day-to-Day Practice", Harvard Anesthesiology Update 2019, Boston, MA
May, 2019	"Measuring Patient Outcomes in the Perioperative Period", Harvard Anesthesiology Update 2019, Boston, MA
Jul, 2019	"Brain Health (Peri-Operative Quality Initiative: POQI 6) - what can we do tomorrow?", Evidence-based Perioperative Medicine, London
Jul, 2019	"Decision making for elective and end of life care", Trainees with an Interest in Peri-Operative Medicine Annual Meeting, London
Jul, 2019	"Communication and Decision-Making in Perioperative Care", Cambridge University THIS Institute, Cambridge, England
Sep, 2020	"From Data to Policy: _My 30 year Journey", Eckenhoff Lecture, Department of Anesthesiology and Critical Care, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA
May, 2021	"The future of the specialty: how the pandemic and policy changes should influence", International Anesthesia Research Society. T.H. Seldon Lecture

May, 2021 "Preoperative cardiac evaluation for non cardiac surgery", Michael E. DeBakey Veterans Medical Center Grand Rounds, Houston, TX

Organizing Roles in Scientific Meetings:

1991 Meeting of Investigators of Heart Rate Variability
Unknown

1992 Meeting of Investigators of Heart Rate Variability
Unknown

1993 Meeting of Investigators of Heart Rate Variability
Unknown

1994 Meeting of Investigators of Heart Rate Variability
Unknown

Oct, 2012 Organizer, Investigators in Perioperative Health Services Research
Washington, DC

Jan, 2018 Planning Committee Member, Building the Evidence Base for Improving Health Care
Contributions, opportunities, and priorities, National Academy of Sciences
Washington, DC

Grants:

Current:

Assessing Hospital Quality of Care for Patients with Multimorbidity, NIH, 11/2019-6/2022 (Jeffrey Silber, PI), $79,433/annual direct costs (Role in grant: Co-I)

Outcomes in Patients with Multimorbidity at Ambulatory Surgical Centers, NIH, 7/2019-6/2022 (Jeffrey Silber, PI: Lee Fleisher, Co-Investigator), $43,300/annual direct costs (Role in grant: Co-I)

Neurocognitive Disorder after Appendectomy in the Elderly: A Natural Experiment , NIA, 4/2017-3/2022 (Jeffrey Silber, PI), $500,000/annual direct costs (Role in grant: Co-I)

A Practical Intervention To Improve Patient-Centered Outcomes After Hip Fractures Among Older Adults (Regain Trial), Patient Centered Outcomes Research Institute (Pcori), 10/2015-7/2022 (Mark D. Neuman, PI), $57,660/annual direct costs (Role in grant: Co-I)

Training In Critical Care Health Policy Research, National Heart, Lung, And Blood Institute/Nih/Dhhs, 5-T32-HL-098054-10, 5/2015-4/2020 (Scott Halpern, PI), $537,348/annual direct costs (Role in grant: Co-PI)

Past:

A matching Study of Outcomes and Costs at Teaching and Non-teaching Hospitals, Association of American Medical Colleges, 1/2016-12/2018 (Jeffrey Silber, M.D., Ph.D., PI: Lee A. Fleisher, M.D., Co-Investigator), $100,000/annual direct costs, 2% effort

(Role in grant: co-P.I.)

Understanding Multimorbidity through Multivariate Template Matching, NIA, 9/2015-9/2016 (Jeffrey Silber, M.D., Ph.D., PI), $238,095/annual direct costs, 1.25% effort (Role in grant: Co-I)

Support For Pharmacoepidemiology Training, Pfizer Inc., N/A, 1/2014-12/2015 (SEAN HENNESSY, PI), $39,352/annual direct costs (Role in grant: Co-PI)

Role Of Hif1a In Inflammation, Tissue Repair, And Cancer Of The Pancreas, American Association For Cancer Research, N/A, 7/2013-6/2016 (M. Celeste Simon, PI), $122,727/annual direct costs (Role in grant: Co-PI)

Mixed-Methods Assessment Of Faer'S Investments In Career Development, Foundation For Anesthesia Education And Research, IMPACT ANALYSIS, 7/2013-12/2014 (LEE A. FLEISHER, PI), $57,402/annual direct costs (Role in grant: PI)

Understanding Racial Disparities in Surgical Outcomes , NIH, 9/2012-8/2015 (Jeff Silber, PI), $387,785/annual direct costs, 5% effort (Role in grant: Co-investigator)

Chronic Disease Clinical Epidemiology Training In Guatemala And Peru, Fogarty International Center/Nih/Dhhs, 5-D43-TW-008317-05, 7/2010-6/2016 (Charles C. Branas, PI), $199,884/annual direct costs (Role in grant: Co-PI)

Improving process measurement, AHRQ, 1 R01 HS018338, 7/2010-6/2013 (Jeffrey H. Silber, PI), $375,000/annual direct costs, 2.5% effort (Role in grant: Co-I)

Training In Critical Care Health Policy Research, National Heart, Lung, And Blood Institute/Nih/Dhhs, 5-T32-HL-098054-05, 5/2010-4/2015 (DAVID A ASCH, PI), $483,132/annual direct costs, 2% effort (Role in grant: Co-PI)

Inspiratory Work Of Breathing During Proportional Assist Ventilation Compared With Assist Control Ventilation (Acv) In Acute Lung Injury (Ali), Tyco Healthcare, #2, 12/2007-8/2009 (Maurizio F. Cereda, PI), $8,829/annual direct costs (Role in grant: Co-PI)

A Prospective, Randomized, Double-Blinded Study Of The Effect On Improved Recovery Using The Sedline For The Titration Of Sevoflurane In Elderly Patients Undergoing Non-Cardiac Surgery After Beta-Adrenergic Blockade, Hospira, CP-09-003, 11/2007-9/2008 (JONATHAN W TANNER, PI), $31,683/annual direct costs (Role in grant: Co-PI)

Plan for Extracting Intraoperative Anesthesia Data to the ACS NSQIP Database, NLM, 8/2007-7/2009 (Clifford Ko, PI), $149,820/annual direct costs (Role in grant: Co-Investigator)

A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study Of Intravenous Methyinaltrexone (Moa-728) For The Treatment Of Post Operative Ileus, Wyeth-Ayerst Research, 3200L2-300-WWW, 3/2007-3/2009 (ASHISH C. SINHA, PI), $20,147/annual direct costs (Role in grant: Co-PI)

Use Of The Sedline Monitor In Gastrointestinal Endoscopy Cases, Hospira, SEDLINE, 9/2006-9/2007 (JONATHAN W TANNER, PI), $37,736/annual direct costs (Role in grant: Co-PI)

Obesity and Surgical Outcomes, NIDDK, 1 R01 DK073671-01A1, 7/2006-6/2011 (Jeffrey Silber, M.D., Ph.D., PI), $511,407/annual direct costs, 5% effort (Role in grant: Investigator)

Cltr: Aprepitant For The Prevention Of Postoperative Nausea And Vomiting, Merck & Co., Inc., 6/2004-3/2005 (LEE A. FLEISHER, PI), $2,869/annual direct costs (Role in grant: PI)

Evaluating patient information prescriptions in different service environments, National Library of Medicine, 10/2003-9/2006 (Nancy Roderer, M.D., PI), $150,000/annual direct costs, 5% effort (Role in grant: Co-Investigator, Single-center)

FOCUS, NIH, 5U01HL073958-02, 9/2003-8/2008 (Jeffrey Carson, PI), $1,000,000/annual direct costs (Role in grant: Consultant/Steering Committee, A randomized trial of two different transfusion triggers in patients with hip fractures to determine return of functional status.)

Phase III, multi-center, placebo-controlled, randomized, double-blind study to evaluate the efficacy of zoniporide administered perioperatively to subjects undergoing vascular surgery, Pfizer, 1/2002-6/2003 (Lee A. Fleisher, PI), $150,000/annual direct costs, 5% effort (Role in grant: PI)

Relationship between discharge hemoglobin level and patient-oriented outcomes during recovery from surgery, Advanced Transfusion Practices and Blood Research, 7/2001-6/2002 (Lee A. Fleisher, PI), $70,429/annual direct costs, 10% effort (Role in grant: PI)

Evidence review of management of atrial fibrillation in the post-coronary artery bypass patient, American College of Chest Physicians, 6/2001-11/2001 (Lee A. Fleisher, PI), $99,863/annual direct costs, 10% effort (Role in grant: PI)

Cost-effectiveness of ambulatory blood pressure monitoring, Agency for Healthcare Quality and Research, 9/2000-9/2001 (Larry Appel, PI), $250,000/annual direct costs, 2.5% effort (Role in grant: Co-Investigator)

Impact of location of care and patient factors on the rate of complication and readmissions after outpatient surgery: a claims analysis, Society of Ambulatory Anesthesia (SAMBA), 7/2000-6/2002 (Lee A. Fleisher, PI), $100,000/annual direct costs,

5% effort (Role in grant: PI)

A cost-findings study of the use of the hemosonic noninvasive cardiac output monitor compared to routine care in whipple surgery, Arrow International, 6/2000-12/2001 (Lee A. Fleisher, M.D., PI), $120,000/annual direct costs, 5% effort (Role in grant: PI)

A randomized study of esmolol versus nitroglycerin in high risk lower extremity procedures, Baxter Pharmaceutical, 6/2000-5/2001 (Lee A. Fleisher, M.D., PI), $100,000/annual direct costs, 5% effort (Role in grant: PI)

An open label, pharmacokinetic study to evaluate the pharmacokinetics, pharmacodynamics, toleration and safety of CP-597,396 administered for 24 hours in subjects undergoing coronary artery bypass (CABG) surgery, Pfizer, 4/2000-12/2001 (Lee A. Fleisher, PI), $200,000/annual direct costs, 5% effort (Role in grant: PI)

Phase II, multi-center, placebo-controlled, randomized, double-blind, dosing regimen optimization and dose-escalation study to evaluate the safety, toleration and clinical pharmacology of CP-597,396 administered in subjects undergoing vascular surgery, Pfizer, 4/2000-12/2001 (Lee A. Fleisher, PI), $300,000/annual direct costs, 5% effort (Role in grant: PI)

Phase III trigger study: A3181007 a double blind, placebo-controlled, parallel group study of the effects of Zoniporide on perioperative cardiac events in high risk subjects undergoing noncardiac vascular surgery, Pfizer, 4/2000-12/2000 (Lee A. Fleisher, PI), $300,000/annual direct costs, 5% effort (Role in grant: PI)

Cost effectiveness of preoperative evaluation before vascular surgery (CEPEVS), Maryland American Heart Association Grant-in-Aid, 1/2000-12/2001 (Lee A. Fleisher, PI), $60,000/annual direct costs, 10% effort (Role in grant: PI)

Perioperative anemia recovery from surgery trial (PARST), International Anesthesia Research Society, 1/2000-12/2001 (Lee A. Fleisher, M.D., PI), $75,000/annual direct costs, 5% effort (Role in grant: PI)

Anesthesia for cataract surgery, Agency for Health Care Policy & Research/Evidence Based Center, 1/2000-12/2000 (Lee A. Fleisher, PI), $249,000/annual direct costs, 10% effort (Role in grant: Co-PI)

Bayesian communication of clinical trials, National Library of Medicine, 10/1999-9/2002 (Harold Lehmann, PI), $249,211/annual direct costs, 1% effort (Role in grant: Evaluator)

Cost-effectiveness of perioperative ROMI protocols, Dade Pharmaceuticals, 1/1999-12/1999 (Lee A. Fleisher, PI), $108,000/annual direct costs, 5% effort (Role in grant: PI)

Pharmacologic modulation of cocaine effects, NIH, 1/1999-12/1999 (George Bigelow, PI), $331,935/annual direct costs, 5% effort (Role in grant: Co-Investigator)

Analysis of the medicare database to assess morbidity and mortality after outpatient anesthesia, Anesthesia Patient Safety Foundation, 1/1998-12/1998 (Lee A. Fleisher, PI), $42,800/annual direct costs, 10% effort (Role in grant: PI)

Remifentanil in microsuspension laryngoscopy, Glaxo Pharmaceuticals, 1/1997-12/1998 (Lee A. Fleisher, PI), $24,902/annual direct costs, 5% effort (Role in grant: PI)

Analysis of short- and long-term costs of cardiovascular disease in patients undergoing major vascular surgery: Analysis of medicare claims data, DuPont Pharmaceuticals, 1/1995-12/1996 (Lee A. Fleisher, PI), $20,000/annual direct costs, 5% effort (Role in grant: PI)

The effect of enalaprilat on heart rate variability, Merck Pharmaceuticals, 1/1995-12/1996 (Lee A. Fleisher, PI), $16,500/annual direct costs, 5% effort (Role in grant: PI)

ACR: A mechanism for disseminating information and improving patient satisfaction, Society of Ambulatory Anesthesia, 1/1994-12/1995 (Lee A. Fleisher, PI), $10,000/annual direct costs, 1% effort (Role in grant: PI)

Outpatient laparoscopic surgery trial, Glaxo Pharmaceuticals, 1/1994-12/1995 (Lee A. Fleisher, PI), $35,000/annual direct costs, 5% effort (Role in grant: PI)

Utilization of information from preoperative cardiac evaluation, Dupont Pharma, CG#94019, 1/1994-12/1995 (Lee A. Fleisher, PI), $15,000/annual direct costs, 5% effort (Role in grant: PI)

Anesthesia as a stress test, Caliber Medical, 1/1993-12/1994 (Lee A. Fleisher, PI), $25,000/annual direct costs, 1% effort (Role in grant: PI)

CAD mechanisms in high risk families: racial differences, NIH, NIH-92-HL-1-H, 1/1992-12/1996 (Lewis Becker, PI), $273,815/annual direct costs, 5% effort (Role in grant: Co-Investigator)

Methods of anesthesia and analgesia for aortic surgery, NIH, GM38177-05, 1/1992-12/1996 (Richard Traystman, PI), $248,355/annual direct costs, 5% effort (Role in grant: Co-Investigator)

Amlodipine and heart rate variability, Pfizer Pharmaceutical, 1/1992-12/1993 (Lee A. Fleisher, PI), $35,000/annual direct costs, 5% effort (Role in grant: PI)

Perioperative body temperature myocardial ischemia trial, Mallinckrodt Medical, 1/1992-12/1993 (Steve Frank, PI), $108,863/annual direct costs, 5% effort (Role in grant: Co-Investigator)

Power spectral analysis and reflex sympathetic activation in high risk patients undergoing

regional anesthesia, Society of Cardiovascular Anesthesiologists Starter Grant, 1/1991-12/1991 (Lee A. Fleisher, PI), $10,000/annual direct costs, 20% effort (Role in grant: PI)

Power spectral analysis and reflex sympathetic activation in high risk patients undergoing regional anesthesia, Foundation of Anesthesia Education and Research Young Investigator Award, 1/1991-12/1991 (Lee A. Fleisher, PI), $20,000/annual direct costs, 20% effort (Role in grant: PI)

Bibliography:

Research Publications, peer reviewed (print or other media):

1. Fleisher LA, Rosenbaum SH, Nelson AH, Barash PG: The predictive value of preoperative silent ischemia for postoperative ischemic cardiac events in vascular and nonvascular surgical patients. Am Heart J 122: 980-986, 1991.

2. Fleisher, L. A., Rosenbaum, S. H., Nelson, A. H., Barash, P. G.: The predictive value of preoperative silent ischemia for postoperative ischemic cardiac events in vascular and nonvascular surgery patients. Am Heart J 122(4 Pt 1): 980-6, 1991.

3. Fleisher LA, Nelson AH, Rosenbaum SH: The failure of negative dipyridamole thallium scans to predict perioperative myocardial ischaemia and infarction. Can J Anaesth 39: 179-183, 1992.

4. Mathew JP, Fleisher LA, Rinehouse JA, Sevarino FB, Sinatra RS, Nelson AH, Prokop EK, Rosenbaum SH: ST-segment depression during labor and delivery. Anesthesiology 77: 179-183, 1992.

5. Fleisher LA, Beattie C: Current practice in preoperative evaluation of patients undergoing major vascular surgery: a survey of cardiovascular anesthesiologists. J Cardiothor Vasc Anesth 7: 650-654, 1993.

6. Fleisher LA, Pincus SM, Rosenbaum SH: Approximate entropy of heart rate as a correlate of postoperative ventricular dysfunction. Anesthesiology 78: 683-692, 1993.

7. Fleisher LA, Rosenbaum SH, Nelson AH, Rosenfeld LE: Gender independence of ambulatory ECG monitoring in predicting perioperative cardiac risk. Am J Cardiol 71: 241-242, 1993.

8. Nelson AH, Fleisher LA, Rosenbaum SH: The relationship between postoperative anemia and cardiac morbidity in the high risk vascular patients in the ICU. Crit Care Med 21: 860-866, 1993.

9. Deutschman C, Harris A, Fleisher LA: Changes in heart rate variability under propofol anesthesia: a possible explanation for propofol induced bradycardia. Anesth Analg 79: 373-377, 1994.

10. Fleisher LA, Frank SM, Shir Y, Estafanous M, Kelly S, Raja SN: Cardiac sympathovagal balance and peripheral sympathetic vasoconstriction: epidural vs. general anesthesia. Anesth Analg 79: 165-171, 1994.

11. Fleisher LA, Skolnick ED, Holroyd K, Lehmann H: Coronary artery revascularization before abdominal aortic aneurysm surgery: A decision analytic approach. Anesth Analg 79: 661-669, 1994.

12. Frank SM, Shir Y, Raja SN, Fleisher LA, Beattie C: Core hypothermia and skin surface temperature gradients: epidural vs. general anesthesia and the effects of age. Anesthesiology 80: 502-508, 1994.

13. Fleisher LA, Nelson AH, Rosenbaum SH: Postoperative myocardial ischemia: etiology of cardiac morbidity or manifestation of underlying disease? J Clin Anesth 7: 97-102, 1995.

14. Fleisher LA, Rosenbaum SH, Nelson AH, Jain D, Wackers FThJ, Zaret BL: Preoperative dipyridamole thallium imaging and ambulatory electrocardiographic monitoring as a predictor of perioperative cardiac events and long term outcome. Anesthesiology 83: 906-917, 1995.

15. Frank SM, Fleisher LA, Gorman, RB, Higgins MS, Breslow MJ, Olson KF, Sitzmann JV, Beattie C: Multivariate determinants of early postoperative oxygen consumption in elderly patients: effects of shivering, body temperature, and gender. Anesthesiology 83: 241-249, 1995.

16. Frank SM, Higgins MS, Breslow MJ, Fleisher LA, Gorman RB, Sitzmann JV, Raff H, Beattie C: The catecholamine, cortisol, and hemodynamic responses to mild perioperative hypothermia: a randomized clinical trial. Anesthesiology 82: 83-93, 1995.

17. Turley SM, Mark LJ, Fisher QA, Schauble JF, Hoehner P, Fleisher L, Beattie C: The Anesthesiology Consultant Report (ACR): a document for effective dissemination of critical information. J AHIMA 66: 71-76, 1995.

18. Fleisher LA, Frank SM, Chang C, Matsukawa T, Vannier CA, Sessler DI: Thermoregulation and changes in heart rate variability. Clin. Sci 90: 97-103, 1996.

19. Godin PJ, Fleisher LA, Eidsath A, Vandivier W, Preas H, Banks SM, Buchman TG, Suffredini AF: Experimental human endotoxemia increases cardiac regularity. Crit Care Med 24: 1117-1124, 1996.

20. L'Italien GL, Paul SD, Hendel RC, Leppo JA, Cohen MC, Fleisher LA, Brown KA, Zarich SW, Cambria RP, Cutler BS, Eagle KA: Development and validation of a

bayesian model for perioperative cardiac risk assessment in vascular surgery patient. J Am Coll Cardiol Page: 779-786, 1996.

21. Fleisher LA, DiPietro JA, Johnson TRB, Pincus S: Complementary and non-coincident increases in heart rate variability and irregularity during fetal development. Clin. Sci 92: 345-349, 1997.

22. Fleisher LA, Langston M, Schulman SP: Perioperative ST segment depression is rare and may not indicate myocardial ischemia in moderate-risk patients undergoing noncardiac surgery. J Cardiothor Vasc Anesth 11: 155-159, 1997.

23. Frank SM, Fleisher LA, Breslow MJ, Higgins MS, Kelly S, Beattie C: Perioperative maintenance of normothermia reduces the incidence of morbid cardiac events. JAMA 277: 1127-1134, 1997.

24. Frank SM, Higgins MS, Fleisher LA, Breslow MJ, Sitzmann J: The adrenergic, respiratory, and cardiovascular effects of mild core hypothermia in humans. Am J Physiol-Reg 272: R557-R562, 1997.

25. Kral BG, Becker LC, Blumenthal RS, Aversano T, Fleisher LA, Yook RM, Becker DM: Exaggerated cardiovascular reactivity to mental stress is associated with exercise-induced myocardial ischemia in an apparently healthy population at risk for premature coronary disease. Circulation 96: 4246-4253, 1997.

26. Yataco AR, Fleisher LA, Katzel LI: Heart rate variability and cardiovascular fitness in senior athletes. Am J Cardiol 80: 1389-1391, 1997.

27. Fleisher LA, Metzger SE, Lam J, Harris A: Perioperative cost-finding analysis of routine use of intraoperative forced-air warming during general anesthesia. Anesthesiology 88: 1357-1364, 1998.

28. Lapuerta P, L'Italien GJ, Paul S, Hendel RC, Leppo JA, Fleisher LA , Cohen MC, Eagle KA, Giugliano RP: Neural network assessment of perioperative cardiac risk in vascular surgery patients. Med Decis Making 18: 70-75, 1998.

29. Fleisher LA , Mark L, Lam J, Pearlman A, Fisher Q, Snyder D, Parker S: Disseminating information using an Anesthesiology Consultant Report: impact on patient satisfaction. J Clin Anesth 11(5): 380-385, Aug 1999.

30. Carter HB, Landis PK, Metter EJ, Fleisher LA, Pearson JD: Prostate specific antigen (PSA) testing of older men. J Nat Cancer Inst 91(20): 1733-1737, 1999.

31. Fleisher LA, Eagle KA, Shaffer T, Anderson GF: Perioperative- and long-term mortality rates after major vascular surgery: the relationship to perioperative testing in the Medicare population. Anesth Analg 89: 849-855, 1999.

32. Fleisher LA, Yee K, Lillemoe KD, Talamini MA, Yeo CJ, Heath R, Bass E, Snyder D,Parker S: Is outpatient laparoscopic cholecystectomy safe and cost-effective?: a model to study transition of care. Anesthesiology 90: 1746-1755, 1999.

33. Lehmann HP, Fleisher LA, Lam J, Frink BA, Bass EB: Patient preferences for early discharge following laparoscopic cholecystectomy. Anesth Analg 88: 1280-1285, 1999.

34. Nelson JB, Nguyen SH, Opgenorth TJ, Fleisher LA , Frank SM: Perioperative plasma endothelin-1 and big endothelin-1 concentrations in patients at risk for morbid cardiac events. Anesth Analg 88: 898-903, 1999.

35. Talamini MA, Coleman J, Sauter P, Stanfield C, Fleisher LA: Outpatient laparoscopic cholecystectomy: patient & nursing perspective. Surg Laparosc Endosc Percutan Tech Page: 333-337, 1999.

36. Fleisher LA, Fleckenstein JF, Frank SM, Thuluvath PJ: Heart rate variability as a predictor of autonomic dysfunction in patients awaiting liver transplantation. Dig Dis Sci 45: 340-344, 2000.

37. Goldschlag B, Afzal N, Carter HB, Fleisher LA: Is pre-donation of autologous bloodrational for radical retropubic prostactectomy? J Urology 164: 1968-1972, 2000.

38. Hogue SL, Reese PR, Colopy M, Fleisher LA, Tuman KJ, Twersky RS, Warner DS, Jamerson B: Assessing a tool of measure patient functional ability after outpatient surgery. Anesth Analg 91: 97-106, 2000.

39. Joshi GP, Jameson B, Roizen MF, Fleisher LA, Twersky RS, Warner DS, Colopy M: Is there a learning curve associated with the use of remifentanil? Anesth Analg 91: 1049-1055, 2000.

40. Katz J, Feldman MA, Bass EB, Lubomski LH, Tielsch JM, Petty BG, Fleisher LA, Schein OD, and the Study of Medical Testing for Cataract Surgery Team: Injectable versus topical anesthesia for cataract surgery: patient perceptions of pain and side effects. Ophthalmology 107: 2054-2060, 2000.

41. Mackey JJ, Parker SD, Nass CM, Snyder DS, Curreri S, Kazim D, Zuckerman RL, Fleisher LA: Remifentanil provides superior hemodynamics compared to a fentanyl based anesthetic in high-risk outpatient surgery. J Clin Anesth 12: 427-432, 2000.

42. Mantha S, Roizen MF, Fleisher LA, Thisted R, Foss J: Comparing methods of measurement: is the statistical reporting appropriate? Anesth Analg 90: 593-602, 2000.

43. Abreu ME, Bigelow GE, Fleisher LA, Walsh SL: Effect of intravenous injection speed on responses to cocaine and hydromorphone in humans. Psychopharmacology 154: 76-84, 2001.

44. Fleisher LA, Hogue S, Colopy M, Twersky RS, Warner DS, Jamerson BD, Tuman KJ, Roizen MA: Does functional ability in the post-operative period differ between remifentanil and fentanyl-based anesthesia? J Clin Anesth 13(6): 401-406, 2001.

45. Friedman DS, Bass EB, Lubomski LH, Fleisher LA, Kempen JH, Magaziner J, Sprintz M, Robinson K, Schein OD: The methodologic quality of clinical trials on regional anesthesia for cataract surgery. Ophthalmology 108: 530-541, 2001.

46. Friedman DS, Bass EB, Lubomski LH, Fleisher LA, Kempen JH, Magaziner J, Sprintz M, Robinson K, Schein OD: Synthesis of the literature on the effectiveness of regional anesthesia for cataract surgery. Ophthalmology 108: 519-529, 2001.

47. Katz J, Feldman MA, Bass EB, Lubomski LH, Tielsch JM, Petty BG, Fleisher LA, Schein OD: Adverse intraoperative medical events and their association with anesthesia management strategies in cataract surgery. Ophthalmology 108: 1721-1726, 2001.

48. Nass CM, Allen JK, Jermyn RM, Fleisher LA: Secondary prevention of coronary artery disease in patients undergoing elective surgery for peripheral vascular disease. J Vasc Med 6: 35-41, 2001.

49. Reeves SW, Friedman DS, Fleisher LA, Lubomski LH, Schein OD, Bass EB: A decision analysis of anesthesia management for cataract surgery. Am J Ophthamol 132(4): 528-536, 2001.

50. Twerksy RS, Jamerson B, Warner DS, Fleisher LA, Hogue S: Hemodynamic and emergence profile for remifentanil vs fentanyl prospectively compared in a large population of surgical patients. J Clin Anesth 13(6): 407-416, 2001.

51. Wu CL, Carter HB, Naqibuddin M, Fleisher LA: The effect of local anesthetics on patient recovery after transrectal biopsy. Urology 57: 925-929, 2001.

52. Wu CL, Naqibuddin M, Fleisher LA: Measurement of patient satisfaction as an outcome of regional anesthesia and analgesia: a systematic review. Reg Anesth Pain Med 26(3): 196-208, 2001.

53. Dexter F, Traub RD, Fleisher LA, Rock P: What sample sizes are required for pooling surgical case durations among facilities to decrease the incidence of procedures with little historical data? Anesthesiology 96: 1230-1236, 2002.

54. Joshi G, Twersky RS, Warner DS, Fleisher LA: A comparison of the remifentanil and fentanyl adverse effect profile in a multicenter phase IV study. J Clin Anesth 14: 494-499, 2002.

55. Kain ZN, Chan K-M, Katz JD, Nigam A, Fleisher LA, Rosenfeld LE: Anesthesiologists and stress: A physiological and behavioral cohort study. Anesth Analg 95: 177-183, 2002.

56. Kaufmann SC, Wu CL, Pronovost PJ, Jermyn RM, Fleisher LA: The effect of intraoperative regional anesthesia on anticipated admission to the intensive care unit. J Clin Anesth 14: 432-436, 2002.

57. Kim LJ, Martinez EA, Faraday N, Fleisher LA, Chan D, Pronovost PJ: Cardiac troponin I predicts the risk of mortality in high-risk surgical patients. Circulation 106: 2366-2371, 2002.

58. Wu CL, Berenholtz SM, Pronovost PJ, Fleisher LA: A systematic review and analysis of postdischarge symptoms following outpatient surgery. Anesthesiology 96: 994-1003, 2002.

59. Elwood T, Morris W, Martin LD, Nespeca M-K, Wilson DA, Fleisher LA, Robotham JL, Nichols DG: Bronchodilator premedication does not decrease respiratory adverse events in pediatric general anesthesia. Can J Anaesth 50: 277-284, 2003.

60. Falcone RA, Jones CE, Nass C, Hale CM, Jermyn R, Walters GL, Stierer T, Fleisher LA: The value of pre-operative pharmacological stress testing before vascular surgery using ACC/AHA guidelines: a prospective, randomized pilot trial. J Cardiothorac Vasc Anesth 17(6): 694-8, Dec 2003.

61. Gupta A, Wu CL, Elkassabany N, Krug C, Parker SD, Fleisher LA: Do prophylactic measures for nausea and nomiting affect post-discharge sequele following ambulatory surgery?: a systematic review of randomized controlled trials. Anesthesiology 99: 488-495, 2003.

62. Katz J, Feldman MA, Bass EB, Lubomski LH, Tielsch JM, Petty BG, Fleisher LA, Schein OD: Risks and benefits of anticoagulant and antiplatelet medication use prior to cataract surgery. Ophthalmology 110(9): 1784-1788, 2003.

63. Mahadevia PJ, Fleisher LA, Frick K, Eng J, Goodman S, Powe NR: Lung-cancer screening with helical computed tomography in older adult smokers - a cost-effectiveness and threshold analysis. JAMA 289: 313-322, 2003.

64. Poldermans D, Bax JJ, Kertai MD, Krenning B, Westerhout CM, Schinkel AFL, Fleisher LA, Klein J, van Urk H, Roelandt JRTC, Boersma E: Statins are associated with a reduced incidence of perioperative mortality in patients undergoing major noncardiac vascular surgery. Circulation 107: 1848-1851, 2003.

65. Wu CL, Anderson GF, Herbert R, Lietman SA, Fleisher LA: The effect of perioperative epidural analgesia on patient mortality and morbidity in the Medicare population undergoing total hip replacement. Reg Anesth Pain Med 28: 271-278, 2003.

66. Wu CL, Naqibuddin M, Lietman SA, Jermyn RM, Fleisher LA: The effect of pain on health-related quality of life in the immediate postoperative period. Anesth Analg 97: 1078-1085, 2003.

67. Friedman DS, Reeves SW, Bass EB, Lubomski LH, Fleisher LA, Schein OD: Patient preferences for anaesthesia management during cataract surgery. Br J Ophthalmol 88(3): 333-5, Mar 2004.

68. Gupta A, Zuckerman R, Stierer T, Sakima N, Parker S, Fleisher LA: Comparison of recovery profile after ambulatory anesthesia with Propofol, Isoflurane, Sevoflurane and Desflurane: a systematic review. Anesth Analg 98(3): 632-41, Mar 2004.

69. Wu CL, Hurley RW, Anderson GF, Herbert R, Rowlingson AJ, Fleisher LA: Effect of postoperative epidural analgesia on morbidity and mortality following surgery in medicare patients. Reg Anesth Pain Med 29(6): 525-33, Nov-Dec 2004.

70. Faraday N, Martinez EA, Scharpf RB, Kasch-Semenza L, Dorman T, Pronovost PJ, Perler B, Gerstenblith G, Bray PF, Fleisher LA: Platelet gene polymorphisms and cardiac risk assessment in vascular surgery patients. Anesthesiology 101(6): 1291-7, December 2004.

71. Fleisher LA, Corbett W, Berry C, Poldermans D: Cost-effectiveness of differing perioperative beta-blockade strategies in vascular surgery patients. J Cardiothor Vasc Anes 18(1): 7-13, 2004.

72. Fleisher LA, Pasternak LR, Herbert R, Anderson GF: Inpatient hospital admission and death after outpatient surgery in elderly patients: importance of patient and system characteristics and location of care. Arch Surg 139: 67-72, 2004.

73. Nicholson WK, Fleisher LA, Fox HE, Powe NR: Screening for gestational diabetes mellitus. Diabetes Care 28(6): 1482-4, June 2005.

74. Creswell LL, Alexander JC, Ferguson TB, Lisbon A, Fleisher LA: ACCP Guidelines for the Prevention and Management of Postoperative Atrial Fibrillation after Cardiac Surgery: Intraoperative Interventions. Chest 128: 28S-35S, 2005.

75. Fleisher LA, Bass EB, McKeown P: ACCP Guidelines for the Prevention and Management of Postoperative Atrial Fibrillation after Cardiac Surgery: Methodological Approach. Chest 128: 17S-23S, 2005.

76. Fleisher LA, Newman MF, St. Aubin LB, Cropp AB, Billing CB, Bonney S, Mackey WC, Poldermans D, Corbalan R, Pereira AH, Coriat P: Efficacy of zoniporide, a Na/H exchange ion inhibitor, for reducing perioperative cardiovascular events in vascular surgery patients. J Cardiothor Vasc Anesth 19: 570-6, 2005.

77. Hogue CW, Creswell LL, Gutterman DD, Fleisher LA: ACCP Guidelines for the Prevention and Management of Postoperative Atrial Fibrillation after Cardiac Surgery: Epidemiology, Mechanisms, and Risks. Chest 128: 9S-16S, 2005.

78. Martinez EA, Nass CM, Jermyn RM, Rosenbaum SH, Akhtar S, Chan DW, Malkus H, Weiss JL, Fleisher LA: Intermittent cardiac troponin-I screening is an effective means of surveillance for a perioperative myocardial infarction. J Cardiothor Vasc Anesth 19: 577-82, 2005.

79. Wu CL, Rowlingson AJ, Partin AW, Kalish MA, Courpas GE, Walsh PC, Fleisher LA: Correlation of Postoperative Pain on Quality of Recovery and Patient-oriented Outcomes in the Immediate Postoperative Period. Reg Anes Pain Med 30: 516-22, 2005.

80. Wu CL, Partin AW, Rowlingson AJ, Kalish MA, Walsh PC, Fleisher LA: Efficacy of continuous local anesthetic infusion for postoperative pain after radical retropubic prostatectomy. Urology 66: 366-70, 2005.

81. Kim DH, Lipsitz LA, Ferrucci L, Varadhan R, Guralnik JM, Carlson M, Fleisher LA, Fried LP, Chaves PHM: Association of Reduced Heart Rate Variability with Cognitive Impairment in Older Disabled Women in the Community: A Pilot Study in the Women's Health and Aging Study I J Am Geriatrics Soc 54: 1751-7, Nov 2006

82. Mackey WC, Fleisher LA, Haider S, Sheikh S, Cappelleri JC, Lee WC, Wang Q, Stephens JM: Perioperative myocardial ischemic injury in high risk vascular surgery patients: Incidence and clinical significance in a prospective clinical trial. J Vasc Surg 43: 533-8, 2006.

83. Vicenzi MN, Meislitzer T, Heitzinger B, Halaj M, Fleisher LA, Metzler H: Coronary artery stenting and noncardiac surgery - a prospective outcome study. Br J Anaesth 96: 686-93, 2006.

84. Wu CL, Rowlingson AJHerbert RRichman JMAndrews RAFleisher LA: Correlation of postoperative epidural analgesia on morbidity and mortality after colectomy in Medicare patients. J Clin Anesth 18(8): 594-9, Dec 2006.

85. Wu CL, Sapirstein A, Herbert R, Rowlingson AJ, Michaels RK, Petrovic MA, Fleisher LA: Effect of postoperative epidural analgesia on morbidity and mortality after lung resection in Medicare patients. J Clin Anesth 18: 515-20,

2006.

86. Fleisher LA, Pasternak LR, Lyles A: A novel index of elevated risk of inpatient hospital admission immediately following outpatient surgery. Arch Surg. 142(3): 263-8, Mar 2007.

87. Chaves Paulo H M, Varadhan Ravi, Lipsitz Lewis A, Stein Phyllis K, Windham B Gwen, Tian Jing, Fleisher Lee A, Guralnik Jack M, Fried Linda P: Physiological complexity underlying heart rate dynamics and frailty status in community-dwelling older women. Journal of the American Geriatrics Society 56(9): 1698-703, Sep 2008. PMCID: PMC2848445

88. Wu, Christopher L. Demeester, James S. Herbert, Robert. Maine, David N. Rowlingson, Andrew J. Fleisher, Lee A.: Correlation of postoperative epidural analgesia with morbidity and mortality following total knee replacement in Medicare patients. American Journal of Orthopedics (Chatham, Nj) 37(10): 524-7, Oct 2008.

89. De Hert, S G. Longrois, D. Yang, H. Fleisher, L A.: Does the use of a volatile anesthetic regimen attenuate the incidence of cardiac events after vascular surgery?. Acta Anaesthesiologica Belgica 59(1): 19-25, 2008.

90. Archan S, Roscher CR, Fairman RM, Fleisher LA: Revised Cardiac Risk Index (Lee) and Perioperative Cardiac Events as Predictors of Long-term Mortality in Patients Undergoing Endovascular Abdominal Aortic Aneurysm Repair. Journal of cardiothoracic and vascular anesthesia 24(1): 84-90, Jun 2009.

91. van Lier Felix, Schouten Olaf, van Domburg Ron T, van der Geest Patrick J, Boersma Eric, Fleisher Lee A, Poldermans Don: Effect of chronic beta-blocker use on stroke after noncardiac surgery. The American journal of cardiology 104(3): 429-33, Aug 2009.

92. Neuman MD, Archan S, Karlawish JH, Schwartz JS, Fleisher LA: The Relationship Between Short-Term Mortality and Quality of Care for Hip Fracture: A Meta-Analysis of Clinical Pathways for Hip Fracture. Journal of the American Geriatrics Society 57(11): 2046-54, Sep 2009.

93. Kim, Michelle M. Barnato, Amber E. Angus, Derek C. Fleisher, Lee A. Kahn, Jeremy M.: The effect of multidisciplinary care teams on intensive care unit mortality. Archives of Internal Medicine 170(4): 369-76, Feb 22 2010.

94. Neuman, Mark D. Fleisher, Lee A. Even-Shoshan, Orit. Mi, Lanyu. Silber, Jeffrey H.: Nonoperative care for hip fracture in the elderly: the influence of race, income, and comorbidities. Medical Care 48(4): 314-20, Apr 2010.

95. Flu Willem-Jan, van Kuijk Jan-Peter, Hoeks Sanne E, Kuiper Ruud, Schouten Olaf,

Goei Dustin, Elhendy Abdou, Verhagen Hence J M, Thomson Ian R, Bax Jeroen J, Fleisher Lee A, Poldermans Don: Prognostic implications of asymptomatic left ventricular dysfunction in patients undergoing vascular surgery. Anesthesiology 112(6): 1316-24, Jun 2010.

96. Ingraham, Angela M. Cohen, Mark E. Bilimoria, Karl Y. Dimick, Justin B. Richards, Karen E. Raval, Mehul V. Fleisher, Lee A. Hall, Bruce L. Ko, Clifford Y.: Association of surgical care improvement project infection-related process measure compliance with risk-adjusted outcomes: implications for quality measurement. Journal of the American College of Surgeons 211(6): 705-14, Dec 2010.

97. McCunn Maureen, Ashburn Michael A, Floyd Thomas F, Schwab C William, Harrington Paul, Hanson C William, Sarani Babak, Mehta Samir, Speck Rebecca M, Fleisher Lee A: An organized, comprehensive, and security-enabled strategic response to the Haiti earthquake: a description of pre-deployment readiness preparation and preliminary experience from an academic anesthesiology department with no preexisting international disaster response program. Anesthesia and analgesia 111(6): 1438-44, Dec 2010.

98. Neuman, Mark D. David, Guy. Silber, Jeffrey H. Schwartz, J Sanford. Fleisher, Lee A.: Changing access to emergency care for patients undergoing outpatient procedures at ambulatory surgery centers: evidence from Florida. Medical Care Research & Review 68(2): 247-58, Apr 2011.

99. Silber, Jeffrey H. Rosenbaum, Paul R. Even-Shoshan, Orit. Mi, Lanyu. Kyle, Fabienne A. Teng, Yun. Bratzler, Dale W. Fleisher, Lee A.: Estimating anesthesia time using the medicare claim: a validation study. Anesthesiology 115(2): 322-33, Aug 2011. PMCID: PMC3273329

100. McCunn Maureen, Speck Rebecca M, Chung Insung, Atkins Joshua H, Raiten Jesse M, Fleisher Lee A: Global health outreach during anesthesiology residency in the United States: a survey of interest, barriers to participation, and proposed solutions. Journal of clinical anesthesia 24(1): 38-43, Feb 2012.

101. Neuman Mark D, Silber Jeffrey H, Elkassabany Nabil M, Ludwig Justin M, Fleisher Lee A: Comparative effectiveness of regional versus general anesthesia for hip fracture surgery in adults. Anesthesiology 117(1): 72-92, Jul 2012.

102. Silber, Jeffrey H. Rosenbaum, Paul R. Kelz, Rachel R. Reinke, Caroline E. Neuman, Mark D. Ross, Richard N. Even-Shoshan, Orit. David, Guy. Saynisch, Philip A. Kyle, Fabienne A. Bratzler, Dale W. Fleisher, Lee A.: Medical and financial risks associated with surgery in the elderly obese. Annals of Surgery 256(1): 79-86, Jul 2012. PMCID: PMC3623296

103. Wijeysundera, Duminda N. Mamdani, Muhammad. Laupacis, Andreas. Fleisher,

Lee A. Beattie, W Scott. Johnson, Sindhu R. Kolstad, Jonathan. Neuman, Mark D.: Clinical evidence, practice guidelines, and beta-blocker utilization before major noncardiac surgery. Circulation. Cardiovascular Quality & Outcomes 5(4): 558-65, Jul 1 2012.

104. Reinke, Caroline E. Kelz, Rachel R. Zubizarreta, Jose R. Mi, Lanyu. Saynisch, Philip. Kyle, Fabienne A. Even-Shoshan, Orit. Fleisher, Lee A. Silber, Jeffrey H.: Obesity and readmission in elderly surgical patients. Surgery 152(3): 355-62, Sep 2012. PMCID: PMC3637915

105. Chuy K, Yan Z, Fleisher L, Liu R: An ICU Preanesthesia Evaluation Form Reduces Missing Preoperative Key Information. J Anesth Clin Res 3: 242, 2012.

106. Liu R, Garcia PS, Fleisher LA: Interest in anesthesia as reflected by keyword searches using common search engines. J Anesthe Clinic Res 3: 187, 2012.

107. Speck RM, Neuman MD, Bond AR, Fleisher LA: Strategies to Promote Reporting of Surgical Care Improvement Project (SCIP) Measures: A Pilot Survey of Anesthesia Department Leaders. Perioperative Medicine 1: 5, 2012.

108. Yan Zhe, Tanner Jonathan W, Lin David, Chalian Ara A, Savino Joseph S, Fleisher Lee A, Liu Renyu: Airway trauma in a high patient volume academic cardiac electrophysiology laboratory center. Anesthesia and analgesia 116(1): 112-7, Jan 2013. PMCID: PMC3530138

109. Silber Jeffrey H, Rosenbaum Paul R, Ross Richard N, Even-Shoshan Orit, Kelz Rachel R, Neuman Mark D, Reinke Caroline E, Ludwig Justin M, Kyle Fabienne A, Bratzler Dale W, Fleisher Lee A: Racial disparities in operative procedure time: the influence of obesity. Anesthesiology 119(1): 43-51, Jul 2013.

110. Clement Rutledge Carter, Derman Peter B, Graham Danielle S, Speck Rebecca M, Flynn David N, Levin Lawrence Scott, Fleisher Lee A: Risk Factors, Causes, and the Economic Implications of Unplanned Readmissions Following Total Hip Arthroplasty. The Journal of arthroplasty 28((8 Suppl)): 7-10, Aug 2013.

111. Kelz Rachel R, Reinke Caroline E, Zubizarreta José R, Wang Min, Saynisch Philip, Even-Shoshan Orit, Reese Peter P, Fleisher Lee A, Silber Jeffrey H: Acute kidney injury, renal function, and the elderly obese surgical patient: a matched case-control study. Annals of surgery 258(2): 359-63, Aug 2013.

112. Liu J, Ma C, Elkassabany N, Fleisher LA, Neuman MD.: Neuraxial Anesthesia Decreases Postoperative Systemic Infection Risk Compared with General Anesthesia in Knee Arthroplasty. Anesth Analg 117(4): 1010-6, 2013.

113. Flynn DN, Speck RM, Mahmoud NN, David G, Fleisher LA.: The impact of complications following open colectomy on hospital finances: a retrospective

cohort study. Perioper Med (Lond). 3: 1, Mar 2014.

114. Silber JH, Rosenbaum PR, Ross RN, Ludwig JM, Wang W, Niknam BA, Mukherjee N, Saynisch PA, Even-Shoshan O, Kelz RR, Fleisher LA.: Template Matching for Auditing Hospital Cost and Quality. Health Serv Res. 49: 1446-74, Mar 2014

115. Speck RM, Foster JJ, Mulher VA, Burke SV, Sullivan PG, Fleisher LA: Culture Change: Establishment of a Professionalism Committee Within an Academic Medical Center. Jt Comm J Qual Patient Saf 40: 161-7, April 2014.

116. Fleisher LA, Linde-Zwirble WL: Incidence Outcome and Attributable Resource Use associated with Pulmonary and Cardiac Complications after Major Small and Large Bowel Procedures. Perioper Med 3: 7, Oct 2014

117. Silber JH, Rosenbaum PR, Ross RN, Ludwig JM, Wang W, Niknam BA, Mukherjee N, Saynisch PA, Even-Shoshan O, Kelz RR, Fleisher LA: A Hospital-Specific Template Matching for Auditing Hospital Cost and Quality. Health Serv Res 49: 1475-97, Oct 2014.

118. Meghan B Lane-Fall, Rinad S Beidas, Jose L Pascual, Meredith L Collard, Hannah G Peifer, Tyler J Chavez, Mark E Barry, Jacob T Gutsche, Scott D Halpern, Lee A Fleisher and Frances K Barg: Handoffs and transitions in critical care (HATRICC): protocol for a mixed methods study of operating room to intensive care unit handoffs BMC Surgery 14: 96, Nov 2014.

119. Clement RC, Kheir MM, Derman PB, Flynn DN, Speck RM, Levin LS, Fleisher LA.: What Are the Economic Consequences of Unplanned Readmissions After TKA? Clin Orthop Relat Res 472(10): 3134-41, 2014.

120. Michael M. Kheir, R. Carter Clement, Peter B. Derman, David N. Flynn, Rebecca M. Speck, L. Scott Levin, Lee A. Fleisher, MD: Are there Identifiable Risk Factors and Causes Associated with Unplanned Readmissions Following Total Knee Arthroplasty? The Journal of Arthroplasty 29: 2192-6. 2014.

121. Neuman MD, Bosk CL, Fleisher LA.: Learning from mistakes in clinical practice guidelines: the case of perioperative β-blockade. BMJ Qual Saf. 23: 957-64, 2014.

122. Onuoha OC, Arkoosh VA, Fleisher LA: "Choosing Wisely" in Anesthesiology: The Gap Between Evidence and Practice. JAMA Intern Med 174: 1391-5, 2014.

123. Weisberg R, Speck R, Fleisher LA: Fostering innovation in medicine: A conceptual framework for Medical Centers. Healthcare 2: 90-93, 2014.

124. Carson JL, Sieber F, Cook DR, Hoover DR, Noveck H, Chaitman BR, Fleisher L, Beaupre L, Macaulay W, Rhoads GG, Paris B, Zagorin A, Sanders DW, Zakriya

KJ, Magaziner J.: Liberal versus restrictive blood transfusion strategy: 3-year survival and cause of death results from the FOCUS randomised controlled trial. Lancet 385: 1183-1189, Mar 2015.

125. Glance LG, Kellermann AL, Hannan EL, FLeisher LA, Eaton MP, Dutton RP, Lustik SJ, Li Y, Dick AW: Impact of Anesthesiologists on CABG Outcomes. Anesth Analg 120(3): 526-533, Mar 2015.

126. Kincaid ML, Fleisher LA, Neuman MD: Presentation of US Hospital websites of risks and benefits of transcatheter aortic valve replacement procedures. Jama Int Med 175: 440-1, Mar 2015. PMCID: PMC4349371

127. Speck RM, Weisberg RW, Fleisher LA: Innovation centers in academic health systems: Varying goals and approaches. Acad Med Mar 2015.

128. Glick HA, McElligott S, Pauly M, Willke RJ, Bergquist H, Doshi JA, Fleisher LA, Kinosian B, Perfetto EM, Polsky DE, Schwartz JS. : Comparative Effectiveness And Cost Effectiveness AnalysesFrequently Agree On Value. Health Aff 34(5): 805-11, 2015.

129. Hyder JA, Niconchuk J, Glance LG, Neuman MD, Cima RR, Dutton RP, Nguyen LL, Fleisher LA, Bader AM: What can the National Quality Forum tell us about performance measurement in anesthesiology? Anesth Analg 120: 440-8, 2015.

130. Onuoha Onyi C, Hatch Michael B, Miano Todd A, Fleisher Lee A: The incidence of un-indicated preoperative testing in a tertiary academic ambulatory center: a retrospective cohort study. Perioperative medicine (London, England) 4: 14, 2015. PMCID: PMC4681056

131. Silber JH, Rosenbaum PR, Kelz RR, Gaskin DJ, Ludwig JM, Ross RN, Niknam BA, Hill A, Wang M, Evan-Shoshan O, Fleisher LA: Examining Causes of Racial Disparities in General Surgical Mortality: Hospital Quality versus Patient Risk. Med Care 53(7): 619-29, 2015.

132. Silber Jeffrey H, Rosenbaum Paul R, McHugh Matthew D, Ludwig Justin M, Smith Herbert L, Niknam Bijan A, Even-Shoshan Orit, Fleisher Lee A, Kelz Rachel R, Aiken Linda H: Comparison of the Value of Nursing Work Environments in Hospitals Across Different Levels of Patient Risk. JAMA surgery 151(6): 527-36, Jan 2016.

133. Jungquist Carla R, Correll Darin J, Fleisher Lee A, Gross Jeffrey, Gupta Rajnish, Pasero Chris, Stoelting Robert, Polomano Rosemary: Avoiding Adverse Events Secondary to Opioid-Induced Respiratory Depression: Implications for Nurse Executives and Patient Safety. The Journal of nursing administration 46(2): 87-94, Feb 2016.

134. Silber Jeffrey H, Rosenbaum Paul R, Ross Richard N, Ludwig Justin M, Wang Wei, Niknam Bijan A, Hill Alexander S, Even-Shoshan Orit, Kelz Rachel R, Fleisher Lee A: Indirect Standardization Matching: Assessing Specific Advantage and Risk Synergy. Health services research 51(6): 2330-2357, Feb 2016.

135. Clement R Carter, Kheir Michael M, Soo Adrianne E, Derman Peter B, Levin L Scott, Fleisher Lee A: What Financial Incentives Will Be Created by Medicare Bundled Payments for Total Hip Arthroplasty? The Journal of arthroplasty 31(9): 1885-9, Mar 2016.

136. Johnstone Robert E, Fleisher Lee A: A 1966 Anesthetic Administered by Robert D. Dripps, M.D., Demonstrated His Experimental Style of Clinical Care. Anesthesiology 124: 1218-21. Mar 2016.

137. Hadler RA, Neuman MD, Raper S, Fleisher LA: Advance Directives and Operating: Room for Improvement? Anesth Analg Case Reports 6(7): 204-7, Apr 2016. PMCID: PMC4816672

138. Glance Laurent G, Hannan Edward L, Fleisher Lee A, Eaton Michael P, Dutton Richard P, Lustik Stewart J, Li Yue, Dick Andrew W: Feasibility of Report Cards for Measuring Anesthesiologist Quality for Cardiac Surgery. Anesthesia and analgesia 122(5): 1603-1613, May 2016.

139. Clement R Carter, Gray Caitlin M, Kheir Michael M, Derman Peter B, Speck Rebecca M, Levin L Scott, Fleisher Lee A: Will Medicare Readmission Penalties Motivate Hospitals to Reduce Arthroplasty Readmissions? The Journal of arthroplasty 32(3): 709-713, Aug 2016.

140. Clement R Carter, Soo Adrianne E, Kheir Michael M, Derman Peter B, Flynn David N, Levin L Scott, Fleisher Lee A: What Incentives Are Created by Medicare Payments for Total Hip Arthroplasty? The Journal of arthroplasty 31(9 Suppl): 69-72, Sep 2016.

141. Neuman Mark D, Ellenberg Susan S, Sieber Frederick E, Magaziner Jay S, Feng Rui, Carson Jeffrey L: Regional versus General Anesthesia for Promoting Independence after Hip Fracture (REGAIN): protocol for a pragmatic, international multicentre trial. BMJ open 6(11): e013473, Nov 2016.

142. Speck Rebecca M, Neuman Mark D, Resnick Kimberly S, Mellers Barbara A, Fleisher Lee A: Anticipated regret in shared decision-making: a randomized experimental study. Perioperative medicine (London, England) 5: 5, 2016. PMCID: PMC4776353

143. Steven E Raper, Lee A Fleisher, David Mayer, Risa V. Ferman, Kevin Steele, John Hollway: Using Root Cause Analysis to Study Prosecutorial Error: A Collaboration Between the Montgomery County (PA) District Attorney's Office

and the Quattrone Center for the Fair Administration of Justice. Tolle Lege - Villanova Law Review Online 2016.

144. Lane-Fall Meghan B, Ramaswamy Tara S, Brown Sydney E S, He Xu, Gutsche Jacob T, Fleisher Lee A, Neuman Mark D: Structural, Nursing, and Physician Characteristics and 30-Day Mortality for Patients Undergoing Cardiac Surgery in Pennsylvania. Critical care medicine 45(9): 1472-1480, Jun 2017. PMCID: PMC5561002

145. Ahmad T, Bouwman R A, Grigoras I, Aldecoa C, Hofer C, Hoeft A, Holt P, Fleisher L A, Buhre W, Pearse R M: Use of failure-to-rescue to identify international variation in postoperative care in low-, middle- and high-income countries: a 7-day cohort study of elective surgery. British journal of anaesthesia 119(2): 258-266, Aug 2017.

146. Gaulton T G, Fleisher L A, Neuman M D: The association between obesity and disability in survivors of joint surgery: analysis of the health and retirement study. British journal of anaesthesia 120(1): 109-116, Jan 2018.

147. Speck Rebecca M, Ward Denham S, Fleisher Lee A: Academic Anesthesiology Career Development: A Mixed-Methods Evaluation of the Role of Foundation for Anesthesiology Education and Research Funding. Anesthesia and analgesia 126(6): 2116-2122, Jan 2018.

148. Liu J, Liu WM, Flynn DN, Fleisher LA, Elkassabany NM: Hospital-Based Acute Care within 7-days of Discharge following Outpatient Arthroscopic Shoulder Surgery. Anesth Analg 126(2): 600-605, Feb 2018.

149. Diraviam Sushmitha P, Sullivan Patricia G, Sestito John A, Nepps Mary Ellen, Clapp Justin T, Fleisher Lee A: Physician Engagement in Malpractice Risk Reduction: A UPHS Case Study. Joint Commission journal on quality and patient safety 44(10): 605-612, Jul 2018.

150. MacKay Emily J, Groeneveld Peter W, Fleisher Lee A, Desai Nimesh D, Gutsche Jacob T, Augoustides John G, Patel Prakash A, Neuman Mark D: Practice Pattern Variation in the Use of Transesophageal Echocardiography for Open Valve Cardiac Surgery. Journal of cardiothoracic and vascular anesthesia Aug 2018.

151. Clapp Justin T, Gordon Emily K B, Baranov Dimitry J, Trey Beulah, Tilin Felice Y, Fleisher Lee A: Encouraging Reflexivity in a Residency Leadership Development Program: Expanding Outside the Competency Approach. Acad Med 93(2): 210-213, Sep 2018.

152. Lane-Fall Meghan B, Pascual Jose L, Massa Scott, Collard Meredith L, Peifer Hannah G, Di Taranti Laura J, Linehan Megan, Fleisher Lee A, Barg Frances K: Developing a Standard Handoff Process for Operating Room-to-ICU Transitions:

Multidisciplinary Clinician Perspectives from the Handoffs and Transitions in Critical Care (HATRICC) Study. Joint Commission journal on quality and patient safety 44(9): 514-525, Sep 2018.

153. Neuman Mark D, Gaskins Lakisha J, Montgomery Brittany, Menio Diane A, Long Judith, Fleisher Lee A, Beaupre Lauren, Ahn Jaimo: Feasibility and Acceptability of a Peer Mentoring Program for Older Adults Following Hospitalization for Hip Fracture. Journal of the American Medical Directors Association Nov 2018.

154. Ashburn, M. A., Fleisher, L. A.: Increasing Evidence for the Limited Role of Opioids to Treat Chronic Noncancer Pain. JAMA 320(23): 2427-2428, 2018.

155. Bampoe Sohail, Cook Tim, Fleisher Lee, Grocott Michael P W, Neuman Mark, Story David, Myles Paul, Haller Guy: Clinical indicators for reporting the effectiveness of patient quality and safety-related interventions: a protocol of a systematic review and Delphi consensus process as part of the international Standardised Endpoints for Perioperative Medicine initiative (StEP). BMJ open 8(11): e023427, Dec 2018.

156. Jeffrey H. Silber, Joseph G. Reiter, Paul R. Rosenbaum, Qingyuan Zhao, Dylan S. Small, Bijan A. Niknam, BS, Alexander S. Hill, BS, Lauren L. Hochman, BA, Rachel R. Kelz, Lee A. Fleisher: Defining Multimorbidity in Older Surgical Patients. Medical Care 56(8): 701-710, 2018.

157. Rachel A. Hadler, Julia F. Lynch, Julia Berenson, Lee A. Fleisher. : Limited Public Support for Team-Based Care Models: Survey Results. Health Management Policy and Innovation 3(2), 2018.

158. Sun Eric, Mello Michelle M, Rishel Chris A, Vaughn Michelle T, Kheterpal Sachin, Saager Leif, Fleisher Lee A, Damrose Edward J, Kadry Bassam, Jena Anupam B: Association of Overlapping Surgery With Perioperative Outcomes. JAMA 321(8): 762-772, Feb 2019.

159. Mehta Samir D, Weber Kristy, Fleisher Lee, Shulman Lawrence N, Gabriel Peter, Trerotola Scott O, Nawas Mohammed, Chi Andrew S, Sebro Ronnie: Assessing the Need for Preprocedural Laboratory Tests and Stopping Non-steroidal Anti-inflammatory Drugs/Aspirin in Patients Undergoing Percutaneous Bone and Soft Tissue Biopsies. Cardiovascular and interventional radiology 42(11): 1588-1596, Jun 2019.

160. Lei Victor J, Kennedy Edward H, Luong ThaiBinh, Chen Xinwei, Polsky Daniel E, Volpp Kevin G, Neuman Mark D, Holmes John H, Fleisher Lee A, Navathe Amol S: Model Performance Metrics in Assessing the Value of Adding Intraoperative Data for Death Prediction: Applications to Noncardiac Surgery. Studies in health technology and informatics 264: 223-227, Aug 2019.

161. Li Joan, Burson Randall C, Clapp Justin T, Fleisher Lee A: Centers of excellence: Are there standards? Healthcare (Amsterdam, Netherlands) 8: 100388, Oct 2019.

162. Ali, Z. S., Flanders, T. M., Ozturk, A. K., Malhotra, N. R., Leszinsky, L., McShane, B. J., Gardiner, D., Rupich, K., Chen, H. I., Schuster, J., Marcotte, P. J., Kallan, M. J., Grady, M. S., Fleisher, L. A., Welch, W. C.: Enhanced recovery after elective spinal and peripheral nerve surgery: pilot study from a single institution. J Neurosurg Spine Page: 1-9, 2019.

163. Arriaga, A. F., Sweeney, R. E., Clapp, J. T., Muralidharan, M., Burson, R. C., 2nd, Gordon, E. K. B., Falk, S. A., Baranov, D. Y., Fleisher, L. A.: Failure to Debrief after Critical Events in Anesthesia Is Associated with Failures in Communication during the Event. Anesthesiology 130(6): 1039-1048, 2019.

164. Clapp Justin T, Arriaga Alexander F, Murthy Sushila, Raper Steven E, Schwartz J Sanford, Barg Frances K, Fleisher Lee A: Surgical Consultation as Social Process: Implications for Shared Decision Making. Ann Surg 269(3): 446-452, Dec 2019.

165. Haller, G., Bampoe, S., Cook, T., Fleisher, L. A., Grocott, M. P. W., Neuman, M., Story, D., Myles, P. S., St, E. P. Compac Group: Systematic review and consensus definitions for the Standardised Endpoints in Perioperative Medicine initiative: clinical indicators. Br J Anaesth 123(2): 228-237, 2019.

166. Lei Victor J, Luong ThaiBinh, Shan Eric, Chen Xinwei, Neuman Mark D, Eneanya Nwamaka D, Polsky Daniel E, Volpp Kevin G, Fleisher Lee A, Holmes John H, Navathe Amol S: Risk Stratification for Postoperative Acute Kidney Injury in Major Noncardiac Surgery Using Preoperative and Intraoperative Data. JAMA network open 2(12): e1916921, Dec 2019. PMCID: PMC6902769

167. Lei, V. J., Kennedy, E. H., Luong, T., Chen, X., Polsky, D. E., Volpp, K. G., Neuman, M. D., Holmes, J. H., Fleisher, L. A., Navathe, A. S.: Model Performance Metrics in Assessing the Value of Adding Intraoperative Data for Death Prediction: Applications to Noncardiac Surgery. Stud Health Technol Inform 264: 223-227, 2019.

168. Neuman, M. D., Gaskins, L. J., Montgomery, B., Menio, D. A., Long, J., Fleisher, L. A., Beaupre, L., Ahn, J.: Feasibility and Acceptability of a Peer Mentoring Program for Older Adults Following Hospitalization for Hip Fracture. J Am Med Dir Assoc 20(2): 218-220 e2, 2019.

169. Sweeney, R. E., Clapp, J. T., Arriaga, A. F., Muralidharan, M., Burson, R. C., 2nd, Gordon, E. K. B., Falk, S. A., Baranov, D. Y., Fleisher, L. A.: Understanding Debriefing: A Qualitative Study of Event Reconstruction at an Academic Medical Center. Acad Med 2019.

170. MacKay Emily J, Neuman Mark D, Fleisher Lee A, Patel Prakash A, Gutsche Jacob T, Augoustides John G, Desai Nimesh D, Groeneveld Peter W: Transesophageal Echocardiography, Mortality, and Length of Hospitalization after Cardiac Valve Surgery. Journal of the American Society of Echocardiography : official publication of the American Society of Echocardiography Mar 2020.

171. Elective surgery cancellations due to the COVID-19 pandemic: global predictive modelling to inform surgical recovery plans. Br J Surg 107(11): 1440-1449, 2020.

172. Clapp, J. T., Diraviam, S. P., Lane-Fall, M. B., Szymczak, J. E., Muralidharan, M., Chung, J. J., Gutsche, J. T., Curley, M. A. Q., Berns, J. S., Fleisher, L. A.: Nephrology in the Academic Intensive Care Unit: A Qualitative Study of Interdisciplinary Collaboration. Am J Kidney Dis 75(1): 61-71, 2020.

173. Deiner, S., Fleisher, L. A., Leung, J. M., Peden, C., Miller, T., Neuman, M. D., A. S. A. Committee on Geriatric Anesthesia, the, A. S. A. Perioperative Brain Health Initiative: Adherence to recommended practices for perioperative anesthesia care for older adults among US anesthesiologists: results from the ASA Committee on Geriatric Anesthesia-Perioperative Brain Health Initiative ASA member survey. Perioper Med (Lond) 9: 6, 2020.

174. Flanders, T. M., Ifrach, J., Sinha, S., Joshi, D. S., Ozturk, A. K., Malhotra, N. R., Pessoa, R., Kallan, M. J., Fleisher, L. A., Ashburn, M. A., Maloney, E., Welch, W. C., Ali, Z. S.: Reduction of Postoperative Opioid Use After Elective Spine and Peripheral Nerve Surgery Using an Enhanced Recovery After Surgery Program. Pain Med 21(12): 3283-3291, 2020.

175. Fleisher, L. A.: The Actions That Define Us: Our Response to Critical Events. Anesthesiol Clin 38(4): xiii, 2020.

176. Gordon, E. K. B., Clapp, J. T., Heins, S. J., Gaulton, T. G., Lane-Fall, M. B., Aysola, J., Baranov, D. Y., Fleisher, L. A.: The role of the interview in residency selection: A mixed-methods study. Med Educ 54(11): 1029-1039, 2020.

177. Gordon, E. K. B., Clapp, J. T., Heins, S. J., Gaulton, T. G., Lane-Fall, M. B., Aysola, J., Baranov, D. Y., Fleisher, L. A.: The Role of the Interview in Residency Selection: A Mixed Methods Study. Med Educ 2020.

178. Jain, S., Rosenbaum, P. R., Reiter, J. G., Hoffman, G., Small, D. S., Ha, J., Hill, A. S., Wolk, D. A., Gaulton, T., Neuman, M. D., Eckenhoff, R. G., Fleisher, L. A., Silber, J. H.: Using Medicare claims in identifying Alzheimer"s disease and related dementias. Alzheimers Dement 2020.

179. Jain, S., Rosenbaum, P. R., Reiter, J. G., Hoffman, G., Small, D. S., Ha, J., Hill, A. S., Wolk, D. A., Gaulton, T., Neuman, M. D., Eckenhoff, R. G., Fleisher, L. A., Silber, J. H.: Using Medicare claims in identifying Alzheimer"s

disease and related dementias. Alzheimers Dement 2020.

180. Jain, S., Rosenbaum, P. R., Reiter, J. G., Hoffman, G., Small, D. S., Ha, J., Hill, A. S., Wolk, D. A., Gaulton, T., Neuman, M. D., Eckenhoff, R. G., Fleisher, L. A., Silber, J. H.: Using Medicare claims in identifying Alzheimer"s disease and related dementias. Alzheimers Dement 2020.

181. Kadakia, K. T., Fleisher, L. A., Stimson, C. J., Aloia, T. A., Offodile, A. C., 2nd: Charting a Roadmap for Value-based Surgery in the Post-pandemic Era. Ann Surg 272(2): e43-e44, 2020.

182. Lane-Fall, M. B., Pascual, J. L., Peifer, H. G., Di Taranti, L. J., Collard, M. L., Jablonski, J., Gutsche, J. T., Halpern, S. D., Barg, F. K., Fleisher, L. A., Hatricc study team: A Partially Structured Postoperative Handoff Protocol Improves Communication in 2 Mixed Surgical Intensive Care Units: Findings From the Handoffs and Transitions in Critical Care (HATRICC) Prospective Cohort Study. Ann Surg 271(3): 484-493, 2020.

183. Liu, R., Gavrin, J. R., Fleisher, L. A.: Online keyword searching in three countries and languages reflects different perceptions and behaviors in response to the name of the novel coronavirus disease. J Glob Health 10(2): 020339, 2020.

184. MacKay, E. J., Neuman, M. D., Fleisher, L. A., Patel, P. A., Gutsche, J. T., Augoustides, J. G., Desai, N. D., Groeneveld, P. W.: Transesophageal Echocardiography, Mortality, and Length of Hospitalization after Cardiac Valve Surgery. J Am Soc Echocardiogr 33(6): 756-762.e1, 2020.

185. Mantha, S., Tripuraneni, S. L., Roizen, M. F., Fleisher, L. A.: Proposed Modifications in the 6-Minute Walk Test for Potential Application in Patients With Mild COVID-19: A Step to Optimize Triage Guidelines. Anesth Analg 131(2): 398-402, 2020.

186. Navathe, A. S., Lei, V. J., Fleisher, L. A., Luong, T., Chen, X., Kennedy, E., Volpp, K. G., Polsky, D. E., Groeneveld, P. W., Weiner, M., Holmes, J. H., Neuman, M. D.: Improving Identification of Patients at Low Risk for Major Cardiac Events After Noncardiac Surgery Using Intraoperative Data. J Hosp Med 15(10): 581-587, 2020.

187. Shannon, A. B., Roberson, J. L., Clapp, J. T., Vaughan, C., Kleid, M., Song, Y., Miura, J. T., Dempsey, D. T., DeMatteo, R. P., Fleisher, L. A., Karakousis, G. C.: What is the patient experience of surgical care during the coronavirus disease 2019 (COVID-19) pandemic? A mixed-methods study at a single institution. Surgery 2020.

188. Silber, J. H., Rosenbaum, P. R., Niknam, B. A., Ross, R. N., Reiter, J. G., Hill, A. S., Hochman, L. L., Brown, S. E., Arriaga, A. F., Fleisher, L. A.:

Comparing Outcomes and Costs of Medical Patients Treated at Major Teaching and Non-teaching Hospitals: A National Matched Analysis. J Gen Intern Med 35(3): 743-752, 2020.

189. Silber, J. H., Rosenbaum, P. R., Niknam, B. A., Ross, R. N., Reiter, J. G., Hill, A. S., Hochman, L. L., Brown, S. E., Arriaga, A. F., Kelz, R. R., Fleisher, L. A.: Comparing Outcomes and Costs of Surgical Patients Treated at Major Teaching and Nonteaching Hospitals: A National Matched Analysis. Ann Surg 271(3): 412-421, 2020.

190. Silber, J. H., Rosenbaum, P. R., Reiter, J. G., Hill, A. S., Jain, S., Wolk, D. A., Small, D. S., Hashemi, S., Niknam, B. A., Neuman, M. D., Fleisher, L. A., Eckenhoff, R.: Alzheimer"s Dementia After Exposure to Anesthesia and Surgery in the Elderly: A Matched Natural Experiment Using Appendicitis. Ann Surg 2020.

191. Silber, J. H., Rosenbaum, P. R., Reiter, J. G., Hill, A. S., Jain, S., Wolk, D. A., Small, D. S., Hashemi, S., Niknam, B. A., Neuman, M. D., Fleisher, L. A., Eckenhoff, R.: Alzheimer"s Dementia After Exposure to Anesthesia and Surgery in the Elderly: A Matched Natural Experiment Using Appendicitis. Ann Surg 2020.

192. Silber, J. H., Rosenbaum, P. R., Reiter, J. G., Hill, A. S., Jain, S., Wolk, D. A., Small, D. S., Hashemi, S., Niknam, B. A., Neuman, M. D., Fleisher, L. A., Eckenhoff, R.: Alzheimer"s Dementia After Exposure to Anesthesia and Surgery in the Elderly: A Matched Natural Experiment Using Appendicitis. Ann Surg 2020.

193. Yao, W., Wang, T., Jiang, B., Gao, F., Wang, L., Zheng, H., Xiao, W., Yao, S., Mei, W., Chen, X., Luo, A., Sun, L., Cook, T., Behringer, E., Huitink, J. M., Wong, D. T., Lane-Fall, M., McNarry, A. F., McGuire, B., Higgs, A., Shah, A., Patel, A., Zuo, M., Ma, W., Xue, Z., Zhang, L. M., Li, W., Wang, Y., Hagberg, C., O'Sullivan, E. P., Fleisher, L. A., Wei, H.: Emergency tracheal intubation in 202 patients with COVID-19 in Wuhan, China: lessons learnt and international expert recommendations. Br J Anaesth 125(1): e28-e37, 2020.

194. Bagchi, S., Mak, J., Li, Q., Sheriff, E., Mungai, E., Anttila, A., Soe, M. M., Edwards, J. R., Benin, A. L., Pollock, D. A., Shulman, E., Ling, S., Moody-Williams, J., Fleisher, L. A., Srinivasan, A., Bell, J. M.: Rates of COVID-19 Among Residents and Staff Members in Nursing Homes - United States, May 25-November 22, 2020. MMWR Morb Mortal Wkly Rep 70(2): 52-55, 2021.

195. Benin, A. L., Soe, M. M., Edwards, J. R., Bagchi, S., Link-Gelles, R., Schrag, S. J., Herzer, K., Verani, J. R., Budnitz, D., Nanduri, S., Jernigan, J.,

Edens, C., Gharpure, R., Patel, A., Wu, H., Golshir, B. C., Jaffe, A., Li, Q., Srinivasan, A., Shulman, E., Ling, S. M., Moody-Williams, J., Fleisher, L. A., Pollock, D. A., Bell, J., Nhsn Team: Ecological Analysis of the Decline in Incidence Rates of COVID-19 Among Nursing Home Residents Associated with Vaccination, United States, December 2020-January 2021. J Am Med Dir Assoc 22(10): 2009-2015, 2021.

196. Damschroder, L. J., Knighton, A. J., Griese, E., Greene, S. M., Lozano, P., Kilbourne, A. M., Buist, D. S. M., Crotty, K., Elwy, A. R., Fleisher, L. A., Gonzales, R., Huebschmann, A. G., Limper, H. M., Ramalingam, N. S., Wilemon, K., Ho, P. M., Helfrichfcr, C. D.: Recommendations for strengthening the role of embedded researchers to accelerate implementation in health systems: Findings from a state-of-the-art (SOTA) conference workgroup. Healthc (Amst) 8 Suppl 1: 100455, 2021.

197. Graff, V., Clapp, J. T., Heins, S. J., Chung, J. J., Muralidharan, M., Fleisher, L. A., Elkassabany, N. M.: Patient Involvement in Anesthesia Decision-making: A Qualitative Study of Knee Arthroplasty. Anesthesiology 2021.

198. Hadler, R. A., Clapp, J. T., Chung, J. J., Gutsche, J. T., Fleisher, L. A.: Escalation and Withdrawal of Treatment for Patients on Extracorporeal Membrane Oxygenation: A Qualitative Study. Ann Surg 2021.

199. Ho, J., Susser, P., Christian, C., DeLisser, H., Scott, M. J., Pauls, L. A., Huffenberger, A. M., Hanson, C. W., 3rd, Chandler, J. M., Fleisher, L. A., Laudanski, K.: Developing the eMedical Student (eMS)-A Pilot Project Integrating Medical Students into the Tele-ICU during the COVID-19 Pandemic and beyond. Healthcare (Basel) 9(1), 2021.

200. Mahajan, A., Esper, S. A., Cole, D. J., Fleisher, L. A.: Anesthesiologists" Role in Value-based Perioperative Care and Healthcare Transformation. Anesthesiology 134(4): 526-540, 2021.

201. Mantha, S., Tripuraneni, S. L., Fleisher, L. A., Roizen, M. F., Mantha, V. R. R., Dasari, P. R.: Relative contribution of vitamin D deficiency to subclinical atherosclerosis in Indian context: Preliminary findings. Medicine (Baltimore) 100(32): e26916, 2021.

202. Neuman, M. D., Feng, R., Carson, J. L., Gaskins, L. J., Dillane, D., Sessler, D. I., Sieber, F., Magaziner, J., Marcantonio, E. R., Mehta, S., Menio, D., Ayad, S., Stone, T., Papp, S., Schwenk, E. S., Elkassabany, N., Marshall, M., Jaffe, J. D., Luke, C., Sharma, B., Azim, S., Hymes, R. A., Chin, K. J., Sheppard, R., Perlman, B., Sappenfield, J., Hauck, E., Hoeft, M. A., Giska, M., Ranganath, Y., Tedore, T., Choi, S., Li, J., Kwofie, M. K., Nader, A., Sanders, R. D., Allen, B. F. S., Vlassakov, K., Kates, S., Fleisher, L. A., Dattilo, J., Tierney, A., Stephens-Shields, A. J., Ellenberg, S.

S., Regain Investigators: Spinal Anesthesia or General Anesthesia for Hip Surgery in Older Adults. N Engl J Med 2021.

203. Onuoha, O., Heins, S. J., Clapp, J. T., Muralidharan, M., Baranov, D. Y., Fleisher, L. A., Gordon, E. K. B.: Improving Formative Feedback in the Operating Room Setting: Developing and Implementing an Initiative to Improve Feedback Quality and Culture. Acad Med 2021.

204. Shannon, A. B., Roberson, J. L., Keele, L., Bharani, T., Song, Y., Miura, J. T., Kelz, R. R., Dempsey, D. T., Fleisher, L. A., DeMatteo, R. P., Karakousis, G. C.: Impact of COVID-19 Restrictions on Demographics and Outcomes of Patients Undergoing Medically Necessary Non-Emergent Surgeries During the Pandemic. World J Surg Page: 1-9, 2021.

205. Williams, C. S., Zheng, Q., White, A. J., Bengtsson, A. I., Shulman, E. T., Herzer, K. R., Fleisher, L. A.: The association of nursing home quality ratings and spread of COVID-19. J Am Geriatr Soc 69(8): 2070-2078, 2021.

Research Publications, peer-reviewed reviews:

1. Flood C, Fleisher LA: Preparation of the cardiac patient for noncardiac surgery. American Family Physician 75(5): 656-665, March 2007.

2. Daumerie G, Fleisher LA: Perioperative beta-blocker and statin therapy. Curr Opin Anaesthesiol. 21: 60-5, 2008.

3. Archan S, Fleisher LA: From creatine kinase-MB to troponin: the adoption of a new standard. Anesthesiology 112(4): 1005-12, Apr 2010.

4. Neuman, Mark D. Schwartz, J Sanford. Fleisher, Lee A.: Commentary: what conclusions can we draw from recent analyses of anesthesia provider model and patient outcomes?. Health Services Research 45(5 Pt 1): 1390-6; discussion 1397-1406, Oct 2010.

5. Gordon EK, Fleisher LA.: Reducing perioperative cardiac morbidity and mortality: is this the right goal? Curr Opin Crit Care 19: 342-5, Aug 2013.

6. Royo Marc B, Fleisher Lee A: Chasing myocardial outcomes: perioperative myocardial infarction and cardiac troponin. Canadian journal of anaesthesia = Journal canadien d'anesthesie 63(2): 227-232, Dec 2015.

7. Fleisher LA: The Value of Preoperative Assessment Before Noncardiac Surgery in the Era of Value-Based Care. Circulation 136(19): 1769-1771, Nov 2017.

8. Fleisher Lee A: Quality Anesthesia: Medicine Measures, Patients Decide. Anesthesiology 129(6): 1063-1069, Sep 2018.

9. Wang, T., Deng, X., Huang, Y., Fleisher, L. A., Xiong, L.: Road to Perioperative Medicine: A Perspective From China. Anesth Analg 129(3): 905-907, 2019.

10. Lane-Fall Meghan B, Gordon Emily K B, Valentine Elizabeth A, Black Stephanie A, Kapur Patricia A, Fleisher Lee A: Fostering belonging in academic anaesthesiology: faculty and department chair perspectives on supporting women anaesthesiologists. British journal of anaesthesia 124(3): e155-e159, Jan 2020.

11. Mantha Srinivas, Tripuraneni Sudha Lakshmi, Fleisher Lee A, Roizen Michael F: Use of Common Carotid Intima-Media Thickness Measured by Ultrasound Echo-Tracking in Cardiovascular Risk Stratification Before Noncardiac Surgery in Low-Risk Category: A Research Idea. A&A practice Jan 2020.

12. Mantha, S., Tripuraneni, S. L., Roizen, M. F., Fleisher, L. A.: Proposed Modifications in the 6-minutue Walk Test for Potential Application in Patients with mild Coronavirus Disease 2019 (COVID-19): A Step to Optimize Triage Guidelines. Anesth Analg 2020.

13. Mahajan, A., Esper, S. A., Cole, D. J., Fleisher, L. A.: Anesthesiologists" Role in Value-based Perioperative Care and Healthcare Transformation. Anesthesiology 134(4): 526-540, 2021.

Contributions to peer-reviewed research publications, participation cited but not by authorship:

1. Carson Jeffrey L, Terrin Michael L, Noveck Helaine, Sanders David W, Chaitman Bernard R, Rhoads George G, Nemo George, Dragert Karen, Beaupre Lauren, Hildebrand Kevin, Macaulay William, Lewis Courtland, Cook Donald Richard, Dobbin Gwendolyn, Zakriya Khwaja J, Apple Fred S, Horney Rebecca A, Magaziner Jay: Liberal or restrictive transfusion in high-risk patients after hip surgery. The New England journal of medicine 365(26): 2453-62, Dec 2011. PMCID: PMC3268062

2. Kahan BC, Koulenti D, Arvaniti K, Beavis V, Campbell D, Chan M, Moreno R, Pearse RM; International Surgical Outcomes Study (ISOS) group: Critical care admission following elective surgery was not associated with survival benefit: prospective analysis of data from 27 countries. Intensive Care Med. 43(7): 971-9, Jul 2017.

3. Abbott T E F, Ahmad T, Phull M K, Fowler A J, Hewson R, Biccard B M, Chew M S, Gillies M, Pearse R M: The surgical safety checklist and patient outcomes after surgery: a prospective observational cohort study, systematic review and meta-analysis. British journal of anaesthesia 120(1): 146-155, Jan 2018.

4. Barnes Jonathan, Hunter Jennifer, Harris Steve, Shankar-Hari Manu, Diouf Elisabeth, Jammer Ib, Kalkman Cor, Klein Andrew A, Corcoran Tomas, Dieleman Stefan, Grocott Michael P W, Mythen Michael G: Systematic review and consensus

definitions for the Standardised Endpoints in Perioperative Medicine (StEP) initiative: infection and sepsis. British journal of anaesthesia 122(4): 500-508, Apr 2019. PMCID: PMC6435904

Abstracts:

1. Archan S, Roscher C, Fairman R, Fleisher LA: Revised cardiac risk index (lee) and perioperative cardiac events as predictors of long-term mortality inpatients undergoing endovascular abdominal aortic aneurysm repair. Eur J Anaesth 26(S45): 56, 2--9.

2. Akhtar S, Fleisher LA, Jermyn R, Chan DW, Rosenbaum SH: Detection of Perioperative Ischemia is Improved by Troponin (TnI) Measurement. Anesthesiology 93: A253, 2000.

3. Akhtar S, Fleisher LA, Jermyn R, Weiss J, Rosenbaum SH: Incidence of perioperative myocardial injury based on ACC/AHA guidelines in vascular surgery patients. Anesthesiology 93: A260, 2000.

4. Fleisher LA, Ferrer JA, Pasternak LR, Barash PG: Safety of outpatient surgery in hospitals versus free-standing facilities in the elderly. Anesthesiology 92: A1176, 2000.

5. Katz J, Feldman MA, Bass EB, Lubomski LH, Tielsch JM, Betty BG, Fleisher LA: Anesthesia for cataract surgery: patient perceptions of pain and side-effects. IOVS 41: S740, 2000.

6. Reeves SW, Fleisher LA, Friedman DS, Lubomski LH, Bass EB, Schein OD: A decision analysis of anesthesia management for cataract surgery. IOVS 41: S740, 2000.

7. Fleisher LA, Naqibuddin M, Yu DL, Thamer M, Carter HB, Walsh PC: Discharge hemoglobin: does it effect quality of life during recovery? Anes Analg 92: S99, 2001.

8. Kim LJ, Martinez EA, Faraday N, Fleisher LA, Chan D, Pronovost PJ: Cardiac troponin I predicts the risk of mortality in high-risk surgical patients. Crit Care Med 29(12): A28, 2001.

9. Wu C, Naquibuddin M, Jermyn RM, Fleisher LA: Does health-related quality-of-life differ according to postoperative analgesic regimen? Anes Analg 92: S272, 2001.

10. Yataco AR, Sung J, Fleisher LA, Bacher AC, Turner KL, Deregis JR, Stewart KJ: Habitual physical activity but not peak aerobic capacity predicts heart rate variability in older adults. Circulation 2001.

11. Ellis JE, Lobato E, Fleisher LA, Ford-Thomas Z, Reno K: Randomized trial of

esmolol vs. nitroglycerin for myocardial ischemia/infarction prophylaxis during high-risk noncardiac surgery. Anesthesiology 96: A210, 2002.

12. Fleisher LA, Pasternak R, Barash PG, Anderson G: Safety of outpatient surgery in the elderly: the importance of the patient, system and location of care. Anesthesiology 96: A1127, 2002.

13. Fleisher LA, Pasternak R, Lyles A: A novel index of elevated risk for hospital admission or death immediately following outpatient surgery. Anesthesiology 07: A38, 2002.

14. Poldermans D, Bax JJ, Kertai MD, Klein J, Fleisher LA, Roelandt JRTC, Eric Boersma E: Statins Are Associated with a Reduced Incidence of perioperative mortality in high-risk patients undergoing non-cardiac surgery. Circulation 2002.

15. Koch M, Goldstein R, Gevirtz C, Showan A, Hoops T, Fleisher L: Office-based anesthesia for colonoscopy by gastroenterologists: higher rates of colon polyp detection. Abstracts of the Society of Ambulatory Anesthesia Annual Meeting 2005 May 2005.

16. Fleisher L, Newman M, St. Aubin L, Cropp A, Billing C, Mackey W, Poldermans D, Corbalan, Pereira A, Coriat P: Efficacy of zoniporide, a Na/H exchange ion inhibitor, for reducing perioperative cardiovascular events in vascular surgery patients Anesth Analg 100: SCA44, 2005.

17. Sheikh S, Haider S, Cappelleri JC, Lee WC, Gold K, Stephens J, Fleisher LA: Health Status in high-risk patients undergoing noncardiac vascular surgery in the United States. Proceedings of the International Society for Pharmacoeconomics and Outcomes Research 2005.

18. Agarwal SJ, Erslon MG, Bloom JD, Fleisher LA: Anesthesia time and risk of postoperative pulmonary complications in orthopedic surgery. Anesthesiology Page: A1498, 2011.

19. Chuy K, Zhe Y, Smith DS, Fleisher LA, Liu R: Newly designed preoperative evaluation form for ICU patients to help reduce missing preoperative information. Anesthesiology Page: A1197, 2011.

20. Liu R, Yan Z Xue W, Brown S, Barnett R, Mullen J, Fleisher LA: Different dynamics of elective case cancellation for inpatient and outpatient in a large academic center. Anesthesiology Page: A742, 2011.

21. Flynn DN, Speck RM, David G, Fleisher LA: Hospital costs associated with complication following open colectomy. Anesthesiology Page: A2057, 2013.

Editorials, Reviews, Chapters, including participation in committee reports (print or other

media):

1. Fleisher LA: Preoperative assessment of the patient with cardiovascular disease. Current Op Anesth 4: 30-34, 1991 Notes: Review.

2. Fleisher LA, Barash PG: Preoperative cardiac evaluation for noncardiac patient for noncardiac surgery: a functional approach. Anesth Analg 74: 586-598, Apr 1992 Notes: Review.

3. Carter J, Fleisher LA, Barash PG: Assessment of perioperative ischemia. In: Advances in Anesthesia. Barash, Stoelting (eds.). 9: 89-120, 1992 Notes: Chapter.

4. Fleisher LA: Perioperative myocardial ischemia and infarction. In: Perioperative Myocardial and Infarction. Beattie, Fleisher (eds.). International Anesthesiology Clinics Winter, 30(1): 1-17, 1992 Notes: Chapter.

5. Fleisher LA: Perioperative assessment of the patient with cardiovascular disease undergoing noncardiac surgery. Current Op Anesth 5: 27-33, 1992 Notes: Review.

6. Jain D, Fleisher LA, Zaret BL: Diagnosis of a perioperative myocardial infarction in noncardiac surgery patients. In: Perioperative Myocardial and Infarction. Beattie, Fleisher (eds.). International Anesthesiology Clinics Winter, 30(1): 199-215, 1992 Notes: Chapter.

7. Rosenbaum SH, Fleisher LA: Was Einthoven a 21st century visionary? J Clin Anesth 4: 263-264, 1992 Notes: Editorial.

8. Fleisher LA, Barash PG: Preoperative evaluation of the cardiac patient for noncardiac surgery. Yale J Bio Med 66: 385-396, 1993 Notes: Review.

9. Fleisher LA, Barash PG: Anesthesia management for noncardiac surgery for the adult. In: Principles and Practice of Cardiac Anesthesia. Estefanous, Reves, Barash (eds.). 1993 Notes: Chapter.

10. Fleisher LA, Hulyalkar A: Cardiovascular testing for the 1990s. In: Advances in Anesthesiology. Barash, Lake (eds.). 11: 27-64, 1993 Notes: Chapter.

11. Fleisher LA: Review of: Manual of cardiac anesthesia, 2nd Edition. Anesth Analg. Thomas S (eds.). 77: 875, 1993 Notes: Book Review.

12. Fleisher LA: Review of: Perioperative management of pacemaker patients. Anesthesiology. Atlee JL, Gombotz H, Tscheliessnnigg KH (eds.). 78: 1199, 1993 Notes: Book Review.

13. Fleisher LA: Perioperative assessment of the patient with cardiovascular disease undergoing noncardiac surgery. Current Op Anesth 6: 24-29, 1993 Notes:

Review.

14. Fleisher LA: Review of: Monitoring in Anesthesia, 3rd Edition. J Cardiothor Vasc Anesth. Saidman LJ Smith NT (eds.). 8: 128, 1994 Notes: Book Review.

15. Fleisher LA, Barash PG: Risk stratification for noncardiac surgery. Circulation 89: 913, 1994 Notes: Letter.

16. Fleisher LA: Review of: Anesthesia and the patient with co-existing heart disease. Anesthesiology. Simpson JI (eds.). 80: 719, 1994 Notes: Book Review.

17. Fleisher LA: Review of: Perioperative Medicine. Anesthesiology. Goldman DR, Brown FH, Guarnieri DM (eds.). 80: 1184, 1994 Notes: Book Review.

18. Frank SM, Raja SN, Fleisher LA, Beattie C, Higgins MS, Breslow MJ: Adrenergic and cardiovascular manifestations of cold stress. In: Thermal Balance in Health and Disease: Recent Basic Research and Clinical Progress. Zeisberger, Schonbaum, Lomax (eds.). 1994 Notes: Chapter.

19. Higgins MS, Fleisher LA: A caution in the interpretation of heart rate variability data. Anesth Analg 79: 812, 1994 Notes: Letter.

20. Norris E, Fleisher LA: Preoperative cardiac risk assessment in patients presenting for major vascular surgery. Sem in Anesth 13: 2-13, 1994 Notes: Review.

21. Fleisher LA, Lehmann H: Comment on: The role of coronary angiography and coronary revascularization before noncardiac surgery. JAMA 274: 1671-1672, 1995 Notes: Letter.

22. Fleisher LA: Preoperative evaluation of the patient undergoing major vascular surgery. In: Anesthesiology Clinics of North America. 13: 53-65, 1995 Notes: Chapter.

23. Fleisher LA: Review of: Decision analysis in the clinical neurosciences, by Diederick Dippel. Med Decision Mak 15: 398-399, 1995 Notes: Book Review.

24. Smith-Stierer T, Fleisher LA: The patient with ischemic heart disease. In: Ambulatory Anesthesiology: A Problem Oriented Approach. McGoldrick (eds.). Williams & Wilkins, Baltimore, MD, Page: 168-179, 1995 Notes: Chapter.

25. Eagle KA, Brundage BH, Caitman BR, Ewy GA, Fleisher LA, Hertzer NR, Leppo LA, Ryan T, Schlant RC, Spencer WH, Spittell JA, Twiss RD: Guidelines for perioperative cardiovascular evaluation of the noncardiac surgery. A report of the American Heart Association/American College of Cardiology Task Force on Assessment of Diagnostic and Therapeutic Cardiovascular Procedures. Circulation 93: 1278-1317, 1996 Notes: Committee Report.

26. Eagle KA, Brundage BH, Chaitman BR, Ewy GA, Fleisher LA, Hertzer NR, Leppo LA, Ryan T, Schlant RC, Spencer WH, Spittell JA, Twiss RD: Guidelines for perioperative cardiovascular evaluation of the noncardiac surgery. A report of the American Heart Association/American College of Cardiology Task Force on Assessment of Diagnostic and Therapeutic Cardiovascular Procedures. J Am Coll Cardiol 27(4): 910-948, 1996 Notes: Committee Report.

27. Fleisher LA, Barash PG: The ROMI Protocol: do we have a rational approach. J Clin Anesth 8(3): 173-174, 1996 Notes: Editorial.

28. Fleisher LA, Eagle KA: Screening for cardiac disease in patients having noncardiac surgery. Ann Intern Med 124: 767-772, 1996 Notes: Editorial.

29. Fleisher LA: Perioperative management of the cardiac patient undergoing noncardiac surgery. American Society of Anesthesiologists (Refresher Course) 24: 71-84, 1996 Notes: Review.

30. Fleisher LA: Heart rate variability as an assessment of cardiovascular status in normal, disease and perioperative states. J Cardiothor Vasc Anesth 10(5): 6599-6671, 1996 Notes: Review.

31. Metzger, SE, Fleisher LA: Cost-Effective Modeling. Anesth Analg 83: 203-204, 1996 Notes: Letter.

32. Roizen MF, Fleisher LA: Medical guidelines by other societies: should we ignore or influence them? Anesth Analg 82: 679-680, 1996 Notes: Editorial.

33. Bernstein WK, Fleisher LA, Chernow B: Priorities in critically ill patients requiring anesthetic care. In: Problems in Anesthesia. 9(3): 277-288, 1997 Notes: Chapter.

34. Fleisher LA, Barash PG: Preoperative preparation of the elderly surgical patient. In: Problems in Anesthesia. 9(4): 525-535, 1997 Notes: Chapter.

35. Fleisher LA, Tuman K: What can we learn from provoking ischemia? Anesth Analg 84: 1177-1179, 1997 Notes: Editorial.

36. Fleisher LA: Preoperative evaluation of cardiac patient: preoperative evaluation in an era of cost containment. In: Problems in Anesthesia. 9(2): 143-152, 1997 Notes: Chapter.

37. Fleisher LA: Preoperative evaluation. In: Clinical Anesthesia, 3rd Edition. Barash, Cullen, Stoelting (eds.). 3: 443-459, 1997 Notes: Chapter.

38. Fleisher LA: Preoperative evaluation. In: Atlas of Anesthesiology. Miller R (eds.). Churchill Livingston, Page: Chapter 3, 1997 Notes: Chapter.

39. Fleisher LA: ...but, is suppression of postoperative ST segment depression an important outcome? Anesth Analg 84: 709-711, 1997 Notes: Editorial.

40. Fleisher LA: Ischemic Heart Disease. In: Anesthesiology Clinics of North America. 15: 49-67, 1997 Notes: Chapter.

41. Gold B, Fleisher LA: Management of outpatients with pre-existing diseases. In: Ambulatory Anesthesia and Surgery. W.B. Saunders, Page: 139-154, 1997 Notes: Chapter.

42. Marcucci C., Fleisher LA: Hypertension--Implications for anesthetic management. Current Op Anesth 10: 229-233, 1997 Notes: Review.

43. Stierer T, Fleisher LA: Preoperative cardiac evaluation of the cardiac patient for noncardiac surgery. Contemporary Surgery 51: 157, 1997 Notes: Review.

44. Fleisher LA, Barash PG: PTCA before noncardiac surgery: current state of the debate. J Cardiothorac Vasc Anesth 12: 499-500, 1998 Notes: Editorial.

45. Fleisher LA, Mantha S, Roizen MF: Medical technology assessment: an overview. Anesth Analg 87: 1271-1282, 1998 Notes: Review.

46. Fleisher LA, Mantha S: Technology assessment and determination of cost-effectiveness. In: Problems in Anesthesia. 10(3): 293-303, 1998 Notes: Chapter.

47. Fleisher LA: Pre-operative cardiac interventions in non-cardiac surgery. In: Bailliere's Clinical Anaesthesiology. Bailliere Tindall (eds.). Harcourt Brace & Company, Philadelphia, PA, 12(3): 419-432, 1998 Notes: Chapter.

48. Fleisher LA: Anesthetic management. In: Progress in Cardiovascular Disease. WB Saunders, 40(5): 441-452, 1998 Notes: Chapter.

49. Fleisher LA: Pre-operative cardiac evaluation before non-cardiac surgery. In: Bailliere's Clinical Anaesthesiology. Bailliere Tindall (eds.). Harcourt Brace & company, Philadelphia, PA, 12(3): 373-390, 1998 Notes: Chapter.

50. Curreri S, Nicholas EJ, Fleisher LA: Testing the limit for outpatient surgery: the importance of procedures. In: Problems in Anesthesia: Ambulatory Anesthesia. Lippincott Williams & Wilkins, Philadelphia, PA, 11: 54-63, 1999 Notes: Chapter.

51. Falcone RA, Zigelstein RC, Fleisher LA: Perioperative evaluation of elderly noncardiac surgical patients. In: Cardiovascular Disease in the Elderly, 2nd Edition. Telsch, Aronow W (eds.). Page: 687-738, 1999 Notes: Chapter.

52. Fleisher LA, Barash PG: Governmental databases, hospital information systems, and clinical outcomes: big brother or big help? Anesth Analg 89(4): 811-813, 1999 Notes: Editorial.

53. Fleisher LA, Bernstein WK: Quality of life and patient satisfaction surrounding cardiovascular surgery. In: Cardiac Anesthesia. Kaplan JA (eds.). WB Saunders, Page: 1337-1346, 1999 Notes: Chapter.

54. Fleisher LA: Preoperative cardiac evaluation before major vascular surgery. In: Problems in Anesthesia: Vascular Anesthesia. Lippincott Williams & Wilkins, Hagerstown, MD, 11(2): 167-178, 1999 Notes: Chapter.

55. Fleisher LA: Principles of outcome prediction in patients with cardiovascular disease. In: Outcome Measurement in Cardiovascular Medicine, Society of Cardiovascular Anesthesiologists Monograph. Kenneth Tuman (eds.). Lippincott Williams & Wilkins, Baltimore, MD, Page: 82-104, 1999 Notes: Chapter.

56. Fleisher LA: Role of the anesthesiologist in the next millennium: perioperative gatekeeper? ASA Newsletter 63(5): 11-12, 1999 Notes: Letter.

57. Frank SM, Fleisher LA: Temperature's importance in patient safety reviewed. APSF Newsletter 14(2): 20-21, 1999 Notes: Letter.

58. Miller ED, Fleisher LA: Antihypertensive therapy. In: Cardiac Anesthesia. Kaplan JA (eds.). WB Saunders, Page: 161-176, 1999 Notes: Chapter.

59. Berry AJ, Fleisher LA: Cause-specific mortality risks of anesthesiologists. Anesthesiology 93: 919-921, 2000 Notes: Editorial.

60. Bynoe TC, Fleisher LA: Anesthetic emergencies. In: Emergencies of the Head and Neck. Eisle D (eds.). Mosby, Page: 97-110, 2000 Notes: Chapter.

61. Fleisher LA: Ischemic heart disease. In: Handbook of preoperative assessment and management. Sweitzer B (eds.). Lippincott Williams & Wilkins, Philadelphia, PA, Page: 39-62, 2000 Notes: Chapter.

62. Fleisher LA: Perioperative cost finding: what are the goals? Am J Anesthesiology 27: 460, 2000 Notes: Editorial.

63. Fleisher LA: Clinical trials report on: A cost comparison in methohexital and propofol for ambulatory anesthesia. Current Anesth Reports 2(5): 398, 2000 Notes: Report.

64. Fleisher LA: Risk of Anesthesia. In: Anesthesia, 5th Edition. Miller R, Miller ED (eds.). Churchill-Livingstone, Page: 795-823, 2000 Notes: Chapter.

65. Fleisher LA: Real-time intraoperative monitoring of myocardial ischemia in noncardiac surgery. Anesthesiology 92: 1183-1188, 2000 Notes: Review.

66. Fleisher LA: Perioperative assessment. In: Cardiac, Thoracic and Vascular Anesthesia. Youngberg (eds.). Churchill Livingstone, Page: 3-19, 2000 Notes: Chapter.

67. Fleisher LA: Effect of perioperative evaluation and consultation on cost and outcome of surgical care. Curr Op Anesth 13: 209-213, 2000 Notes: Review.

68. Fleisher LA: Risks of anesthesia: do we continue to be as safe after we leave the hospitalenvironment? In: Problems in Anesthesia. 12: 102-109, 2000 Notes: Chapter.

69. Fleisher LA: Preoperative cardiac evaluation before noncardiac surgery. In: Current Reviews in Clinical Anesthesia 13: 209-213, 2000 Notes: Chapter.

70. Fleisher LA: Anesthesiologists as perioperative physicians: the con perspective. In: Problems in Anesthesia. 12: 46-48, 2000 Notes: Chapter.

71. Frank SM, Tran KM, Fleisher LA, Elrahmany HK: Clinical importance of body temperature in the surgical patient. J Thermal Biology 25: 151-155, 2000 Notes: Review.

72. Mantha A, Fleisher LA, Roizen MF, Foss JF: Cost-effectiveness and benefit of preoperative work-up and preparation for vascular surgery, Chapter 2. In: Cardiac, Thoracic and Vascular Anesthesia. Youngberg JA, Lake CL, Roizen MF, Wilson RS (eds.). Churchill Livingstone, Page: 20-40, 2000 Notes: Chapter.

73. Sen D, Sweitzer B, Fleisher LA: Nonischemic heart disease. In: Handbook of Preoperative Assessment and Management. Sweitzer B (eds.). Lippincott Williams & Wilkins, Philadelphia, PA, Page: 63-96, 2000 Notes: Chapter.

74. Wu CL, Fleisher LA: Outcomes research in regional anesthesia and analgesia. Anesth Analg 91: 1232-1242, 2000 Notes: Review.

75. Wu CL, Fleisher LA: Outcomes in perioperative medicine and anesthesiology: into the next millennium. In: Anesthesiology Clinics of North America. 18: 633-645, 2000 Notes: Chapter.

76. Fleisher LA, Barash PG: The Adult Noncardiac Patient. Cardiac Anesthesia: principles and clinical practice. Estafanous FG, Barash PG, Reves JG (eds.). Lippincott Williams & Wilkins, Page: 911-930, 2001.

77. Fleisher LA, Eagle KA: Lowering cardiac risks of noncardiac surgery: strategies to lower risk. N Engl J Med 345: 1677-1682, 2001 Notes: Review.

78. Fleisher LA: Assessment of patients with heart disease for fitness for noncardiac surgery. In: Essential Cardiology: Principles and Practice. Rosendorff C (eds.). WB Saunders, Philadelphia, PA, Page: 764-779, 2001 Notes: Chapter.

79. Fleisher LA: Routine laboratory testing in the elderly: is it indicated? Anesth Analg 93: 249-250, 2001 Notes: Editorial.

80. Fleisher LA: Risk Indices: what is their value to the clinician and patient? Anesthesiology 94: 191-193, 2001 Notes: Editorial.

81. Fleisher LA: Preoperative evaluation. In: Clinical Anesthesia, 4th Edition. Barash P, Cullen B, Stoelting R. (eds.). Lippincott Williams & Wilkins, Page: 473-490, 2001 Notes: Chapter.

82. Fleisher LA: Wahr J: Epidemiology and future of cardiothoracic anesthesia. In: Textbooks of Cardiovascular Anesthesia. Daniel Thys (eds.). McGraw Hill, Page: 3-10, 2001 Notes: Chapter.

83. Pronovost P, Berenholtz S, Fleisher LA: How to apply the principles of evidence based medicine. In: Conducting Research in Anaesthesia and Intensive Care Medicine. Zbinden AM, Thomson D (eds.). Butterworth Heinemann, Page: 278-298, 2001 Notes: Chapter.

84. Wu CL, Carter HB, Naqibuddin M, Fleisher LA: Technique determines efficacy of local anesthetic for outpatient prostate biopsy. Urology 8: 636, 2001 Notes: Letter.

85. Watson TA, Fleisher LA: Acute heart failure in the postoperative period. Acute Heart Failure Mebazaa A, Gheorghiade M, Zannad F, Parrillo J (eds.). Springer, 200.

86. Appel LJ., Robinson KA., Guallar E., Erlinger T., Masood SO., Jehn M., Fleisher L., Powe NR., Bass EB.: Utility of blood pressure monitoring outside of the clinic setting. [Review] [0 refs] Evidence Report: Technology Assessment (Summary) (63): 1-5, Nov 2002.

87. Berry C, Wu CL, Fleisher LA: Outcomes research: the effect of recent clinical research on perioperative anesthesia practice. Clin Researcher 2: 2-6, 2002 Notes: Review.

88. Eagle KA, Berger PB, Calkins H, Chaitman BR, Ewy GA, Fleischmann KE, Fleisher LA, Foehlich JB, Gusberg RJ, Leppo JA, Ryan T, Schalnt RC,Winters WL: ACC/AHA Guidelines for perioperative cardiovascular evaluation for noncardiac surgery update- executive summary. J Am Coll Cardiol 39(3): 542-553, 2002 Notes: Committee Report.

89. Fleisher LA, Anderson GF: Perioperative risk: how can we study the influence of provider characteristics? Anesthesiology 96: 1044-1052, 2002 Notes: Editorial.

90. Fleisher LA, Eagle KA: Guidelines on perioperative cardiovascular evaluation: what have we learned over the past 6 years to warrant an update? Anesth Analg 94: 1378-1379, 2002 Notes: Editorial.

91. Fleisher LA: Review of: Anesthesia for the cardiac patient, by Christopher A. Troianos. Anesth Analg 95: 1468-1469, 2002 Notes: Book Review.

92. Fleisher LA: Why did my attending cancel the case, and was he correct in doing so? Inspirations 2002 Notes: Letter.

93. Fleisher LA: Preoperative evaluation of the patient with hypertension. JAMA 287: 2043-2046, 2002 Notes: Review.

94. Fleisher LA: Evaluation of the patient with cardiac disease undergoing noncardiac surgery: an update on the original AHA/ACC Guidelines. International Anesthesiology Clinics 40(2): 109-120, 2002 Notes: Review.

95. Nass C, Fleisher LA: Diagnosing perioperative myocardial infarction in cardiothoracic and vascular surgery. Seminars Cardiothorac Vasc Anes 6(3): 219-227, 2002 Notes: Review.

96. Pasternak LR, Arens JF, Caplan RA, Connis RT, Fleisher LA, Flowerdew R, Gold BS, Mahew JF, Nickinovich DG, Rice LJ, Roizen MF, Twersky RS: Practice advisory for preanesthesia evaluation: a report by the American Society of Anesthesiologists Task Force on Preanesthesia Evaluation. Anesthesiology 96: 485-496, 2002 Notes: Committee Report.

97. Fleisher LA, Barash PG: Treatment of coronary artery disease in the year 2003. J Cardiothorac Vasc Anesth 17: 258-259, 2003 Notes: Editorial.

98. Stierer S, Fleisher LA: Challenging patients in an ambulatory setting. In: Anesthesiology Clinics of North America. 21: 243-261, 2003 Notes: Chapter.

99. Fleisher LA: Preoperative cardiac evaluation. Anesthesiol Clin North America 22(1): 59-75, Mar 2004.

100. Falcone R, Ziegelstein R, Fleisher LA: Assessment of patients with heart disease for noncardiac surgery. In: Essential Cardiology: Principles and Practice. Rosendorff C (eds.). WB Saunders, Philadelphia, PA, Page: In Press, 2004 Notes: Chapter.

101. Fleisher LA: Is outcomes research a waste of time? Anesth Analg 98, 2004 Notes: Review.

102. Fleisher LA: Preoperative cardiac evaluation before major vascular surgery. In: Vascular Anesthesia, 2nd Edition. Kaplan JA (eds.). Churchill Livingstone, Page: 93-105, 2004 Notes: Chapter.

103. Stevens RD., Fleisher LA.: Strategies in the high-risk cardiac patient undergoing non-cardiac surgery. [Review] [106 refs] Best Practice & Research in Clinical Anesthesiology 18(4): 549-63, December 2004.

104. Floyd T, Fleisher LA: Off-pump coronary artery bypass and the hypothesis from which it grew: is it yet to be tested? What are the downsides of the lingering questions? Anesthesiology 102(1): 3-5, Jan 2005.

105. Landesberg G, Mosseri M, Fleisher LA: Coronary revascularization before vascular surgery. N Engl J Med 352(14): 1492-5, April 2005.

106. Fleisher LA: Cardiac risk in noncardiac surgery: new insights in management. American College of Cardiology Current Journal REview 14: 5-8, May 2005.

107. Augoustides J, Fleisher LA: Comments on "Randomized controlled trials of aprotonin in cardiac surgery: could clinical equipoise have stopped the bleeding? Clinical Trials 2: 229-232, 2005.

108. Fleisher LA, Eagle KA: Anesthesia and noncardiac surgery in patients with heart disease. Braunwald's Heart Disease 7th edition. Zipes DP, Libby P, Bonow RO, Braunwald E (eds.). Elsevier Saunders, Page: 2021-2035, 2005.

109. Gupta A, Fleisher LA: What outcomes are important in ambulatory anesthesia? Ambulatory anesthesia & perioperative analgesia. Steele SM, Nielsen KC, Klein SM (eds.). McGraw-Hill, 2005.

110. Savino J, Fleisher LA: Assessment of patients with heart disease for fitness for noncardiac surgery. Essential Cardiology: principles and practice 2nd edition. Rosendorff C (eds.). Humana Press, Totowa, NJ, Page: 747-762, 2005.

111. Thomsen R, Fleisher LA: Anesthesia and Patient Positioning. Advanced Therapy in Minimally Invasive Surgery. Talamini M (eds.). BD Decker, Inc. 2005.

112. Fleisher LA, Eckenhoff RG.: Image not living up to goal. Anesthesiology. 105(3): 626-7, Sep 2006.

113. Ochroch EA, Fleisher LA: Retrospective analysis: looking backward to point the way forward. Anesthesiology 105(4): 643-4, Oct 2006.

114. American College of Cardiology; American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2002 Guidelines on

Perioperative Cardiovascular Evaluation for Noncardiac Surgery); American Society of Echocardiography; American Society of Nuclear Cardiology; Heart Rhythm Society; Society of Cardiovascular Anesthesiologists; Society for Cardiovascular Angiography and Interventions; Society for Vascular Medicine and Biology; Fleisher LA, Beckman JA, Brown KA, Calkins H, Chaikof E, Fleischmann KE, Freeman WK, Froehlich JB, Kasper EK, Kersten JR, Riegel B, Robb JF, Smith SC Jr, Jacobs AK, Adams CD, Anderson JL, Antman EM, Faxon DP, Fuster V, Halperin JL, Hiratzka LF, Hunt SA, Lytle BW, Nishimura R, Page RL, Riegel B.: ACC/AHA 2006 guideline update on perioperative cardiovascular evaluation for noncardiac surgery: focused update on perioperative beta-blocker therapy: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery) J Am Coll Cardiol 47(11): 2343-55, 2006.

115. Fleisher LA, Beckman JA, Brown KA, Calkins H, Chaikof E, Fleischmann KE, Freeman WK, Froehlich JB, Kasper EK, Kersten JR, Riegel B, Robb JF, Smith SC Jr, Jacobs AK, Adams CD, Anderson JL, Antman EM, Faxon DP, Fuster V, Halperin JL, Hiratzka LF, Hunt SA, Lytle BW, Nishimura R, Page RL, Riegel B; American College of Cardiology/American Heart Association Task Force on Practice Guidelines Writing Committee to Update the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery; American Society of Echocardiography; American Society of Nuclear Cardiology; Heart Rhythm Society; Society of Cardiovascular Anesthesiologists; Society for Cardiovascular Angiography and Interventions; Society for Vascular Medicine and Biology.: ACC/AHA 2006 guideline update on perioperative cardiovascular evaluation for noncardiac surgery: focused update on perioperative beta-blocker therapy: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines Circulation 113(22): 2662-74, 2006.

116. Gutsche JT, Fleisher: Hypertension after noncardiac vascular surgery. Advanced therapy in Hypertension and Vascular Disease. Mohler ER, Townsend RR (eds.). BC Becker, Page: 690-701, 2006.

117. Hecker JG, Laslett L, Campbell E, Nunnally M, O'connor A, Ellis JE, Frogel JK, Fleisher LA. : Case 2-2006Catastrophic Cardiovascular Collapse During Carotid Endarterectomy. J Cardiothorac Vasc Anesth 20: 259-68, 2006.

118. Horak J, Fleisher LA: Assessment of cardiac risk and cardiology consultation: examining, imaging, optimizing, and recommending. Kaplan's cardiac anesthesia (5th edition). Kaplan JA (eds.). Elsevier Saunders, 2006.

119. John AD, Fleisher LA: Electrocardiography: the ECG. Anesthesiol Clin. 24(4): 697-715, Dec 2006.

120. Kersten JR, Fleisher LA: Statins: The Next Advance in Cardioprotection? Anesthesiology 105: 1079-80, 2006.

121. Kukafka JD, Fleisher LA: Anesthesia. General Surgery Review Illustrated, 2nd edition 2006.

122. Macario A, Fleisher LA: Is There Value in Obtaining a Patient's Willingness to Pay for a Particular Anesthetic Intervention? Anesthesiology 104: 906-9, 2006.

123. Macario A, Fleisher LA.: Is There Value in Obtaining a Patient's Willingness to Pay for a Particular Anesthetic Intervention? Anesthesiology 104: 906-9, 2006.

124. Neligan PJ, Fleisher LA: Obesity and Diabetes: Evidence of Increased Perioperative Risk? Anesthesiology 104: 398-400, 2006.

125. Thomsen R, Fleisher LA: Anesthesia and patient positioning. Advanced Therapy in Minimally Invasive Surgery. Talamini MA (eds.). BC Decker, Inc., Hamilton, Page: 11-20, 2006.

126. Kersten JR, Fleisher LA: Drug-eluting coronary stents: what are the risks? Anesthesiology 106(5): 898-900, May 2007.

127. Augoustides JFleisher LA: Advancing Perioperative Prediction of Cardiac Risk after Vascular Surgery: Does Postoperative N-terminal Pro-brain Natriuretic Peptide Do the Trick? Anesthesiology 106: 1080-2, Jun 2007.

128. Augoustides J, Fleisher LA: Advancing perioperative prediction of cardiac risk after vascular surgery: does postoperative N-terminal pro-brain natriuretic peptide do the trick? Anesthesiology 106(6): 1080-2, Jun 2007.

129. Fleisher LA: The preoperative evaluation: an opportunity for education and other strategies to improve care. J Cardiothorac Vasc Anesth 21(3): 323-4, Jun 2007.

130. Fleisher LA: The preoperative electrocardiogram: what is the role in 2007? Ann Surg 246(2): 171-2, Aug 2007.

131. Fleisher LA: Perioperative {beta-Blockade: How Best to Translate Evidence into Practice. Anesth Analg 104: 1-3, 2007.

132. Fleisher LA: Should my outpatient center have a beta blocker protocol? Curr Opin Anesth 20: 526-30, 2007.

133. Fleisher LA, Beckman JA, Brown KA, Calkins H, Chaikof E, Fleischmann KE, Freeman WK, Froehlich JB, Kasper EK, Kersten JR, Riegel B, Robb JF, Smith SC Jr, Jacobs AK, Adams CD, Anderson JL, Antman EM, Faxon DP, Fuster V, Halperin JL, Hiratzka LF, Hunt SA, Lytle BW, Nishimura R, Page RL, Riegel B:

ACC/AHA 2006 Guideline Update on Perioperative Cardiovascular Evaluation for Noncardiac Surgery: Focused Update on Perioperative Beta-Blocker Therapy -- A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery). Anesth Analg 104: 15-26, 2007.

134. Vernick W, Fleisher LA: "Beta blockade" Geriatric Anesthesia. Sieber FE (eds.). McGraw-Hill, Page: 233-46, 2007.

135. Augoustides JG, Fleisher LA: The future for B-type natriuretic peptide in preoperative assessment. Anesthesiology 108(2): 332-3, Feb 2008.

136. Fleisher Lee A, Beckman Joshua A, Brown Kenneth A, Calkins Hugh, Chaikof Elliott, Fleischmann Kirsten E, Freeman William K, Froehlich James B, Kasper Edward K, Kersten Judy R, Riegel Barbara, Robb John F, Smith Sidney C, Jacobs Alice K, Adams Cynthia D, Anderson Jeffrey L, Antman Elliott M, Buller Christopher E, Creager Mark A, Ettinger Steven M, Faxon David P, Fuster Valentin, Halperin Jonathan L, Hiratzka Loren F, Hunt Sharon A, Lytle Bruce W, Nishimura Rick, Ornato Joseph P, Page Richard L, Riegel Barbara, Tarkington Lynn G, Yancy Clyde W: ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery). Anesthesia and analgesia 106(3): 685-712, Mar 2008.

137. Fleisher LA, Poldermans D: Perioperative beta blockade: where do we go from here? Lancet 371(9627): 1813-4, May 2008.

138. Fleisher LA: Implications of preoperative heart failure: the next frontier in perioperative medicine? Anesthesiology 51(13): 1321-2, 2008.

139. Fleisher LA, Eagle KA: Anesthesia and noncardiac surgery in patients with heart disease. Braunwald's Heart Disease 8th edition. Libby P, Bonow RO, Mann DL, Zipes DP, Baunwald E (eds.). Saunders Elsevier, Page: 2013-2032, 2008.

140. Fleisher LA, Newman MF: Implications of perioperative morbidity on long-term outcomes. Perioperative medicine: managing for outcome. Newman MF, Fleisher LA, Fink MP (eds.). Saunders Elsevier, Page: 3-10, 2008.

141. Kwon E, Fleisher LA, Eagle KA: Cardiac risk assessment in noncardiac surgery. Perioperative medicine: managing for outcomes. Newman MF, Fleisher LA, Fink MP (eds.). Saunders Elsevier, Page: 45-60, 2008.

142. Miller J, Fleisher LA, Carson JL: Fluid management. Geriatric Anesthesiology 2nd

edition. Silverstein JH, Rooke GA, Reves JG, McLeskey CH (eds.). Springer, 2008.

143. Smith DS, Fleisher LA: Approaches to Quality Improvement in Anesthesia Care. Anesthesiology: Principles and Practice. Longnecker DE, Brown DL, Newman MF, Zapol WM (eds.). McGraw-Hill, Page: 452-64, 2008.

144. Stearns JD, Fleisher LA: Epidemiology and Predictors. Complications in Anesthesiology (3rd edition). Labato E, Gravenstein N, Kirby RR (eds.). Wolters Kluwer Lippincott Williams & Wilkens, Page: 204-219, 2008.

145. Vernick W, Fleisher LA: Risk stratification. Best Practice & Research Clinical Anaesthesiology 22(1): 1-21, 2008.

146. Watson TA, Fleisher LA: Acute heart failure in the postoperative period. Acute Heart Failure. Mebazaa A, Gheorghiade M, Zannad FM, Parrillo JE (eds.). Springer, Page: 323-32, 2008.

147. Neuman Mark D, Fleisher Lee A: Using quality improvement databases to advance medical knowledge: opportunities and challenges. Anesthesiology 110(3): 449-50, Mar 2009.

148. Poirier Paul, Alpert Martin A, Fleisher Lee A, Thompson Paul D, Sugerman Harvey J, Burke Lora E, Marceau Picard, Franklin Barry A, : Cardiovascular evaluation and management of severely obese patients undergoing surgery: a science advisory from the American Heart Association. Circulation 120(1): 86-95, Jul 2009.

149. Froehlich James B, Fleisher Lee A: Noncardiac surgery in the patient with heart disease. The Medical clinics of North America 93(5): 995-1016, Sep 2009.

150. Poldermans D, Schouten O, van Lier F, Hoeks SE, van de Ven L, Stolker RJ, Fleisher LA: Perioperative Strokes and beta-Blockade. Anesthesiology Sep 2009.

151. , , , , , , , , , Fleischmann KE, Beckman JA, Buller CE, Calkins H, Fleisher LA, Freeman WK, Froehlich JB, Kasper EK, Kersten JR, Robb JF, Valentine RJ: 2009 ACCF/AHA Focused Update on Perioperative Beta Blockade. Journal of the American College of Cardiology 54(22): 2102-2128, Nov 2009.

152. , , , , , , , , , Fleisher LA, Beckman JA, Brown KA, Calkins H, Chaikof EL, Fleischmann KE, Freeman WK, Froehlich JB, Kasper EK, Kersten JR, Riegel B, Robb JF: 2009 ACCF/AHA Focused Update on Perioperative Beta Blockade Incorporated Into the ACC/AHA 2007 Guidelines on Perioperative Cardiovascular Evaluation and Care for Noncardiac Surgery. Journal of the American College of Cardiology 54(22): e13-e118, Nov 2009.

153. Ballantyne JC, Fleisher LA: Ethical issues in opioid prescribing for chronic pain. Pain Nov 2009.

154. Elkassabany N, Muravchick S, Fleisher LA: Thinking clearly about postoperative delirium and perioperative medications: how concerned should we be? Canadian journal of anaesthesia = Journal canadien d'anesthesie 56: 785-8, Nov 2009.

155. Fleischmann KE, Beckman JA, Buller CE, Calkins H, Fleisher LA, Freeman WK, Froehlich JB, Kasper EK, Kersten JR, Robb JF, Valentine RJ: 2009 ACCF/AHA Focused Update on Perioperative Beta Blockade. A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation Nov 2009.

156. Fleisher LA, Beckman JA, Brown KA, Calkins H, Chaikof EL, Fleischmann KE, Freeman WK, Froehlich JB, Kasper EK, Kersten JR, Riegel B, Robb JF: 2009 ACCF/AHA Focused Update on Perioperative Beta Blockade Incorporated Into the ACC/AHA 2007 Guidelines on Perioperative Cardiovascular Evaluation and Care for Noncardiac Surgery. A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation Nov 2009.

157. Fleisher Lee A, : Cardiac risk stratification for noncardiac surgery: update from the American College of Cardiology/American Heart Association 2007 guidelines. Cleveland Clinic journal of medicine 76 Suppl 4: S9-15, Nov 2009.

158. Augoustidies JGT, Riha H, Fleisher LA: How long should you wait after percutaneous coronary intervention for noncardiac surgery? Evidence-based practice of Anesthesiology, 2nd edition. Fleisher LA (eds.). Elsevier, Philadelphia, PA, Page: 79-86, 2009.

159. Fleisher LA: Anesthesia and the pateint with cardiovascular disease. Oxford Desk Reference- Cardiology. Oxford University Press, 2009.

160. Fleisher LA: Preoperative cardiac evaluation. Atlas of Cardiothoracic Anesthesia, 2nd edition. Reves JG, Reeves ST, Abernathy JH (eds.). Springer, 2009.

161. Fleisher LA: Risk of Anesthesia. Miller's Anesthesia, 7th edition. Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Young WL (eds.). Elsevier, Philadelphia, PA, Page: 969-1000, 2009.

162. Fleisher, LA: Preoperative cardiovascular evaluation and care for noncardiac surgery. The AHA Guidelines and Scientific Statements Handbook. Fuster V (eds.). Wiley-Blackwell, 2009.

163. Roizen MF, Fleisher LA: Anesthetic implications of concurrent diseases. Miller's Anesthesia, 7th edition. Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish JP,

Young WL (eds.). Elsevier, Philadelphia, PA, Page: 1067-1150, 2009.

164. Fleisher LA: Improving perioperative outcomes: my journey into risk, patient preferences, guidelines, and performance measures: Ninth Honorary FAER Research Lecture. Anesthesiology 112(4): 794-801, Apr 2010.

165. Fleisher LA: Preoperative cardiac evaluation. Cardiology secrets, 3rd. Glenn N. Levine (eds.). Mosby, Page: 409-413, 2010.

166. Fleisher LA: Risk of Reinfarction. Ann Surg Mar 2011.

167. Shander Aryeh, Fleisher Lee A, Barie Philip S, Bigatello Luca M, Sladen Robert N, Watson Charles B: Clinical and economic burden of postoperative pulmonary complications: patient safety summit on definition, risk-reducing interventions, and preventive strategies. Critical care medicine 39(9): 2163-72, Sep 2011.

168. Fleisher LA, Barnett K: Perioperative management of patients with cardiovascular disease. McGraw-Hill Specialty Board Review Cardiology. Baliga RR (eds.). McGraw Hill, 2011.

169. Fleisher LA, Beckman J: Anesthesia and noncardiac surgery in patients with heart disease, 9th edition. Braunwald's Heart Disease: A Textbook of Cardiovascular Medicien. Bonow RO, Mann DL, Zipes DP, Libby P (eds.). Elsevier, 2011.

170. Horak J, Mohler ER, Fleisher LA: Assessment of cardiac risk and the cardiology consultant. Kaplan's Cardiac Anesthesia: The Echo Era, 6th edition. Kaplan JA, Reich DL, Savino JS (eds.). Elsevier, 2011.

171. Apfelbaum Jeffrey L, Connis Richard T, Nickinovich David G, Pasternak L Reuven, Arens James F, Caplan Robert A, Connis Richard T, Fleisher Lee A, Flowerdew Richard, Gold Barbara S, Mayhew James F, Nickinovich David G, Rice Linda Jo, Roizen Michael F, Twersky Rebecca S: Practice advisory for preanesthesia evaluation: an updated report by the American Society of Anesthesiologists Task Force on Preanesthesia Evaluation. Anesthesiology 116(3): 522-38, Mar 2012.

172. Fleisher Lee A: Assessing the value of "discretionary" clinical care: the case of anesthesia services for endoscopy. JAMA : the journal of the American Medical Association 307(11): 1200-1, Mar 2012.

173. Rupp Stephen M, Apfelbaum Jeffrey L, Blitt Casey, Caplan Robert A, Connis Richard T, Domino Karen B, Fleisher Lee A, Grant Stuart, Mark Jonathan B, Morray Jeffrey P, Nickinovich David G, Tung Avery: Practice guidelines for central venous access: a report by the American Society of Anesthesiologists Task Force on Central Venous Access. Anesthesiology 116(3): 539-73, Mar 2012.

174. Fleisher Lee A, Beattie W Scott: Perioperative statin therapy: understanding the

evidence in a Bayesian context. Canadian journal of anaesthesia = Journal canadien d'anesthésie 59(6): 511-5, Jun 2012.

175. Lentine Krista L, Costa Salvatore P, Weir Matthew R, Robb John F, Fleisher Lee A, Kasiske Bertram L, Carithers Robert L, Ragosta Michael, Bolton Kline, Auerbach Andrew D, Eagle Kim A: Cardiac Disease Evaluation and Management Among Kidney and Liver Transplantation Candidates: A Scientific Statement From the American Heart Association and the American College of Cardiology Foundation. Circulation 126(5): 617-663, Jul 2012.

176. Lentine Krista L, Costa Salvatore P, Weir Matthew R, Robb John F, Fleisher Lee A, Kasiske Bertram L, Carithers Robert L, Ragosta Michael, Bolton Kline, Auerbach Andrew D, Eagle Kim A: Cardiac disease evaluation and management among kidney and liver transplantation candidates: a scientific statement from the american heart association and the american college of cardiology foundation. Journal of the American College of Cardiology 60(5): 434-80, Jul 2012.

177. Fleisher L A: The application of evidence to clinical decision-making in anaesthesia as a means of delivering value to patients. European journal of anaesthesiology 29(8): 357-9, Aug 2012.

178. Fleisher Lee A, Evers Alex S, Wiener-Kronish Jeanine, Ulatowski John A: What Are We Looking For?: The Question of Resident Selection. Anesthesiology 117(2): 230-231, Aug 2012.

179. Blike GT, Fleisher LA: Approaches to Quality Improvement in Anesthesia Care. Anesthesiology (second edition). Longnecker DE, Brown DL, Newman MF, Zapol WM (eds.). McGraw Hill 2012.

180. Augoustides John G T, Neuman Mark D, Fleisher Lee A: Estimated glomerular filtration rate: more bang for the buck. Anesthesiology 118(4): 775-6, Apr 2013.

181. Fleisher LA, Savino JS: Assessment of patients with heart disease for fitness for noncardiac surgery. Essential Cardiology: Principles and Practice, Third edition. Rosendorff C (eds.). Springer, Page: 727-736, 2013.

182. Fleisher LA, Trey B: Turning Mission-Based Academic-Department Leaders into a Leadership Team: A Case Study in Creating Value N Engl J Med Leading Healthcare Innovation HBR Insight Center 2013 Notes: http://images.nejm.org/editorial/supplementary/2013/hbr16-fleisher.pdf.

183. Neuman MD, Fleisher LA: Evaluating Outcomes and Costs in Perioperative Care JAMA Surg 2013.

184. Todd MM, Fleisher LA.: Avoiding professional extinction. Anesthesiology 120: 2-3, Jan 2014.

185. Glance LG, Fleisher LA.: Anesthesiologists and the Transformation of the Healthcare System: A Call to Action. Anesthesiology 120: 257-9, Feb 2014.

186. Fleisher LA.: Preoperative Consultation Before Cataract Surgery: Are We Choosing Wisely or Is This Simply Low-Value Care? JAMA Intern Med 174(3): 389-90, Mar 2014

187. Anderson Jeffrey L, Heidenreich Paul A, Barnett Paul G, Creager Mark A, Fonarow Gregg C, Gibbons Raymond J, Halperin Jonathan L, Hlatky Mark A, Jacobs Alice K, Mark Daniel B, Masoudi Frederick A, Peterson Eric D, Shaw Leslee J: ACC/AHA statement on cost/value methodology in clinical practice guidelines and performance measures: a report of the American College of Cardiology/American Heart Association Task Force on Performance Measures and Task Force on Practice Guidelines. Circulation 129(22): 2329-45, Jun 2014.

188. Jacobs Alice K, Anderson Jeffrey L, Halperin Jonathan L, Anderson Jeffrey L, Halperin Jonathan L, Albert Nancy M, Bozkurt Biykem, Brindis Ralph G, Curtis Lesley H, DeMets David, Fleisher Lee A, Gidding Samuel, Hochman Judith S, Kovacs Richard J, Ohman E Magnus, Pressler Susan J, Sellke Frank W, Shen Win-Kuang, Wijeysundera Duminda N: The evolution and future of ACC/AHA clinical practice guidelines: a 30-year journey: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. Circulation 130(14): 1208-17, Sep 2014.

189. Amsterdam Ezra A, Wenger Nanette K, Brindis Ralph G, Casey Donald E, Ganiats Theodore G, Holmes David R, Jaffe Allan S, Jneid Hani, Kelly Rosemary F, Kontos Michael C, Levine Glenn N, Liebson Philip R, Mukherjee Debabrata, Peterson Eric D, Sabatine Marc S, Smalling Richard W, Zieman Susan J: 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation 130(25): e344-426, Dec 2014.

190. Amsterdam Ezra A, Wenger Nanette K, Brindis Ralph G, Casey Donald E, Ganiats Theodore G, Holmes David R, Jaffe Allan S, Jneid Hani, Kelly Rosemary F, Kontos Michael C, Levine Glenn N, Liebson Philip R, Mukherjee Debabrata, Peterson Eric D, Sabatine Marc S, Smalling Richard W, Zieman Susan J: 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation 130(25): 2354-94, Dec 2014.

191. Fleisher LA: Preoperative cardiac evaluation before non cardiac surgery. Evidence-based cardiology consult. Stergiopoulos K (eds.). Springer, 2014.

192. Fleisher LA: Preoperative cardiac evaluation. Cardiology Secrets, 4th edition. Levine GM (eds.). Elsevier Saunders, Page: 409-414, 2014.

193. Fleisher Lee A, Fleischmann Kirsten E, Auerbach Andrew D, Barnason Susan A, Beckman Joshua A, Bozkurt Biykem, Davila-Roman Victor G, Gerhard-Herman Marie D, Holly Thomas A, Kane Garvan C, Marine Joseph E, Nelson M Timothy, Spencer Crystal C, Thompson Annemarie, Ting Henry H, Uretsky Barry F, Wijeysundera Duminda N: 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation 130(24): 2215-45, Dec 2014.

194. Fleisher Lee A, Fleischmann Kirsten E, Auerbach Andrew D, Barnason Susan A, Beckman Joshua A, Bozkurt Biykem, Davila-Roman Victor G, Gerhard-Herman Marie D, Holly Thomas A, Kane Garvan C, Marine Joseph E, Nelson M Timothy, Spencer Crystal C, Thompson Annemarie, Ting Henry H, Uretsky Barry F, Wijeysundera Duminda N: 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. Journal of the American College of Cardiology 64(22): e77-137, Dec 2014.

195. Fleisher Lee A, Fleischmann Kirsten E, Auerbach Andrew D, Barnason Susan A, Beckman Joshua A, Bozkurt Biykem, Davila-Roman Victor G, Gerhard-Herman Marie D, Holly Thomas A, Kane Garvan C, Marine Joseph E, Nelson M Timothy, Spencer Crystal C, Thompson Annemarie, Ting Henry H, Uretsky Barry F, Wijeysundera Duminda N: 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation 130(24): e278-333, Dec 2014.

196. Kukafka JD, Fleisher LA: Anesthesia. Surgery review, 3rd edition. Makary M, Cooper M (eds.). Wolters Kluwer, Page: 491-503, 2014.

197. Patel PA, Fleisher LA: Aspirin, Clopidogrel and the Surgeon. Adv Surgery. Cameron JL, Evers BM, Fong Y, Herndon D, Lillemoe K, Mannick JA, Yeo CJ (eds.). Elsevier, 48: 211-222, 2014.

198. Prasanna V, Litwack AJ, Fleisher LA: Perioperative cardiovascular evaluation and treatment of elderly patients undergoing noncardiac surgery. Cardiovascular disease in the elderly. Aronow WS, Fleg JL, Rich MW (eds.). CRC Press, 2014.

199. Wijeysundera Duminda N, Duncan Dallas, Nkonde-Price Chileshe, Virani Salim S, Washam Jeffrey B, Fleischmann Kirsten E, Fleisher Lee A: Perioperative beta

blockade in noncardiac surgery: a systematic review for the 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation 130(24): 2246-64, Dec 2014.

200. Wijeysundera Duminda N, Duncan Dallas, Nkonde-Price Chileshe, Virani Salim S, Washam Jeffrey B, Fleischmann Kirsten E, Fleisher Lee A: Perioperative beta blockade in noncardiac surgery: a systematic review for the 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. Journal of the American College of Cardiology 64(22): 2406-25, Dec 2014.

201. Fleisher Lee A: Geriatric Anesthesia: Can We Achieve the Goal of Returning our Elderly to Baseline or Improved Function? Anesthesiology clinics 33(3): xiii-xiv, Sep 2015.

202. Halperin Jonathan L, Levine Glenn N, Al-Khatib Sana M, Birtcher Kim K, Bozkurt Biykem, Brindis Ralph G, Cigarroa Joaquin E, Curtis Lesley H, Fleisher Lee A, Gentile Federico, Gidding Samuel, Hlatky Mark A, Ikonomidis John, Joglar José, Pressler Susan J, Wijeysundera Duminda N: Further Evolution of the ACC/AHA Clinical Practice Guideline Recommendation Classification System: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Journal of the American College of Cardiology Sep 2015.

203. Fleisher Lee A: Value of Sequels: Is It Safe to Include Nitrous Oxide in Your Anesthetic? Anesthesiology 123(6): 1229-30, Oct 2015.

204. Atkins Joshua H, Fleisher Lee A: Value from the Patients' and Payers' Perspectives. Anesthesiology clinics 33(4): 651-8, Dec 2015.

205. Fleisher Lee A: Value-The Current Cure for Health Care's Ailments? Anesthesiology clinics 33(4): xv-xvi, Dec 2015.

206. Fosnot Caroline D, Fleisher Lee A, Keogh John: Providing Value in Ambulatory Anesthesia in 2015. Anesthesiology clinics 33(4): 731-8, Dec 2015.

207. Fosnot Caroline D, Fleisher Lee A, Keogh John: Providing value in ambulatory anesthesia. Current opinion in anaesthesiology 28(6): 617-22, Dec 2015.

208. Hiratzka Loren F, Creager Mark A, Isselbacher Eric M, Svensson Lars G, Nishimura Rick A, Bonow Robert O, Guyton Robert A, Sundt Thoralf M, Halperin Jonathan L, Levine Glenn N, Anderson Jeffrey L, Albert Nancy M, Al-Khatib Sana M, Birtcher Kim K, Bozkurt Biykem, Brindis Ralph G, Cigarroa Joaquin E, Curtis

Lesley H, Fleisher Lee A, Gentile Federico, Gidding Samuel, Hlatky Mark A, Ikonomidis John, Joglar José, Kovacs Richard J, Ohman E Magnus, Pressler Susan J, Sellke Frank W, Shen Win-Kuang, Wijeysundera Duminda N: Surgery for Aortic Dilatation in Patients With Bicuspid Aortic Valves: A Statement of Clarification From the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation 133(7): 680-6, Feb 2016.

209. Ashburn Michael A, Fleisher Lee A: Does assessment of patient satisfaction with pain care lead to patient harm? Healthcare (Amsterdam, Netherlands) 4(1): 6-8, Mar 2016.

210. Fleisher Lee A: Preoperative Assessment of the Patient with Cardiac Disease Undergoing Noncardiac Surgery. Anesthesiology clinics 34(1): 59-70, Mar 2016.

211. Fleisher Lee A, Wiener-Kronish Jeanine P: Ensuring the Future of the Specialty: What Is the Best Strategy to Ensure a Pipeline of Physician-scientists? Anesthesiology Mar 2016.

212. Levine Glenn N, Bates Eric R, Bittl John A, Brindis Ralph G, Fihn Stephan D, Fleisher Lee A, Granger Christopher B, Lange Richard A, Mack Michael J, Mauri Laura, Mehran Roxana, Mukherjee Debabrata, Newby L Kristin, O'Gara Patrick T, Sabatine Marc S, Smith Peter K, Smith Sidney C: 2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Journal of the American College of Cardiology Mar 2016.

213. Fleisher Lee A: Chronic Pain and Its Treatment in an Era of Increased Scrutiny. Anesthesiology clinics 34(2): xi-xii, Jun 2016.

214. Fleisher Lee A: Anesthesiologists as Clinical Neuroscientists-One Future for Our Specialty. Anesthesiology clinics 34(3): xiii-xiv, Sep 2016.

215. Graham Danielle S, Fleisher Lee A: The potential unintended consequences of linking insurance coverage decisions to quality metrics. Healthcare (Amsterdam, Netherlands) 4(3): 135-7, Sep 2016.

216. Liao Joshua M, Fleisher Lee A, Navathe Amol S: Increasing the Value of Social Comparisons of Physician Performance Using Norms. JAMA 316(11): 1151-1152, Sep 2016.

217. Gerhard-Herman Marie D, Gornik Heather L, Barrett Coletta, Barshes Neal R, Corriere Matthew A, Drachman Douglas E, Fleisher Lee A, Fowkes Francis Gerry R, Hamburg Naomi M, Kinlay Scott, Lookstein Robert, Misra Sanjay, Mureebe Leila, Olin Jeffrey W, Patel Rajan A G, Regensteiner Judith G, Schanzer

Andres, Shishehbor Mehdi H, Stewart Kerry J, Treat-Jacobson Diane, Walsh M Eileen: 2016 AHA/ACC Guideline on the Management of Patients With Lower Extremity Peripheral Artery Disease: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Journal of the American College of Cardiology 69(11): 1465-1508, Nov 2016.

218. Gerhard-Herman Marie D, Gornik Heather L, Barrett Coletta, Barshes Neal R, Corriere Matthew A, Drachman Douglas E, Fleisher Lee A, Fowkes Francis Gerry R, Hamburg Naomi M, Kinlay Scott, Lookstein Robert, Misra Sanjay, Mureebe Leila, Olin Jeffrey W, Patel Rajan A G, Regensteiner Judith G, Schanzer Andres, Shishehbor Mehdi H, Stewart Kerry J, Treat-Jacobson Diane, Walsh M Eileen: 2016 AHA/ACC Guideline on the Management of Patients With Lower Extremity Peripheral Artery Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Journal of the American College of Cardiology 69(11): e71-e126, Nov 2016.

219. Levine Glenn N, Bates Eric R, Bittl John A, Brindis Ralph G, Fihn Stephan D, Fleisher Lee A, Granger Christopher B, Lange Richard A, Mack Michael J, Mauri Laura, Mehran Roxana, Mukherjee Debabrata, Newby L Kristin, O'Gara Patrick T, Sabatine Marc S, Smith Peter K, Smith Sidney C, Halperin Jonathan L, Levine Glenn N, Al-Khatib Sana M, Birtcher Kim K, Bozkurt Biykem, Brindis Ralph G, Cigarroa Joaquin E, Curtis Lesley H, Fleisher Lee A, Gentile Federico, Gidding Samuel, Hlatky Mark A, Ikonomidis John S, Joglar José A, Pressler Susan J, Wijeysundera Duminda N: 2016 ACC/AHA guideline focused update on duration of dual antiplatelet therapy in patients with coronary artery disease: A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. The Journal of thoracic and cardiovascular surgery 152(5): 1243-1275, Nov 2016.

220. Fleisher Lee A: The Patient with Multimorbidities: Does 1 + 1 Always Simply Equal 2? Anesthesiology clinics 34(4): xiii-xiv, Dec 2016.

221. Fleisher Lee A: Anesthesiologists in Obstetric Care: Beyond Labor Epidurals and C-Section Care. Anesthesiology clinics 35(1): xiii-xiv, Mar 2017.

222. Fleisher Lee A: What Can the Use of Anesthesia Services for Endoscopy in the Veterans Health Administration Teach Us About Appropriate Care? JAMA internal medicine 177(3): 438, Mar 2017.

223. Nishimura Rick A, Otto Catherine M, Bonow Robert O, Carabello Blase A, Erwin John P, Fleisher Lee A, Jneid Hani, Mack Michael J, McLeod Christopher J, O'Gara Patrick T, Rigolin Vera H, Sundt Thoralf M, Thompson Annemarie: 2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: A Report of the American

College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Journal of the American College of Cardiology 70(2): 252-289, Mar 2017.

224. Fleisher Lee A: Transplantation Anesthesia: The Role of the Anesthesiologist. Anesthesiology clinics 35(3): xiii, Sep 2017.

225. Ashburn Michael A, Fleisher Lee A: The Role of Gabapentin in Multimodal Postoperative Pain Management. JAMA surgery Dec 2017.

226. Fleisher LA: Preoperative Cardiac Evaluation. Cardiology Secrets, 5th edition. Levine GN (eds.). Elsevier, 2017.

227. Fleisher Lee A: Anesthesia Outside of the Operating Room: The Wild West or the New Frontier? Anesthesiology clinics 35(4): xv-xvi, Dec 2017.

228. Fleisher L A: Anaesthesia quality metrics: do they achieve the goals of evidence to improve patient care? British journal of anaesthesia 120(1): 2-4, Jan 2018.

229. Clapp Justin T, Fleisher Lee A: What is the Realistic Scope of Informed Consent? Joint Commission journal on quality and patient safety 44(6): 341-342, Jun 2018.

230. Fleisher Lee A, Ko Clifford Y: Enhanced Recovery After Surgery: Is It Time to Drive Patient-Reported Outcomes Through Robust Measurement? Anesthesia and analgesia 126(6): 1801-1802, Jun 2018.

231. Gordon Emily K, Baranov Dimitry Y, Fleisher Lee A: The role of feedback in ameliorating burnout. Current opinion in anaesthesiology 31(3): 361-365, Jun 2018.

232. Ashburn Michael A, Fleisher Lee A: Perioperative Opioid Management-An Opportunity to Put the Genie Back Into the Bottle. JAMA surgery Jul 2018.

233. Fleisher Lee A: Preoperative Cardiac Evaluation before Noncardiac Surgery: Reverend Bayes's Risk Indices and Optimal Variables. Anesthesiology Sep 2018.

234. Fleisher Lee A: Regional Anesthesia: What We Need to Know in the Era of Enhanced Recovery After Surgery Protocols and the Opioid Epidemic. Anesthesiology clinics 36(3): xi-xii, Sep 2018.

235. The Future of Health Services Research: Advancing Health Systems Research and Practice in the United States. _ Danielle Whicher, Kristin Rosengran, Lisa Simpson,Sameer Siddiqi (eds.). National Academy of Medicine, 2018.

236. Fleisher Lee A: Preoperative Evaluation: Is It Time to View It as a Component of Perioperative Optimization? Anesthesiology clinics 36(4): xv-xvi, Dec 2018.

237. Gordon EK, Baranov DY, Fleisher LA: The role of feedback in ameliorating burnout. Curr Opin Anesthesiol 31: (in press), 2018.

238. Lane-Fall Meghan B, Fleisher Lee A: Untangling the Web of Health Care Access and Racial Disparities After Coronary Artery Bypass Grafting. Journal of cardiothoracic and vascular anesthesia Dec 2018.

239. National Academies of Sciences, Engineering, Medicine Committee on Reproductive Health Services: Assessing the Safety and Quality of Abortion Care in the U.S.: The Safety and Quality of Abortion Care in the United States. The National Academies Press 2018.

240. Sturgess J, Clapp J T, Fleisher L A: Shared decision-making in peri-operative medicine: a narrative review. Anaesthesia 74 Suppl 1: 13-19, Jan 2019.

241. Fleisher Lee A, Beckman Joshua A, Wijeysundera Duminda N: Does Following Perioperative Cardiovascular Evaluation Guidelines Increase Perioperative Costs? Anesthesia and analgesia 128(2): 202-203, Feb 2019.

242. Santhirapala Ramai, Fleisher Lee A, Grocott Michael P W: Choosing Wisely: just because we can, does it mean we should? British journal of anaesthesia 122(3): 306-310, Mar 2019.

243. Levine Glenn N, O'Gara Patrick T, Beckman Joshua A, Al-Khatib Sana M, Birtcher Kim K, Cigarroa Joaquin E, de Las Fuentes Lisa, Deswal Anita, Fleisher Lee A, Gentile Federico, Goldberger Zachary D, Hlatky Mark A, Joglar José A, Piano Mariann R, Wijeysundera Duminda N: Recent Innovations, Modifications, and Evolution of ACC/AHA Clinical Practice Guidelines: An Update for Our Constituencies: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Journal of the American College of Cardiology 73(15): 1990-1998, Apr 2019.

244. Levine Glenn N, O'Gara Patrick T, Beckman Joshua A, Al-Khatib Sana M, Birtcher Kim K, Cigarroa Joaquin E, de Las Fuentes Lisa, Deswal Anita, Fleisher Lee A, Gentile Federico, Goldberger Zachary D, Hlatky Mark A, Joglar José A, Piano Mariann R, Wijeysundera Duminda N: Recent Innovations, Modifications, and Evolution of ACC/AHA Clinical Practice Guidelines: An Update for Our Constituencies: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation 139(17): e879-e886, Apr 2019.

245. Clapp Justin T, Fleisher Lee A, Lane-Fall Meghan B: Decision Aids Are a Solution, but to Which Problem? Anesthesia and analgesia 128(5): 837-838, May 2019.

246. Ashburn Michael A, Fleisher Lee A: Do Gabapentinoids Cause More Harm Than

Good? Annals of surgery 270(6): e68, Dec 2019.

247. Lane-Fall, M. B., Fleisher, L. A.: Untangling the Web of Health Care Access and Racial Disparities After Coronary Artery Bypass Grafting. J Cardiothorac Vasc Anesth 33(7): 1899-1900, 2019.

248. Khachaturian Ara S, Hayden Kathleen M, Devlin John W, Fleisher Lee A, Lock Sarah Lenz, Cunningham Colm, Oh Esther S, Fong Tamara G, Fick Donna Marie, Marcantonio Edward R, Iyengar Vijeth, Rockwood Kenneth, Kuchel George A, Eckenhoff Roderic G, MacLullich Alasdair M J, Jones Richard N, Davis Daniel, D'Antonio Patricia M, Fargo Keith N, Albert Marilyn S, Williamson Jeff D, Ling Shari M, Weiss Joan, Karlawish Jason, Petersen Ronald C, Blazer Dan G, Khachaturian Zaven S, Inouye Sharon K: International drive to illuminate delirium: A developing public health blueprint for action. Alzheimer's & dementia : the journal of the Alzheimer's Association Mar 2020.

249. Yao Wenlong, Wang Tingting, Jiang Bailing, Gao Feng, Wang Li, Zheng Hongbo, Xiao Weimin, Yao Shanglong, Mei Wei, Chen Xiangdong, Luo Ailin, Sun Liang, Cook Tim, Behringer Elizabeth, Huitink Johannes M, Wong David T, Lane-Fall Meghan, McNarry Alistair F, McGuire Barry, Higgs Andrew, Shah Amit, Patel Anil, Zuo Mingzhang, Ma Wuhua, Xue Zhanggang, Zhang Li-Ming, Li Wenxian, Wang Yong, Hagberg Carin, O'Sullivan Ellen P, Fleisher Lee A, Wei Huafeng: Emergency tracheal intubation in 202 patients with COVID-19 in Wuhan, China: lessons learnt and international expert recommendations. British journal of anaesthesia Apr 2020.

250. Ayesha D'Avena, Shantanu Agrawal, Kenneth W. Kizer, Lee A. Fleisher, Nancy Foster, Donald M. Berwick: Normalizing High-Value Care: Findings of the National Quality Task Force. NEJM Catalyst May 2020.

251. Hughes, C. G., Boncyk, C. S., Culley, D. J., Fleisher, L. A., Leung, J. M., McDonagh, D. L., Gan, T. J., McEvoy, M. D., Miller, T. E., Perioperative Quality Initiative, Workgroup: American Society for Enhanced Recovery and Perioperative Quality Initiative Joint Consensus Statement on Postoperative Delirium Prevention. Anesth Analg 130(6): 1572-1590, 2020.

252. Kushal Kadakia, Lee A Fleisher, Cary J Stimson, Thomas Aloia, Anaeze C. Offodile: Charting a Roadmap for Value-Based Surgery in the Post-Pandemic Era. Ann Surg 2020.

253. Lee, K. C., Walling, A. M., Senglaub, S. S., Bernacki, R., Fleisher, L. A., Russell, M. M., Wenger, N. S., Cooper, Z.: Improving Serious Illness Care for Surgical Patients: Quality Indicators for Surgical Palliative Care. Ann Surg 2020.

254. Liu, R., Fleisher, L. A.: Getting to a New Normal: Mandating That Patients Wear Masks as Hospitals Fully Reopen during the Coronavirus Pandemic.

Anesthesiology 2020.

255. Mantha, S., Tripuraneni, S. L., Fleisher, L. A., Roizen, M. F.: Use of Common Carotid Intima-Media Thickness Measured by Ultrasound Echo-Tracking in Cardiovascular Risk Stratification Before Noncardiac Surgery in Low-Risk Category: A Research Idea. A A Pract 14(5): 166-169, 2020.

256. Beattie, W. S., Lalu, M., Bocock, M., Feng, S., Wijeysundera, D. N., Nagele, P., Fleisher, L. A., Kurz, A., Biccard, B., Leslie, K., Howell, S., Landoni, G., Grocott, H., Lamy, A., Richards, T., Myles, P.: Systematic review and consensus definitions for the Standardized Endpoints in Perioperative Medicine (StEP) initiative: cardiovascular outcomes. Br J Anaesth 126(1): 56-66, 2021.

257. Benesch, C., Glance, L. G., Derdeyn, C. P., Fleisher, L. A., Holloway, R. G., Messe, S. R., Mijalski, C., Nelson, M. T., Power, M., Welch, B. G., American Heart Association Stroke, Council, Council on Arteriosclerosis, Thrombosis, Vascular, Biology, Council on, Cardiovascular, Stroke, Nursing, Council on Clinical, Cardiology, Council on, Epidemiology, Prevention,: Perioperative Neurological Evaluation and Management to Lower the Risk of Acute Stroke in Patients Undergoing Noncardiac, Nonneurological Surgery: A Scientific Statement From the American Heart Association/American Stroke Association. Circulation 143(19): e923-e946, 2021.

258. Clapp, J. T., Schwarze, M. L., Fleisher, L. A.: Surgical Overtreatment and Shared Decision-making-The Limits of Choice. JAMA Surg 2021.

259. Peden, C. J., Miller, T. R., Deiner, S. G., Eckenhoff, R. G., Fleisher, L. A.: Improving perioperative brain health: an expert consensus review of key actions for the perioperative care team. Br J Anaesth 126(2): 423-432, 2021.

260. Writing Committee, Members, Ommen, S. R., Mital, S., Burke, M. A., Day, S. M., Deswal, A., Elliott, P., Evanovich, L. L., Hung, J., Joglar, J. A., Kantor, P., Kimmelstiel, C., Kittleson, M., Link, M. S., Maron, M. S., Martinez, M. W., Miyake, C. Y., Schaff, H. V., Semsarian, C., Sorajja, P., Acc Aha Joint Committee Members, O'Gara, P. T., Beckman, J. A., Levine, G. N., Al-Khatib, S. M., Armbruster, A., Birtcher, K. K., Ciggaroa, J., Dixon, D. L., de Las Fuentes, L., Deswal, A., Fleisher, L. A., Gentile, F., Goldberger, Z. D., Gorenek, B., Haynes, N., Hernandez, A. F., Hlatky, M. A., Joglar, J. A., Jones, W. S., Marine, J. E., Mark, D., Palaniappan, L., Piano, M. R., Tamis-Holland, J., Wijeysundera, D. N., Woo, Y. J.: 2020 AHA/ACC guideline for the diagnosis and treatment of patients with hypertrophic cardiomyopathy: A report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. J Thorac Cardiovasc Surg 2021.

261. Writing Committee, Members, Otto, C. M., Nishimura, R. A., Bonow, R. O.,

Carabello, B. A., Erwin, J. P., 3rd, Gentile, F., Jneid, H., Krieger, E. V., Mack, M., McLeod, C., O'Gara, P. T., Rigolin, V. H., Sundt, T. M., 3rd, Thompson, A., Toly, C., Acc Aha Joint Committee Members, O'Gara, P. T., Beckman, J. A., Levine, G. N., Al-Khatib, S. M., Armbruster, A., Birtcher, K. K., Ciggaroa, J., Deswal, A., Dixon, D. L., Fleisher, L. A., de Las Fuentes, L., Gentile, F., Goldberger, Z. D., Gorenek, B., Haynes, N., Hernandez, A. F., Hlatky, M. A., Joglar, J. A., Jones, W. S., Marine, J. E., Mark, D., Palaniappan, L., Piano, M. R., Spatz, E. S., Tamis-Holland, J., Wijeysundera, D. N., Woo, Y. J.: 2020 ACC/AHA guideline for the management of patients with valvular heart disease: A report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. J Thorac Cardiovasc Surg 2021.

Books:

1. Perioperative Myocardial Ischemia. International Anesthesiology Clinics. Beattie C, Fleisher LA (eds.). Little Brown, 1992.

2. Preoperative Evaluation in an Era of Cost Containment. Problems in Anesthesia. Fleisher LA (eds.). Lippincott Raven, Philadelphia, PA, 1997.

3. Essence of Anesthesia Practice. Roizen MF, Fleisher LA (eds.). W.B. Saunders, Philadelphia, PA, 1997.

4. Frontiers in Anesthesia. Problems in Anesthesia. Fleisher LA (eds.). Lippincott Williams & Wilkins, Philadelphia, PA, 2000.

5. Quality, Safety, Risk and Outcomes in Anesthesiology. Problems in Anesthesia. Fleisher LA, Prough D (eds.). Lippincott Williams & Wilkins, Philadelphia, PA, 2001.

6. Essence of Anesthesia Practice, 2nd Edition for Palm OS. Roizen MF, Fleisher LA (eds.). WB Saunders, Philadelphia, PA, 2001.

7. Essence of Anesthesia Practice, 2nd Edition. Roizen MF, Fleisher LA (eds.). WB Saunders, Philadelphia, PA, 2001.

8. Evidence-Based Practice of Anesthesia. Fleisher LA (eds.). WB Saunders, Philadelphia, PA, 2004.

9. Miller's Anesthesia 6th edition. Miller RD, Consulting editors: Fleisher LA, Johns RA, Savarese JJ, Wiener-Kronish JP, Young WL (eds.). Elevier Churchill Livingston, 2005.

10. Anesthesia and Uncommon Diseases. Fleisher LA (eds.). Elsevier, Philadelphia, PA, 2006.

11. Perioperative medicine: managing for outcome. Newman MF, Fleisher LA, Fink MP (eds.). Saunders Elsevier, 2008.

12. Miller's Anesthesia, 7th edition. _ Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Young, WL (eds.). Elsevier, Philadelphia, PA, 2009.

13. Fleisher LA: Evidence-based Practice of Anesthesiology, 2nd edition. _ Fleisher LA (eds.). Elsevier, Philadelphia, PA, 2009.

14. Fleisher LA, Roizen MF: Essence of Anesthesia Practice, 3rd edition. Elsevier Fleisher LA, Roizen MF (eds.). Elsevier, 2011.

15. Fleisher LA: Evidence based practice of Anesthesiology 3rd edition. _ Fleisher LA (eds.). Elsevier, 2013.

16. Fleisher LA, Roizen MF, Roizen JD: Essence of Anesthesia Practice, 4th Edition. _ Elsevier, 2017.

17. Lane-Fall M.B., Fleisher L.A.: Quality improvement and implementation science. Anesthesiology Clinics. Elsevier, 36, Mar 2018.

18. Gropper MA, Miller RD, Cohen NH, Eriksson LI, Fleisher, LA, Leslie K, Wiener-Kronish JP: Miller's Anesthesia 9th edition. __ Elsevier, 2020.

19. Newman MF, Fleisher LA, Ko C, MythenM: Perioperative medicine: managing for outcome 2nd edition. __ Elsevier, 2021.

20. Fleisher LA: Evidence based practice of Anesthesiology 4th edition. _ Fleisher LA (eds.). Elsevier, 2022.

Alternative Media:

1. Augoustides JGT, Neligan P, Fleisher LA: Perioperative management of Hypertension. American College of Physicians- Physicians Information and Education Resource. American College of Physicians, April 2006 Notes: website.

2. Fleisher LA, Gaiser RG: Procedures Consult- Anesthesiology. www.proceduresconsult.com. Fleisher LA, Gaiser RG (eds.). Elsevier, 2009.

3. Fleisher LA: Clinical Decision Support: Anesthesiology. Fleisher LA, Davis PJ, Hawkins J, McGoldrick KE, Newman M, Wiener-Kronish JP (eds.). Decision Support in Medicine, LLC. Wilmington, DE 2012.

4. Ibrahim AM, Fleisher LA: Rethinking The Challenges of Healthcare: Time to Cultivate More Tri-SectorLeaders. NEJM Catalyst Website: Leadership Section June 2016 Notes: https://catalyst.nejm.org/rethinking-challenges-of-health-care-time-cultivate-more-tri-sector-leaders/

5. Clapp JT, Diraviam SP, Fleisher LA: The "Stranger Effect" - A Look at Interactions Between Consultants and Care Teams Through the Lens of Social Science. NEJM Catalyst December 2017 Notes: https://catalyst.nejm.org/stranger-effect-interactions-physician-consultants-care-teams/

6. Handley NR, Fleisher LA: Physicians In Training: An Untapped Resource for Health Care Innovation. NEJM Catalyst April 5 2018.

7. Fleisher LA, Trey B: Building a Culture of Team Trust: The Shark Tank Method. https://executiveeducation.wharton.upenn.edu/thought-leadership/wharton-at-work/2019/01/building-team-trust/ Jan 2019.

FLEISHER DECLARATION: EXHIBIT B

The American College of Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

INTERIM UPDATE

ACOG PRACTICE BULLETIN

Clinical Management Guidelines for Obstetrician–Gynecologists

NUMBER 193, MARCH 2018

(Replaces Practice Bulletin Number 191, February 2018)

Committee on Practice Bulletins—Gynecology. This Practice Bulletin was developed by the Committee on Practice Bulletins—Gynecology in collaboration with Kurt T. Barnhart, MD, MSCE; and Jason M. Franasiak, MD, TS (ABB).

INTERIM UPDATE: This Practice Bulletin is updated as highlighted to clarify the guidance on the assessment of hCG levels after uterine aspiration in women with a pregnancy of unknown location.

Tubal Ectopic Pregnancy

Ectopic pregnancy *is defined as a pregnancy that occurs outside of the uterine cavity. The most common site of ectopic pregnancy is the fallopian tube. Most cases of tubal ectopic pregnancy that are detected early can be treated successfully either with minimally invasive surgery or with medical management using methotrexate. However, tubal ectopic pregnancy in an unstable patient is a medical emergency that requires prompt surgical intervention. The purpose of this document is to review information on the current understanding of tubal ectopic pregnancy and to provide guidelines for timely diagnosis and management that are consistent with the best available scientific evidence.*

Background

Epidemiology

According to the Centers for Disease Control and Prevention, ectopic pregnancy accounts for approximately 2% of all reported pregnancies (1). However, the true current incidence of ectopic pregnancy is difficult to estimate because many patients are treated in an outpatient setting where events are not tracked, and national surveillance data on ectopic pregnancy have not been updated since 1992 (1). Despite improvements in diagnosis and management, ruptured ectopic pregnancy continues to be a significant cause of pregnancy-related mortality and morbidity. In 2011–2013, ruptured ectopic pregnancy accounted for 2.7% of all pregnancy-related deaths and was the leading cause of hemorrhage-related mortality (2). The prevalence of ectopic pregnancy among women presenting to an emergency department with first-trimester vaginal bleeding, or abdominal pain, or both, has been reported to be as high as 18% (3).

Etiology

The fallopian tube is the most common location of ectopic implantation, accounting for more than 90% of cases (4). However, implantation in the abdomen (1%), cervix (1%), ovary (1–3%), and cesarean scar (1–3%) can occur and often results in greater morbidity because of delayed diagnosis and treatment (4). An ectopic pregnancy also can co-occur with an intrauterine pregnancy, a condition known as heterotopic pregnancy. The risk of heterotopic pregnancy among women with a naturally achieved pregnancy is estimated to range from 1 in 4,000 to 1 in 30,000, whereas the risk among women who have undergone in vitro fertilization is estimated to be as high as 1 in 100 (5, 6).

Risk Factors

One half of all women who receive a diagnosis of an ectopic pregnancy do not have any known risk factors (3). Women with a history of ectopic pregnancy are at increased risk of recurrence. The chance of a repeat ectopic pregnancy in a woman with a history of one ectopic pregnancy is approximately 10% (odds ratio [OR] 3.0; 95% CI, 2.1–4.4). In a woman with two or more prior ectopic pregnancies, the risk of recurrence increases to more than 25% (OR, 11.17; 95% CI, 4.0–29.5) (3). Other important risk factors for ectopic pregnancy include previous damage to the fallopian tubes, factors secondary to ascending pelvic infection, and prior pelvic or fallopian tube surgery (3, 7). Among women who become pregnant through the use of assisted reproductive technology, certain factors such as tubal factor infertility and multiple

embryo transfer are associated with an increased risk of ectopic pregnancy (8, 9). Women with a history of infertility also are at increased risk of ectopic pregnancy independent of how they become pregnant (7). Other less significant risk factors include a history of cigarette smoking and age older than 35 years (7).

Women who use an intrauterine device (IUD) have a lower risk of ectopic pregnancy than women who are not using any form of contraception because IUDs are highly effective at preventing pregnancy. However, up to 53% of pregnancies that occur with an IUD in place are ectopic (10). Factors such as oral contraceptive use, emergency contraception failure, previous elective pregnancy termination, pregnancy loss, and cesarean delivery have not been associated with an increased risk of ectopic pregnancy (3, 7, 11, 12).

Clinical Considerations and Recommendations

▶ *How is an ectopic pregnancy diagnosed?*

The minimum diagnostic evaluation of a suspected ectopic pregnancy is a transvaginal ultrasound evaluation and confirmation of pregnancy. Serial evaluation with transvaginal ultrasonography, or serum hCG level measurement, or both, often is required to confirm the diagnosis.

Women with clinical signs and physical symptoms of a ruptured ectopic pregnancy, such as hemodynamic instability or an acute abdomen, should be evaluated and treated urgently. Early diagnosis is aided by a high index of suspicion. Every sexually active, reproductive-aged woman who presents with abdominal pain or vaginal bleeding should be screened for pregnancy, regardless of whether she is currently using contraception (13, 14). Women who become pregnant and have known significant risk factors should be evaluated for possible ectopic pregnancy even in the absence of symptoms.

Transvaginal Ultrasonography

Ultrasonography can definitively diagnose an ectopic pregnancy when a gestational sac with a yolk sac, or embryo, or both, is noted in the adnexa (15, 16); however, most ectopic pregnancies do not progress to this stage (15). The ultrasound findings of a mass or a mass with a hypoechoic area that is separate from the ovary should raise suspicion for the presence of an ectopic pregnancy; however, its positive predictive value is only 80% (15) because these findings can be confused with pelvic structures, such as a paratubal cyst, corpus luteum, hydrosalpinx, endometrioma, or bowel. Although an early intrauterine gestational sac may be visualized as early as 5 weeks of gestation (17), definitive ultrasound evidence of an intrauterine pregnancy includes visualization of a gestational sac with a yolk sac or embryo (16). Visualization of a definitive intrauterine pregnancy eliminates ectopic pregnancy except in the rare case of a heterotopic pregnancy. Although a hypoechoic "sac-like" structure (including a "double sac sign") (18) in the uterus likely represents an intrauterine gestation, it also may represent a pseudogestational sac, which is a collection of fluid or blood in the uterine cavity that is sometimes visualized with ultrasonography in women with an ectopic pregnancy (19, 20).

Serum Human Chorionic Gonadotropin Measurement

Measurement of the serum hCG level aids in the diagnosis of women at risk of ectopic pregnancy. However, serum hCG values alone should not be used to diagnose an ectopic pregnancy and should be correlated with the patient's history, symptoms, and ultrasound findings (21, 22). Accurate gestational age calculation, rather than an absolute hCG level, is the best determinant of when a normal pregnancy should be seen within the uterus with transvaginal ultrasonography (23, 24). An intrauterine gestational sac with a yolk sac should be visible between 5 weeks and 6 weeks of gestation regardless of whether there are one or multiple gestations (25, 26). In the absence of such definitive information, the serum hCG level can be used as a surrogate for gestational age to help interpret a nondiagnostic ultrasonogram.

The "discriminatory level" is the concept that there is a hCG value above which the landmarks of a normal intrauterine gestation should be visible on ultrasonography. The absence of a possible gestational sac on ultrasound examination in the presence of a hCG measurement above the discriminatory level strongly suggests a nonviable gestation (an early pregnancy loss or an ectopic pregnancy). In 50–70% of cases, these findings are consistent with an ectopic pregnancy (27–29). However, the utility of the hCG discriminatory level has been challenged (24) in light of a case series that noted ultrasonography confirmation of an intrauterine gestational sac on follow-up when no sac was noted on initial scan and the serum hCG level was above the discriminatory level (30–32). If the concept of the hCG discriminatory level is to be used as a diagnostic aid in women at risk of ectopic pregnancy, the value should be conservatively high (eg, as high as 3,500 mIU/mL) to avoid the potential for misdiagnosis and possible interruption of an intrauterine pregnancy that a woman hopes to continue (24, 32). Women with a multiple gestation have higher hCG levels than those with a single gestation at any given gestational age and may have hCG levels above traditional discriminatory hCG levels before ultrasonography recognition (24).

Trends of Serial Serum Human Chorionic Gonadotropin

A single hCG concentration measurement cannot diagnose viability or location of a gestation. Serial hCG concentration measurements are used to differentiate normal from abnormal pregnancies (21, 22, 33, 34). When clinical findings suggest an abnormal gestation, a second hCG value measurement is recommended 2 days after the initial measurement to assess for an increase or decrease. Subsequent assessments of hCG concentration should be obtained 2–7 days apart, depending on the pattern and the level of change.

In early pregnancy, serum hCG levels increase in a curvilinear fashion until a plateau at 100,000 mIU/mL by 10 weeks of gestation. Guidelines regarding the minimal increase in hCG for a potentially viable intrauterine pregnancy have become more conservative (ie, slower increase) (21, 22) and have been demonstrated to be dependent on the initial value (35). There is a slower than expected increase in serum hCG levels for a normal gestation when initial values are high. For example, the expected rate of increase is 49% for an initial hCG level of less than 1,500 mIU/mL, 40% for an initial hCG level of 1,500–3,000 mIU/mL, and 33% for an initial hCG level greater than 3,000 mIU/mL (35). In early pregnancy, an increase in serum hCG of less than a minimal threshold in 48 hours is suspicious of an abnormal pregnancy (ectopic or early pregnancy loss) because 99% of normal intrauterine pregnancies will have a rate of increase faster than this minimum. However, even hCG patterns consistent with a growing or resolving gestation do not eliminate the possibility of an ectopic pregnancy (36).

Decreasing hCG values suggest a failing pregnancy and may be used to monitor spontaneous resolution, but this decrease should not be considered diagnostic. Approximately 95% of women with a spontaneous early pregnancy loss will have a decrease in hCG concentration of 21–35% in 2 days depending on initial hCG levels (34). A woman with decreasing hCG values and a possible ectopic pregnancy should be monitored until nonpregnant levels are reached because rupture of an ectopic pregnancy can occur while levels are decreasing or are very low.

Pregnancy of Unknown Location

A pregnant woman without a definitive finding of an intrauterine or ectopic pregnancy on ultrasound examination has a "pregnancy of unknown location" (37). A pregnancy of unknown location should not be considered a diagnosis, rather it should be treated as a transient state and efforts should be made to establish a definitive diagnosis when possible (16). A woman with a pregnancy of unknown location who is clinically stable and has a desire to continue the pregnancy, if intrauterine, should have a repeat transvaginal ultrasound examination, or serial measurement of hCG concentration, or both, to confirm the diagnosis and guide management (22, 37). Follow-up to confirm a diagnosis of ectopic pregnancy in a stable patient, especially at first clinical encounter, is recommended to eliminate misdiagnosis and to avoid unnecessary exposure to methotrexate, which can lead to interruption or teratogenicity of an ongoing intrauterine pregnancy (16, 38, 39). The first step is to assess for the possibility that the gestation is advancing.

When the possibility of a progressing intrauterine gestation has been reasonably excluded, uterine aspiration can help to distinguish early intrauterine pregnancy loss from ectopic pregnancy by identifying the presence or absence of intrauterine chorionic villi. Choosing the appropriate time and intervention should be done through shared decision making, incorporating the patient's values and preferences regarding maternal risk and the possibility of interrupting a progressing pregnancy. If chorionic villi are found, then failed intrauterine pregnancy is confirmed and no further evaluation is necessary. If chorionic villi are not confirmed, hCG levels should be monitored, with the first measurement taken 12–24 hours after aspiration. A plateau or increase in hCG postprocedure suggests that evacuation was incomplete or there is a nonvisualized ectopic pregnancy, and further treatment is warranted. Although the change at which hCG is considered to have plateaued is not precisely defined, it would be reasonable to consider levels to have plateaued if they have decreased by less than 10–15%. Large decreases in hCG levels are more consistent with failed intrauterine pregnancy than ectopic pregnancy. In two small series of women undergoing uterine aspiration for pregnancy of unknown location, nearly all women with a decrease in hCG levels of 50% or greater within 12–24 hours after aspiration had failed intrauterine pregnancies (29, 40). Patients with a decrease in hCG of 50% or greater can be monitored with serial hCG measurements, with further treatment reserved for those whose levels plateau or increase, or who develop symptoms of ectopic pregnancy. Management of patients with an hCG decrease of less than 50% should be individualized, as while failed intrauterine pregnancy is more frequent, ectopic pregnancy risk is appreciable. One study (29) noted 55.6% of patients with ectopic pregnancies had an hCG decrease of more than 10%, 23.5% had a decrease of more than 30%, and 7.1% had a decrease of more than 50%. In a series of patients who had an initial decrease of hCG levels between 15% and 50% 12–24 hours after office uterine aspiration for pregnancy

of unknown location who were monitored with serial hCG measurement, 3 of 46 patients had rising or plateauing hCG levels necessitating treatment for ectopic pregnancy (41). The other patients had resolving hCG levels, and were presumed to have failed intrauterine pregnancies. Patients with an hCG decline between 15% and 50% 12–24 hours after aspiration require at least close follow-up with serial hCG measurement, with consideration of treatment for ectopic pregnancy based on clinical factors such as plateau or increase in hCG, development of symptoms, or high clinical suspicion or strong risk factors for ectopic pregnancy (29, 40, 41).

There is debate among experts about the need to determine pregnancy location by uterine aspiration before providing methotrexate (42, 43). Proponents cite the importance of confirming the diagnosis to avoid unnecessary exposure to methotrexate and to help guide management of the current pregnancy and future pregnancies (37, 42). Arguments against the need for a definitive diagnosis include concern about the increased risk of tubal rupture because of delay in treatment while diagnosis is established and the increased health-care costs associated with additional tests and procedures (43). However, with close follow-up during this diagnostic phase, the risk of rupture is low. In one large series with serial hCG measurement of women with pregnancies of unknown location, the risk of rupture of an ectopic pregnancy during surveillance to confirm diagnosis was as low as 0.03 % among all women at risk and as low as 1.7% among all ectopic pregnancies diagnosed (22). In addition, presumptive treatment with methotrexate has not been found to confer a significant cost savings or to decrease the risk of complications (44). The choice of performing a uterine aspiration before treatment with methotrexate should be guided by a discussion with the patient regarding the benefits and risks, including the risk of teratogenicity in the case of an ongoing intrauterine pregnancy and exposure to methotrexate.

▶ *Who are candidates for medical management of ectopic pregnancy?*

Medical management with methotrexate can be considered for women with a confirmed or high clinical suspicion of ectopic pregnancy who are hemodynamically stable, who have an unruptured mass, and who do not have absolute contraindications to methotrexate administration (45). These patients generally also are candidates for surgical management. The decision for surgical management or medical management of ectopic pregnancy should be guided by the initial clinical, laboratory, and radiologic data as well as patient-informed choice based on a discussion of the benefits and risks of each approach. Women who choose methotrexate therapy should be counseled about the importance of follow-up surveillance.

Methotrexate

Methotrexate is a folate antagonist that binds to the catalytic site of dihydrofolate reductase, which interrupts the synthesis of purine nucleotides and the amino acids serine and methionine, thereby inhibiting DNA synthesis and repair and cell replication. Methotrexate affects actively proliferating tissues, such as bone marrow, buccal and intestinal mucosa, respiratory epithelium, malignant cells, and trophoblastic tissue. Systemic methotrexate has been used to treat gestational trophoblastic disease since 1956 and was first used to treat ectopic pregnancy in 1982 (46). There are no recommended alternative medical treatment strategies for ectopic pregnancy beyond intramuscular methotrexate. Although oral methotrexate therapy for ectopic pregnancy has been studied, the outcomes data are sparse and indicate that benefits are limited (47).

Contraindications

Box 1 lists absolute and relative contraindications to methotrexate therapy (45). Before administering methotrexate, it is important to reasonably exclude the presence of an intrauterine pregnancy. In addition, methotrexate administration should be avoided in patients with clinically significant elevations in serum creatinine, liver transaminases, or bone marrow dysfunction indicated by significant anemia, leukopenia, or thrombocytopenia. Because methotrexate affects all rapidly dividing tissues within the body, including bone marrow, the gastrointestinal mucosa, and the respiratory epithelium, it should not be given to women with blood dyscrasias or active gastrointestinal or respiratory disease. However, asthma is not an exclusion to the use of methotrexate. Methotrexate is directly toxic to the hepatocytes and is cleared from the body by renal excretion; therefore, methotrexate typically is not used in women with liver or kidney disease.

Relative contraindications for the use of methotrexate (Box 1) do not serve as absolute cut-offs but rather as indicators of potentially reduced effectiveness in certain settings. For example, a high initial hCG level is considered a relative contraindication. Systematic review evidence shows a failure rate of 14.3% or higher with methotrexate when pretreatment hCG levels are higher than 5,000 mIU/mL compared with a 3.7% failure rate for hCG levels less than 5,000 mIU/mL (48). Of note, studies often have excluded patients from methotrexate treatment when hCG levels are greater than

Box 1. Contraindications to Methotrexate Therapy

Absolute Contraindications

- Intrauterine pregnancy
- Evidence of immunodeficiency
- Moderate to severe anemia, leukopenia, or thrombocytopenia
- Sensitivity to methotrexate
- Active pulmonary disease
- Active peptic ulcer disease
- Clinically important hepatic dysfunction
- Clinically important renal dysfunction
- Breastfeeding
- Ruptured ectopic pregnancy
- Hemodynamically unstable patient
- Inability to participate in follow-up

Relative Contraindications

- Embryonic cardiac activity detected by transvaginal ultrasonography
- High initial hCG concentration
- Ectopic pregnancy greater than 4 cm in size as imaged by transvaginal ultrasonography
- Refusal to accept blood transfusion

Modified from Medical treatment of ectopic pregnancy: a committee opinion. Practice Committee of American Society for Reproductive Medicine. Fertil Steril 2013;100:638–44.

5,000 mIU/mL based on expert opinion that these levels are a relative contraindication to medical management. Other predictors of methotrexate treatment failure include the presence of an advanced or rapidly growing gestation (as evidenced by fetal cardiac activity) and a rapidly increasing hCG concentration (greater than 50% in 48 hours) (48–50).

▶ ***What methotrexate regimens are used in the management of ectopic pregnancy, and how do they compare in effectiveness and risk of adverse effects?***

There are three published protocols for the administration of methotrexate to treat ectopic pregnancy: 1) a single-dose protocol (51), 2) a two-dose protocol (52), and 3) a fixed multiple-dose protocol (53) (Box 2). The single-dose regimen is the simplest of the three regimens; however, an additional dose may be required to ensure resolution in up to one quarter of patients (54, 55). The two-dose regimen was first proposed in 2007 in an effort to combine the efficacy of the multiple-dose protocol with the favorable adverse effect profile of the single-dose regimen (55). The two-dose regimen adheres to the same hCG monitoring schedule as the single-dose regimen, but a second dose of methotrexate is administered on day 4 of treatment. The multiple-dose methotrexate regimen involves up to 8 days of treatment with alternating administration of methotrexate and folinic acid, which is given as a rescue dose to minimize the adverse effects of the methotrexate.

The overall treatment success of systemic methotrexate for ectopic pregnancy, defined as resolution of the ectopic pregnancy without the need for surgery, in observational studies ranges from approximately 70% to 95% (55). Resolution of an ectopic pregnancy may depend on the methotrexate treatment regimen used and the initial hCG level. However, there is no clear consensus in the literature regarding the optimal methotrexate regimen for the management of ectopic pregnancy. The choice of methotrexate protocol should be guided by the initial hCG level and discussion with the patient regarding the benefits and risks of each approach. In general, the single-dose protocol may be most appropriate for patients with a relatively low initial hCG level or a plateau in hCG values, and the two-dose regimen may be considered as an alternative to the single-dose regimen, particularly in women with an initial high hCG value.

Single-Dose Versus Multiple-Dose

Observational studies that compared the single-dose and multiple-dose regimens have indicated that although the multiple-dose regimen is statistically more effective (92.7% versus 88.1%, respectively; P=.035) (single-dose

Box 2. Methotrexate Treatment Protocols

Single-dose regimen*

- Administer a single dose of methotrexate at a dose of 50 mg/m^2 intramuscularly on day 1
- Measure hCG level on posttreatment day 4 and day 7
  - If the decrease is greater than 15%, measure hCG levels weekly until reaching nonpregnant level
  - If decrease is less than 15%, readminister methotrexate at a dose of 50 mg/m^2 intramuscularly and repeat hCG level
  - If hCG does not decrease after two doses, consider surgical management
- If hCG levels plateau or increase during follow-up, consider administering methotrexate for treatment of a persistent ectopic pregnancy

Two-dose regimen†

- Administer methotrexate at a dose of 50 mg/m^2 intramuscularly on day 1
- Administer second dose of methotrexate at a dose of 50 mg/m^2 intramuscularly on day 4
- Measure hCG level on posttreatment day 4 and day 7
  - If the decrease is greater than 15%, measure hCG levels weekly until reaching nonpregnant level
  - If decrease is less than 15%, readminister methotrexate 50 mg/m^2 intramuscularly on day 7 and check hCG levels on day 11
  - If hCG levels decrease 15% between day 7 and day 11, continue to monitor weekly until reaching nonpregnant levels
  - If the decrease is less than 15% between day 7 and day 11, readminister dose of methotrexate 50 mg/m^2 intramuscularly on day 11 and check hCG levels on day 14
  - If hCG does not decrease after four doses, consider surgical management
- If hCG levels plateau or increase during follow-up, consider administering methotrexate for treatment of a persistent ectopic pregnancy

Fixed multiple-dose regimen‡

- Administer methotrexate 1 mg/kg intramuscularly on days 1, 3, 5, 7; alternate with folinic acid 0.1 mg/kg intramuscularly on days 2, 4, 6, 8
- Measure hCG levels on methotrexate dose days and continue until hCG has decreased by 15% from its previous measurement
  - If the decrease is greater than 15%, discontinue administration of methotrexate and measure hCG levels weekly until reaching nonpregnant levels (may ultimately need one, two, three, or four doses)
  - If hCG does not decrease after four doses, consider surgical management
- If hCG levels plateau or increase during follow-up, consider administering methotrexate for treatment of a persistent ectopic pregnancy

Abbreviation: hCG, human chorionic gonadotropin.

*Stovall TG, Ling FW. Single-dose methotrexate: an expanded clinical trial. Am J Obstet Gynecol 1993;168:1759-62; discussion 1762–5.

†Barnhart K, Hummel AC, Sammel MD, Menon S, Jain J, Chakhtoura N. Use of "2-dose" regimen of methotrexate to treat ectopic pregnancy. Fertil Steril 2007;87:250–6.

‡Rodi IA, Sauer MV, Gorrill MJ, Bustillo M, Gunning JE, Marshall JR, et al. The medical treatment of unruptured ectopic pregnancy with methotrexate and citrovorum rescue: preliminary experience. Fertil Steril 1986;46:811–3.

failure OR, 1.71; 95% CI, 1.04–2.82), the single-dose regimen is associated with a decreased risk of adverse effects (OR, 0.44; 95% CI, 0.31–0.63) (55). However, a more recent systematic review of randomized controlled trials showed similar rates of successful resolution with the single-dose and multiple-dose regimens (relative risk [RR], 1.07; 95% CI, 0.99–1.17) and an increased risk of adverse effects with the multiple-dose protocol (RR, 1.64; 95% CI, 1.15–2.34) (56).

Single-Dose Versus Two-Dose

A systematic review and meta-analysis of three randomized controlled trials showed similar rates of successful resolution for the two-dose and single-dose protocols (RR, 1.09; 95% CI 0.98–1.20) and comparable risk of adverse effects (RR, 1.33; 95% CI, 0.92–1.94) (56). However, in two of the three trials included in the review, the two-dose regimen was associated with greater success among women with high initial hCG levels. In the first trial, there was a nonstatistically significant trend toward greater success for the two-dose regimen in the subgroup with an initial hCG level greater than 5,000 mIU/mL (80.0% versus 58.8%, P=.279) (RR, 0.74; 95% CI, 0.47–1.16) (57). The second trial reported a statistically significant higher success rate for the two-dose regimen versus the single-dose regimen in patients with initial serum hCG levels between 3,600 mIU/mL and 5,500 mIU/mL (88.9% versus 57.9%, P=.03) (OR 5.80; 95% CI, 1.29–26.2) (58).

▶ *What surveillance is needed after methotrexate treatment?*

After administration of methotrexate treatment, hCG levels should be serially monitored until a nonpregnancy level (based upon the reference laboratory assay) is reached (51). Close monitoring is required to ensure disappearance of trophoblastic activity and to eliminate the possibility of persistent ectopic pregnancy. During the first few days after treatment, the hCG level may increase to levels higher than the pretreatment level but then should progressively decrease to reach a nonpregnant level (51). Failure of the hCG level to decrease by at least 15% from day 4 to day 7 after methotrexate administration is associated with a high risk of treatment failure and requires additional methotrexate administration (in the case of the single-dose or two-dose regimen) or surgical intervention (51). Methotrexate treatment failure in patients who did not undergo pretreatment uterine aspiration should raise concern for the presence of an abnormal intrauterine gestation. In these patients, uterine aspiration should be considered before repeat methotrexate administration or surgical management, unless there is clear evidence of a tubal ectopic pregnancy. Ultrasound surveillance of resolution of an ectopic pregnancy is not routinely indicated because findings do not predict rupture or time to resolution (59, 60). Resolution of serum hCG levels after medical management is usually complete in 2–4 weeks but can take up to 8 weeks (55). The resolution of hCG levels is significantly faster in patients successfully treated with the two-dose methotrexate regimen compared with the single-dose regimen (25.7±13.6 versus 31.9±14.1 days; P>.025) (57).

▶ *What are the potential adverse effects of systemic methotrexate administration?*

Adverse effects of methotrexate usually are dependent on dose and treatment duration. Because methotrexate affects rapidly dividing tissues, gastrointestinal problems (eg, nausea, vomiting, and stomatitis) are the most common adverse effects after multiple doses. Vaginal spotting is expected. It is not unusual for women treated with methotrexate to experience abdominal pain 2–3 days after administration, presumably from the cytotoxic effect of the drug on the trophoblastic tissue. In the absence of signs and symptoms of overt tubal rupture and significant hemoperitoneum, abdominal pain usually can be managed expectantly by monitoring a woman's hemoglobin level and intraperitoneal fluid amount with transvaginal ultrasonography.

Elevation of liver enzymes is a less commonly reported adverse effect and typically resolves after discontinuing methotrexate use (61). Alopecia also is a rare adverse effect of the low doses used to treat ectopic pregnancy. Cases of pneumonitis also have been reported, and women should be counseled to report any fever or respiratory symptoms to their physicians (62).

▶ *How should women be counseled regarding the treatment effects of methotrexate?*

Patients treated with methotrexate should be counseled about the risk of ectopic pregnancy rupture; about avoiding certain foods, supplements, or drugs that can decrease efficacy; and about the importance of not becoming pregnant again until resolution has been confirmed. It is important to educate patients about the symptoms of tubal rupture and to emphasize the need to seek immediate medical attention if these symptoms occur. Vigorous activity and sexual intercourse should be avoided until confirmation of resolution because of the theoretical risk of inducing rupture of the ectopic pregnancy. Additionally, practitioners should limit pelvic and ultrasound examinations when possible. Patients should be advised to avoid folic acid supplements, foods

that contain folic acid, and nonsteroidal antiinflammatory drugs during therapy because these products may decrease the efficacy of methotrexate. Avoidance of narcotic analgesic medications, alcohol, and gas-producing foods are recommended so as not to mask, or be confused with, escalation of symptoms of rupture. Sunlight exposure also should be avoided during treatment to limit the risk of methotrexate dermatitis (63).

Before treatment with methotrexate, women should be counseled about the potential for fetal death or teratogenic effects when administered during pregnancy. The product labeling approved by the U.S. Food and Drug Administration recommends that women avoid pregnancy during treatment and for at least one ovulatory cycle after methotrexate therapy (63). Methotrexate is cleared from the serum before the 4–12 weeks necessary for the resolution of the ectopic gestation and ovulation in the next cycle (64, 65). However, there are reports of methotrexate detectable in liver cells 116 days past exposure (66). Limited evidence suggests that the frequency of congenital anomalies or early pregnancy loss is not elevated in women who have become pregnant shortly after methotrexate exposure (66). However, perhaps based on the timing of methotrexate's clearance from the body, some experts continue to recommend that women delay pregnancy for at least 3 months after the last dose of methotrexate (67).

▶ *How does methotrexate treatment affect subsequent fertility?*

Patients can be counseled that available evidence, although limited, suggests that methotrexate treatment of ectopic pregnancy does not have an adverse effect on subsequent fertility or on ovarian reserve. A prospective observational study noted no difference in anti-müllerian hormone levels or reproductive outcomes after administration of methotrexate (68). Furthermore, a systematic review of women undergoing fertility treatment found no significant differences in the mean number of oocytes retrieved during the cycles before and after methotrexate administration (69).

▶ *Who are candidates for surgical management of ectopic pregnancy?*

In clinically stable women in whom a nonruptured ectopic pregnancy has been diagnosed, laparoscopic surgery or intramuscular methotrexate administration are safe and effective treatments. The decision for surgical management or medical management of ectopic pregnancy should be guided by the initial clinical, laboratory, and radiologic data as well as patient-informed choice based on a discussion of the benefits and risks of each approach. Surgical management of ectopic pregnancy is required when a patient is exhibiting any of the following: hemodynamic instability, symptoms of an ongoing ruptured ectopic mass (such as pelvic pain), or signs of intraperitoneal bleeding.

Surgical management is necessary when a patient meets any of the absolute contraindications to medical management listed in Box 1 and should be considered when a patient meets any of the relative contraindications. Surgical management should be employed when a patient who initially elects medical management experiences a failure of medical management. Surgical treatment also can be considered for a clinically stable patient with a nonruptured ectopic pregnancy or when there is an indication for a concurrent surgical procedure, such as tubal sterilization or removal of hydrosalpinx when a patient is planning to undergo subsequent in vitro fertilization.

Surgical management generally is performed using laparoscopic salpingectomy (removal of part or all of the affected fallopian tube) or laparoscopic salpingostomy (removal of the ectopic pregnancy while leaving the affected fallopian tube in situ). Laparotomy typically is reserved for unstable patients, patients with a large amount of intraperitoneal bleeding, and patients in whom visualization has been compromised at laparoscopy.

▶ *How do medical management and surgical management of ectopic pregnancy compare in effectiveness and risk of complications?*

Medical management of ectopic pregnancy avoids the inherent risks of surgery and anesthesia. However, compared with laparoscopic salpingectomy, medical management of ectopic pregnancy has a lower success rate and requires longer surveillance, more office visits, and phlebotomy. Randomized trials that compared medical management of ectopic pregnancy with methotrexate to laparoscopic salpingostomy have demonstrated a statistically significant lower success rate with the use of single-dose methotrexate (relative rate for success, 0.82; 95% CI, 0.72–0.94) and no difference with the use of multidose methotrexate (relative rate for success, 1.8; 95% CI, 0.73–4.6) (70). Comparing systemic methotrexate with tube-sparing laparoscopic surgery, randomized trials have shown no difference in overall tubal preservation, tubal patency, repeat ectopic pregnancy, or future pregnancies (70).

Medical management of ectopic pregnancy is cost effective when laparoscopy is not needed to make the diagnosis and hCG values are less 1,500 mIU/mL (71). Surgical management of ectopic pregnancy is more cost

effective if time to resolution is expected to be prolonged, or there is a relatively high chance of medical management failure, such as in cases with high or increasing hCG values or when embryonic cardiac activity is detected (72, 73).

How do salpingostomy and salpingectomy compare in effectiveness and fertility outcomes in the management of ectopic pregnancy?

The decision to perform a salpingostomy or salpingectomy for the treatment of ectopic pregnancy should be guided by the patient's clinical status, her desire for future fertility, and the extent of fallopian tube damage. Randomized controlled trials that compared salpingectomy with salpingostomy for the management of ectopic pregnancy have found no statistically significant difference in the rates of subsequent intrauterine pregnancy (RR, 1.04; 95% CI, 0.899–1.21) or repeat ectopic pregnancy (RR, 1.30; 95% CI, 0.72–2.38) (74). In contrast, cohort study findings indicate that salpingostomy is associated with a higher rate of subsequent intrauterine pregnancy (RR, 1.24; 95% CI, 1.08–1.42) but also with an increased risk of repeat ectopic pregnancy (10% versus 4%; RR, 2.27; 95% CI, 1.12–4.58) compared with salpingectomy (74).

In general, salpingectomy is the preferred approach when severe fallopian tube damage is noted and in cases in which there is significant bleeding from the proposed surgical site. Salpingectomy can be considered in cases of desired future fertility when the patient has a healthy contralateral fallopian tube. However, salpingostomy should be considered in patients who desire future fertility but have damage to the contralateral fallopian tube and in whom removal would require assisted reproduction for future childbearing. When salpingostomy is performed, it is important to monitor the patient with serial hCG measurement to ensure resolution of ectopic trophoblastic tissue. If there is concern for incomplete resection, a single prophylactic dose of methotrexate may be considered (45).

Who are candidates for expectant management of diagnosed ectopic pregnancy?

There may be a role for expectant management of ectopic pregnancy in specific circumstances. Candidates for successful expectant management of ectopic pregnancy should be asymptomatic; should have objective evidence of resolution (generally, manifested by a plateau or decrease in hCG levels); and must be counseled and willing to accept the potential risks, which include tubal rupture, hemorrhage, and emergency surgery. If the initial hCG level is less than 200 mIU/mL, 88% of patients will experience spontaneous resolution; lower spontaneous resolution rates can be anticipated with higher hCG levels (75). In a single small randomized trial of women with hCG levels less than 2,000 mIU/mL, expectant management was not associated with a statistically significant lower treatment success than single-dose methotrexate for the management of ectopic pregnancy (59% versus 76%, respectively) (RR, 1.3; 95% CI, 0.9–1.8) (76). Reasons for abandoning expectant management include intractable or significantly increased pain, insufficient decrease of hCG levels, or tubal rupture with hemoperitoneum.

Summary of Recommendations

The following recommendations are based on good and consistent scientific evidence (Level A):

- In clinically stable women in whom a nonruptured ectopic pregnancy has been diagnosed, laparoscopic surgery or intramuscular methotrexate administration are safe and effective treatments. The decision for surgical management or medical management of ectopic pregnancy should be guided by the initial clinical, laboratory, and radiologic data as well as patient-informed choice based on a discussion of the benefits and risks of each approach.
- Surgical management of ectopic pregnancy is required when a patient is exhibiting any of the following: hemodynamic instability, symptoms of an ongoing ruptured ectopic mass (such as pelvic pain), or signs of intraperitoneal bleeding.

The following recommendations are based on limited or inconsistent scientific evidence (Level B):

- Serum hCG values alone should not be used to diagnose an ectopic pregnancy and should be correlated with the patient's history, symptoms, and ultrasound findings.
- If the concept of the hCG discriminatory level is to be used as a diagnostic aid in women at risk of ectopic pregnancy, the value should be conservatively high (eg, as high as 3,500 mIU/mL) to avoid the potential for misdiagnosis and possible interruption of an intrauterine pregnancy that a woman hopes to continue.
- The decision to perform a salpingostomy or salpingectomy for the treatment of ectopic pregnancy

should be guided by the patient's clinical status, her desire for future fertility, and the extent of fallopian tube damage.

- The choice of methotrexate protocol should be guided by the initial hCG level and discussion with the patient regarding the benefits and risks of each approach. In general, the single-dose protocol may be most appropriate for patients with a relatively low initial hCG level or a plateau in hCG values, and the two-dose regimen may be considered as an alternative to the single-dose regimen, particularly in women with an initial high hCG value.
- Failure of the hCG level to decrease by at least 15% from day 4 to day 7 after methotrexate administration is associated with a high risk of treatment failure and requires additional methotrexate administration (in the case of the single-dose or two-dose regimen) or surgical intervention.
- Patients can be counseled that available evidence, although limited, suggests that methotrexate treatment of ectopic pregnancy does not have an adverse effect on subsequent fertility or on ovarian reserve.
- There may be a role for expectant management of ectopic pregnancy in specific circumstances.

The following recommendations are based primarily on consensus and expert opinion (Level C):

- The minimum diagnostic evaluation of a suspected ectopic pregnancy is a transvaginal ultrasound evaluation and confirmation of pregnancy. Serial evaluation with transvaginal ultrasonography, or serum hCG level measurement, or both, often is required to confirm the diagnosis.
- A woman with a pregnancy of unknown location who is clinically stable and has a desire to continue the pregnancy, if intrauterine, should have a repeat transvaginal ultrasound examination, or serial measurement of hCG concentration, or both, to confirm the diagnosis and guide management.
- Medical management with methotrexate can be considered for women with a confirmed or high clinical suspicion of ectopic pregnancy who are hemodynamically stable, who have an unruptured mass, and who do not have absolute contraindications to methotrexate administration.
- After administration of methotrexate treatment, hCG levels should be serially monitored until a nonpregnancy level (based upon the reference laboratory assay) is reached.
- Patients treated with methotrexate should be counseled about the risk of ectopic pregnancy rupture; about avoiding certain foods, supplements, or drugs that can decrease efficacy; and about the importance of not becoming pregnant again until resolution has been confirmed.

References

1. Ectopic pregnancy--United States, 1990-1992. Centers for Disease Control and Prevention (CDC). MMWR Morb Mortal Wkly Rep. 1995;44:46–8. (Level II-2) ⇦
2. Creanga AA, Syverson C, Seed K, Callaghan WM. Pregnancy-related mortality in the United States, 2011-2013. Obstet Gynecol 2017;130:366–73. (Level II-2) ⇦
3. Barnhart KT, Sammel MD, Gracia CR, Chittams J, Hummel AC, Shaunik A. Risk factors for ectopic pregnancy in women with symptomatic first-trimester pregnancies. Fertil Steril 2006;86:36–43 (Level II-2) ⇦
4. Bouyer J, Coste J, Fernandez H, Pouly JL, Job-Spira N. Sites of ectopic pregnancy: a 10 year population-based study of 1800 cases. Hum Reprod 2002;17:3224–30. (Level II-3) ⇦
5. Maymon R, Shulman A. Controversies and problems in the current management of tubal pregnancy. Hum Reprod Update 1996;2:541–51. (Level III) ⇦
6. Barrenetxea G, Barinaga-Rementeria L, Lopez de Larruzea A, Agirregoikoa JA, Mandiola M, Carbonero K. Heterotopic pregnancy: two cases and a comparative review. Fertil Steril 2007;87:417.e9–15. (Level III) ⇦
7. Ankum WM, Mol BW, Van der Veen F, Bossuyt PM. Risk factors for ectopic pregnancy: a meta-analysis. Fertil Steril 1996;65:1093–9. (Meta-Analysis) ⇦
8. Clayton HB, Schieve LA, Peterson HB, Jamieson DJ, Reynolds MA, Wright VC. Ectopic pregnancy risk with assisted reproductive technology procedures. Obstet Gynecol 2006;107:595–604. (Level II-3) ⇦
9. Perkins KM, Boulet SL, Kissin DM, Jamieson DJ. Risk of ectopic pregnancy associated with assisted reproductive technology in the United States, 2001-2011. National ART Surveillance (NASS) Group. Obstet Gynecol 2015;125:70–8. (Level II-3) ⇦
10. Backman T, Rauramo I, Huhtala S, Koskenvuo M. Pregnancy during the use of levonorgestrel intrauterine system. Am J Obstet Gynecol 2004;190:50–4. (Level II-3) ⇦
11. Cleland K, Raymond E, Trussell J, Cheng L, Zhu H. Ectopic pregnancy and emergency contraceptive pills: a systematic review. Obstet Gynecol 2010;115:1263–6. (Systematic Review) ⇦
12. Emergency contraception. Practice Bulletin No. 152. American College of Obstetricians and Gynecologists. Obstet Gynecol 2015;126:e1–11. (Level III) ⇦
13. Kirk E, Papageorghiou AT, Condous G, Tan L, Bora S, Bourne T. The diagnostic effectiveness of an initial transvaginal scan in detecting ectopic pregnancy. Hum Reprod 2007;22:2824–8. (Level II-3) ⇦

14. van Mello NM, Mol F, Opmeer BC, Ankum WM, Barnhart K, Coomarasamy A, et al. Diagnostic value of serum hCG on the outcome of pregnancy of unknown location: a systematic review and meta-analysis. Hum Reprod Update 2012;18:603–17. (Systematic Review and Meta-Analysis)

15. Barnhart KT, Fay CA, Suescum M, Sammel MD, Appleby D, Shaunik A, et al. Clinical factors affecting the accuracy of ultrasonography in symptomatic first-trimester pregnancy. Obstet Gynecol 2011;117:299–306. (Level II-3)

16. Barnhart K, van Mello NM, Bourne T, Kirk E, Van Calster B, Bottomley C, et al. Pregnancy of unknown location: a consensus statement of nomenclature, definitions, and outcome. Fertil Steril 2011;95:857–66. (Level III)

17. Goldstein SR, Snyder JR, Watson C, Danon M. Very early pregnancy detection with endovaginal ultrasound. Obstet Gynecol 1988;72:200–4. (Level III)

18. Doubilet PM, Benson CB. Double sac sign and intradecidual sign in early pregnancy: interobserver reliability and frequency of occurrence. J Ultrasound Med 2013;32:1207–14. (Level II-3)

19. Ackerman TE, Levi CS, Lyons EA, Dashefsky SM, Lindsay DJ, Holt SC. Decidual cyst: endovaginal sonographic sign of ectopic pregnancy. Radiology 1993;189:727–31. (Level II-3)

20. Ahmed AA, Tom BD, Calabrese P. Ectopic pregnancy diagnosis and the pseudo-sac. Fertil Steril 2004;81:1225–8. (Level III)

21. Seeber BE, Sammel MD, Guo W, Zhou L, Hummel A, Barnhart KT. Application of redefined human chorionic gonadotropin curves for the diagnosis of women at risk for ectopic pregnancy. Fertil Steril 2006;86:454–9. (Level II-3)

22. Morse CB, Sammel MD, Shaunik A, Allen-Taylor L, Oberfoell NL, Takacs P, et al. Performance of human chorionic gonadotropin curves in women at risk for ectopic pregnancy: exceptions to the rules. Fertil Steril 2012;97:101–6.e2. (Level II-3)

23. Early pregnancy loss. Practice Bulletin No. 150. American College of Obstetricians and Gynecologists. Obstet Gynecol 2015;125:1258–67. (Level III)

24. Doubilet PM, Benson CB, Bourne T, Blaivas M, Barnhart KT, Benacerraf BR, et al. Diagnostic criteria for nonviable pregnancy early in the first trimester. Society of Radiologists in Ultrasound Multispecialty Panel on Early First Trimester Diagnosis of Miscarriage and Exclusion of a Viable Intrauterine Pregnancy. N Engl J Med 2013;369:1443–51. (Level III)

25. Goldstein I, Zimmer EA, Tamir A, Peretz BA, Paldi E. Evaluation of normal gestational sac growth: appearance of embryonic heartbeat and embryo body movements using the transvaginal technique. Obstet Gynecol 1991;77:885–8. (Level II-3)

26. Rossavik IK, Torjusen GO, Gibbons WE. Conceptual age and ultrasound measurements of gestational sac and crown-rump length in in vitro fertilization pregnancies. Fertil Steril 1988;49:1012–7. (Level III)

27. Barnhart KT, Katz I, Hummel A, Gracia CR. Presumed diagnosis of ectopic pregnancy. Obstet Gynecol 2002;100:505–10. (Level II-3)

28. Chung K, Chandavarkar U, Opper N, Barnhart K. Reevaluating the role of dilation and curettage in the diagnosis of pregnancy of unknown location. Fertil Steril 2011;96:659–62. (Level II-3)

29. Shaunik A, Kulp J, Appleby DH, Sammel MD, Barnhart KT. Utility of dilation and curettage in the diagnosis of pregnancy of unknown location. Am J Obstet Gynecol 2011;204:130.e1–6. (Level II-3)

30. Doubilet PM, Benson CB. Further evidence against the reliability of the human chorionic gonadotropin discriminatory level. J Ultrasound Med 2011;30:1637–42. (Level II-3)

31. Mehta TS, Levine D, Beckwith B. Treatment of ectopic pregnancy: is a human chorionic gonadotropin level of 2,000 mIU/mL a reasonable threshold? Radiology 1997;205:569–73. (Level II-3)

32. Connolly A, Ryan DH, Stuebe AM, Wolfe HM. Reevaluation of discriminatory and threshold levels for serum beta-hCG in early pregnancy. Obstet Gynecol 2013;121:65–70. (Level II-3)

33. Barnhart KT, Sammel MD, Rinaudo PF, Zhou L, Hummel AC, Guo W. Symptomatic patients with an early viable intrauterine pregnancy: HCG curves redefined. Obstet Gynecol 2004;104:50–5. (Level II-3)

34. Barnhart K, Sammel MD, Chung K, Zhou L, Hummel AC, Guo W. Decline of serum human chorionic gonadotropin and spontaneous complete abortion: defining the normal curve. Obstet Gynecol 2004;104:975–81. (Level II-3)

35. Barnhart KT, Guo W, Cary MS, Morse CB, Chung K, Takacs P, et al. Differences in serum human chorionic gonadotropin rise in early pregnancy by race and value at presentation. Obstet Gynecol 2016;128:504–11. (Level II-3)

36. Silva C, Sammel MD, Zhou L, Gracia C, Hummel AC, Barnhart K. Human chorionic gonadotropin profile for women with ectopic pregnancy. Obstet Gynecol 2006;107:605–10. (Level II-3)

37. Barnhart KT. Early pregnancy failure: beware of the pitfalls of modern management. Fertil Steril 2012;98:1061–5. (Level III)

38. Nurmohamed L, Moretti ME, Schechter T, Einarson A, Johnson D, Lavigne SV, et al. Outcome following high-dose methotrexate in pregnancies misdiagnosed as ectopic. Am J Obstet Gynecol 2011;205:533.e1–3. (Level III)

39. Addar MH. Methotrexate embryopathy in a surviving intrauterine fetus after presumed diagnosis of ectopic pregnancy: case report. J Obstet Gynaecol Can 2004;26:1001–3. (Level III)

40. Rivera V, Nguyen PH, Sit A. Change in quantitative human chorionic gonadotropin after manual vacuum aspiration in women with pregnancy of unknown location. Am J Obstet Gynecol 2009;200:e56–9.

41. Insogna IG, Farland LV, Missmer SA, Ginsburg ES, Brady PC. Outpatient endometrial aspiration: an alternative to

methotrexate for pregnancy of unknown location. Am J Obstet Gynecol 2017;217:185.e1–9.

42. Rubal L, Chung K. Do you need to definitively diagnose the location of a pregnancy of unknown location? The case for "yes." Fertil Steril 2012;98:1078–84. (Level III)
43. Reid S, Condous G. Is there a need to definitively diagnose the location of a pregnancy of unknown location? The case for "no." Fertil Steril 2012;98:1085–90. (Level III)
44. Ailawadi M, Lorch SA, Barnhart KT. Cost-effectiveness of presumptively medically treating women at risk for ectopic pregnancy compared with first performing a dilatation and curettage. Fertil Steril 2005;83:376–82. (Cost-analysis)
45. Medical treatment of ectopic pregnancy: a committee opinion. Practice Committee of American Society for Reproductive Medicine. Fertil Steril 2013;100:638–44. (Level III)
46. Tanaka T, Hayashi H, Kutsuzawa T, Fujimoto S, Ichinoe K. Treatment of interstitial ectopic pregnancy with methotrexate: report of a successful case. Fertil Steril 1982; 37:851–2. (Level III)
47. Lipscomb GH, Meyer NL, Flynn DE, Peterson M, Ling FW. Oral methotrexate for treatment of ectopic pregnancy. Am J Obstet Gynecol 2002;186:1192–5. (Level II-2)
48. Menon S, Colins J, Barnhart KT. Establishing a human chorionic gonadotropin cutoff to guide methotrexate treatment of ectopic pregnancy: a systematic review. Fertil Steril 2007;87:481–4. (Systematic Review)
49. Lipscomb GH, Bran D, McCord ML, Portera JC, Ling FW. Analysis of three hundred fifteen ectopic pregnancies treated with single-dose methotrexate. Am J Obstet Gynecol 1998;178:1354–8. (Level II-3)
50. Cohen A, Zakar L, Gil Y, Amer-Alshiek J, Bibi G, Almog B, et al. Methotrexate success rates in progressing ectopic pregnancies: a reappraisal. Am J Obstet Gynecol 2014;211:128.e1–5. (Level II-3)
51. Stovall TG, Ling FW. Single-dose methotrexate: an expanded clinical trial. Am J Obstet Gynecol 1993;168:1759-62; discussion 1762–5. (Level II-3)
52. Barnhart K, Hummel AC, Sammel MD, Menon S, Jain J, Chakhtoura N. Use of "2-dose" regimen of methotrexate to treat ectopic pregnancy. Fertil Steril 2007;87:250–6. (Level III)
53. Rodi IA, Sauer MV, Gorrill MJ, Bustillo M, Gunning JE, Marshall JR, et al. The medical treatment of unruptured ectopic pregnancy with methotrexate and citrovorum rescue: preliminary experience. Fertil Steril 1986;46:811–3. (Level III)
54. Lipscomb GH, Givens VM, Meyer NL, Bran D. Comparison of multidose and single-dose methotrexate protocols for the treatment of ectopic pregnancy. Am J Obstet Gynecol 2005;192:1844-7; discussion 1847–8. (Level II-3)
55. Barnhart KT, Gosman G, Ashby R, Sammel M. The medical management of ectopic pregnancy: a meta-analysis comparing "single dose" and "multidose" regimens. Obstet Gynecol 2003;101:778–84. (Meta-Analysis)
56. Yang C, Cai J, Geng Y, Gao Y. Multiple-dose and double-dose versus single-dose administration of methotrexate for the treatment of ectopic pregnancy: a systematic review and meta-analysis. Reprod Biomed Online 2017;34:383–91. (Systematic Review and Meta-Analysis)
57. Song T, Kim MK, Kim ML, Jung YW, Yun BS, Seong SJ. Single-dose versus two-dose administration of methotrexate for the treatment of ectopic pregnancy: a randomized controlled trial. Hum Reprod 2016;31:332–8. (Level I)
58. Hamed HO, Ahmed SR, Alghasham AA. Comparison of double- and single-dose methotrexate protocols for treatment of ectopic pregnancy. Int J Gynaecol Obstet 2012;116:67–71. (Level I)
59. Atri M, Bret PM, Tulandi T, Senterman MK. Ectopic pregnancy: evolution after treatment with transvaginal methotrexate. Radiology 1992;185:749–53. (Level III)
60. Brown DL, Doubilet PM. Transvaginal sonography for diagnosing ectopic pregnancy: positivity criteria and performance characteristics. J Ultrasound Med 1994;13: 259–66. (Level III)
61. Pisarska MD, Carson SA, Buster JE. Ectopic pregnancy. Lancet 1998;351:1115–20. (Level III)
62. Dasari P, Sagili H. Life-threatening complications following multidose methotrexate for medical management of ectopic pregnancy. BMJ Case Rep 2012;2012. (Level III)
63. Methotrexate – injection. In: Drug facts and comparisons. St. Louis (MO): Wolters Kluwer; 2017. p. 3883–90. (Level III)
64. Huffman DH, Wan SH, Azarnoff DL, Hogstraten B. Pharmacokinetics of methotrexate. Clin Pharmacol Ther 1973;14:572–9. (Level III)
65. Shen DD, Azarnoff DL. Clinical pharmacokinetics of methotrexate. Clin Pharmacokinet 1978;3:1–13. (Level III)
66. Svirsky R, Rozovski U, Vaknin Z, Pansky M, Schneider D, Halperin R. The safety of conception occurring shortly after methotrexate treatment of an ectopic pregnancy. Reprod Toxicol 2009;27:85–7. (Level II-3)
67. Hackmon R, Sakaguchi S, Koren G. Effect of methotrexate treatment of ectopic pregnancy on subsequent pregnancy. Can Fam Physician 2011;57:37–9. (Level III)
68. Oriol B, Barrio A, Pacheco A, Serna J, Zuzuarregui JL, Garcia-Velasco JA. Systemic methotrexate to treat ectopic pregnancy does not affect ovarian reserve. Fertil Steril 2008;90:1579–82. (Level III)
69. Ohannessian A, Loundou A, Courbiere B, Cravello L, Agostini A. Ovarian responsiveness in women receiving fertility treatment after methotrexate for ectopic pregnancy: a systematic review and meta-analysis. Hum Reprod 2014;29:1949–56. (Systematic Review and Meta-Analysis)
70. Hajenius PJ, Mol F, Mol BW, Bossuyt PM, Ankum WM, Van der Veen F. Interventions for tubal ectopic pregnancy. Cochrane Database of Systematic Reviews 2007, Issue 1. Art. No.: CD000324. DOI: 10.1002/14651858. CD000324.pub2. (Meta-Analysis)
71. Mol BW, Swart P, Bossuyt PM, van der Veen F. Prognostic significance of diagnostic laparoscopy for spontaneous fertility. J Reprod Med 1999;44:81–6. (Level II-2)

72. Morlock RJ, Lafata JE, Eisenstein D. Cost-effectiveness of single-dose methotrexate compared with laparoscopic treatment of ectopic pregnancy. Obstet Gynecol 2000;95:407–12. (Cost-analysis)

73. Sowter MC, Farquhar CM, Gudex G. An economic evaluation of single dose systemic methotrexate and laparoscopic surgery for the treatment of unruptured ectopic pregnancy. BJOG 2001;108:204–12. (Cost-analysis)

74. Cheng X, Tian X, Yan Z, Jia M, Deng J, Wang Y, et al. Comparison of the fertility outcome of salpingotomy and salpingectomy in women with tubal pregnancy: a systematic review and meta-analysis. PLoS One 2016;11:e0152343. (Systematic Review and Meta-Analysis)

75. Korhonen J, Stenman UH, Ylostalo P. Serum human chorionic gonadotropin dynamics during spontaneous resolution of ectopic pregnancy. Fertil Steril 1994;61:632–6. (Level II-3)

76. van Mello NM, Mol F, Verhoeve HR, van Wely M, Adriaanse AH, Boss EA, et al. Methotrexate or expectant management in women with an ectopic pregnancy or pregnancy of unknown location and low serum hCG concentrations? A randomized comparison. Hum Reprod 2013;28:60–7. (Level I)

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Tubal ectopic pregnancy. ACOG Practice Bulletin No. 193. American College of Obstetricians and Gynecologists. Obstet Gynecol 2018; 131:e91–103.

The MEDLINE database, the Cochrane Library, and ACOG's own internal resources and documents were used to conduct a literature search to locate relevant articles published between January 2000 and September 2017. The search was restricted to articles published in the English language. Priority was given to articles reporting results of original research, although review articles and commentaries also were consulted. Abstracts of research presented at symposia and scientific conferences were not considered adequate for inclusion in this document. Guidelines published by organizations or institutions such as the National Institutes of Health and the American College of Obstetricians and Gynecologists were reviewed, and additional studies were located by reviewing bibliographies of identified articles. When reliable research was not available, expert opinions from obstetrician–gynecologists were used.

Studies were reviewed and evaluated for quality according to the method outlined by the U.S. Preventive Services Task Force:

I	Evidence obtained from at least one properly designed randomized controlled trial.
II-1	Evidence obtained from well-designed controlled trials without randomization.
II-2	Evidence obtained from well-designed cohort or case–control analytic studies, preferably from more than one center or research group.
II-3	Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.
III	Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Based on the highest level of evidence found in the data, recommendations are provided and graded according to the following categories:

Level A—Recommendations are based on good and consistent scientific evidence.

Level B—Recommendations are based on limited or inconsistent scientific evidence.

Level C—Recommendations are based primarily on consensus and expert opinion.

FLEISHER DECLARATION: EXHIBIT C

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Clinical Management Guidelines for Obstetrician–Gynecologists

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Committee on Practice Bulletins—Obstetrics. This Practice Bulletin was developed by the American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Obstetrics in collaboration with Jimmy Espinoza, MD, MSc; Alex Vidaeff, MD, MPH; Christian M. Pettker, MD; and Hyagriv Simhan, MD.

INTERIM UPDATE: The content of this Practice Bulletin has been updated as highlighted (or removed as necessary) to include limited, focused editorial corrections to platelet counts, diagnostic criteria for preeclampsia (Box 2), and preeclampsia with severe features (Box 3).

Gestational Hypertension and Preeclampsia

Hypertensive disorders of pregnancy constitute one of the leading causes of maternal and perinatal mortality worldwide. It has been estimated that preeclampsia complicates 2–8% of pregnancies globally (1). In Latin America and the Caribbean, hypertensive disorders are responsible for almost 26% of maternal deaths, whereas in Africa and Asia they contribute to 9% of deaths. Although maternal mortality is much lower in high-income countries than in developing countries, 16% of maternal deaths can be attributed to hypertensive disorders (1, 2). In the United States, the rate of preeclampsia increased by 25% between 1987 and 2004 (3). Moreover, in comparison with women giving birth in 1980, those giving birth in 2003 were at 6.7-fold increased risk of severe preeclampsia (4). This complication is costly: one study reported that in 2012 in the United States, the estimated cost of preeclampsia within the first 12 months of delivery was $2.18 billion ($1.03 billion for women and $1.15 billion for infants), which was disproportionately borne by premature births (5). This Practice Bulletin will provide guidelines for the diagnosis and management of gestational hypertension and preeclampsia.

Background

Risk Factors

A variety of risk factors have been associated with increased probability of preeclampsia (Box 1) (6–12). Nonetheless, it is important to remember that most cases of preeclampsia occur in healthy nulliparous women with no obvious risk factors. Although the precise role of genetic–environmental interactions on the risk and incidence of preeclampsia is unclear, emerging data suggest the tendency to develop preeclampsia may have some genetic component (13–16).

Definitions and Diagnostic Criteria for Hypertensive Disorders of Pregnancy

Preeclampsia (With and Without Severe Features)

Preeclampsia is a disorder of pregnancy associated with new-onset hypertension, which occurs most often after 20 weeks of gestation and frequently near term. Although often accompanied by new-onset proteinuria, hypertension and other signs or symptoms of preeclampsia may present in some women in the absence of proteinuria (17). Reliance on maternal symptoms may be occasionally problematic in clinical practice. Right upper quadrant or epigastric

Box 1. Risk Factors for Preeclampsia

Nulliparity
Multifetal gestations
Preeclampsia in a previous pregnancy
Chronic hypertension
Pregestational diabetes
Gestational diabetes
Thrombophilia
Systemic lupus erythematosus
Prepregnancy body mass index greater than 30
Antiphospholipid antibody syndrome
Maternal age 35 years or older
Kidney disease
Assisted reproductive technology
Obstructive sleep apnea

pain is thought to be due to periportal and focal parenchymal necrosis, hepatic cell edema, or Glisson's capsule distension, or a combination. However, there is not always a good correlation between the hepatic histopathology and laboratory abnormalities (18). Similarly, studies have found that using headache as a diagnostic criterion for preeclampsia with severe features is unreliable and nonspecific. Thus, an astute and circumspect diagnostic approach is required when other corroborating signs and symptoms indicative of severe preeclampsia are missing (19, 20). Of note, in the setting of a clinical presentation similar to preeclampsia, but at gestational ages earlier than 20 weeks, alternative diagnoses should to be considered, including but not limited to thrombotic thrombocytopenic purpura, hemolytic–uremic syndrome, molar pregnancy, renal disease or autoimmune disease.

Although hypertension and proteinuria are considered to be the classical criteria to diagnose preeclampsia, other criteria are also important. In this context, it is recommended that women with gestational hypertension in the absence of proteinuria are diagnosed with preeclampsia if they present with any of the following severe features: thrombocytopenia (platelet count less than 100,~~000~~ $\times$ 10^9/L); impaired liver function as indicated by abnormally elevated blood concentrations of liver enzymes (to twice the upper limit of normal concentration); severe persistent right upper quadrant or epigastric pain and not accounted for by alternative diagnoses; renal insufficiency (serum creatinine concentration greater than 1.1 mg/dL or a doubling of the serum creatinine concentration in the absence of other renal disease); pulmonary edema; or new-onset headache unresponsive to acetaminophen and not accounted for by alternative diagnoses or visual disturbances (Box 2). *Gestational hypertension* is defined as a systolic blood pressure of 140 mm Hg or more or a diastolic blood pressure of 90 mm Hg or more, or both, on two occasions at least 4 hours apart after 20 weeks of gestation in a woman with a previously normal blood pressure (21). Women with gestational hypertension with severe range blood pressures (a systolic blood pressure of 160 mm Hg or higher, or diastolic blood pressure of 110 mm Hg or higher) should be diagnosed with preeclampsia with severe features. These severe ranges of blood pressure or any of the severe features listed in Box 3 increase the risk of morbidity and mortality (22).

Box 2. Diagnostic Criteria for Preeclampsia

Blood pressure

- Systolic blood pressure of 140 mm Hg or more or diastolic blood pressure of 90 mm Hg or more on two occasions at least 4 hours apart after 20 weeks of gestation in a woman with a previously normal blood pressure
- Systolic blood pressure of 160 mm Hg or more or diastolic blood pressure of 110 mm Hg or more. (Severe hypertension can be confirmed within a short interval (minutes) to facilitate timely antihypertensive therapy).

and

Proteinuria

- 300 mg or more per 24 hour urine collection (or this amount extrapolated from a timed collection) or
- Protein/creatinine ratio of 0.3 ~~mg/dL~~ or more or
- Dipstick reading of 2+ (used only if other quantitative methods not available)

Or in the absence of proteinuria, new-onset hypertension with the new onset of any of the following:

- Thrombocytopenia: Platelet count less than 100,~~000~~ $\times$ 10^9/L
- Renal insufficiency: Serum creatinine concentrations greater than 1.1 mg/dL or a doubling of the serum creatinine concentration in the absence of other renal disease
- Impaired liver function: Elevated blood concentrations of liver transaminases to twice normal concentration
- Pulmonary edema
- New-onset headache unresponsive to medication and not accounted for by alternative diagnoses or visual symptoms

Box 3. Preeclampsia with Severe Features

- Systolic blood pressure of 160 mm Hg or more, or diastolic blood pressure of 110 mm Hg or more on two occasions at least 4 hours apart (unless antihypertensive therapy is initiated before this time)
- Thrombocytopenia (platelet count less than 100,000 $\times$ 10^9/L
- Impaired liver function that is not accounted for by alternative diagnoses and as indicated by abnormally elevated blood concentrations of liver enzymes (to more than twice the upper limit normal concentrations), or by severe persistent right upper quadrant or epigastric pain unresponsive to medications
- Renal insufficiency (serum creatinine concentration more than 1.1 mg/dL or a doubling of the serum creatinine concentration in the absence of other renal disease)
- Pulmonary edema
- New-onset headache unresponsive to medication and not accounted for by alternative diagnoses
- Visual disturbances

Proteinuria during pregnancy is defined as 300 mg/dL of protein or more in a 24-hour urine collection (21, 23) or a protein -to-creatinine ratio of 0.30 or more (24). When quantitative methods are not available or rapid decisions are required, a urine protein dipstick reading can be substituted. However, dipstick urinalysis has high false–positive and false–negative test results. A test result of 1+ proteinuria is false–positive in 71% of cases compared with the 300 mg cutoff on 24-hour urine collection, and even 3+ proteinuria test results may be false–positive in 7% of cases. Using the same 24-hour urine collection standard, the false–negative rate for dipstick urinalysis is 9% (25). If urinalysis is the only available means of assessing proteinuria then overall accuracy is better using 2+ as the discriminant value (25, 26).

Gestational Hypertension

Gestational hypertension is defined as a systolic blood pressure 140 mm Hg or more or a diastolic blood pressure of 90 mm Hg or more, or both, on two occasions at least 4 hours apart after 20 weeks of gestation, in a woman with a previously normal blood pressure (21). Gestational hypertension is considered severe when the systolic level reaches 160 mm Hg or the diastolic level reaches 110 mm Hg, or both. On occasion, especially when faced with severe hypertension, the diagnosis may need to be confirmed within a shorter interval (minutes) than 4 hours to facilitate timely antihypertensive therapy (27). Gestational hypertension occurs when hypertension without proteinuria or severe features develops after 20 weeks of gestation and blood pressure levels return to normal in the postpartum period (21). It appears that this diagnosis is more of an exercise of nomenclature than a pragmatic one because the management of gestational hypertension and that of preeclampsia without severe features is similar in many aspects, and both require enhanced surveillance. Outcomes in women with gestational hypertension usually are good, but the notion that gestational hypertension is intrinsically less concerning than preeclampsia is incorrect. Gestational hypertension is associated with adverse pregnancy outcomes (17) and may not represent a separate entity from preeclampsia (28). Up to 50% of women with gestational hypertension will eventually develop proteinuria or other end-organ dysfunction consistent with the diagnosis of preeclampsia, and this progression is more likely when the hypertension is diagnosed before 32 weeks of gestation (29, 30). Although investigators have reported a higher perinatal mortality rate in women with nonproteinuric hypertension compared with proteinuric preeclampsia (31), in a cohort of 1,348 hypertensive pregnant patients, the women with proteinuria progressed more frequently to severe hypertension and had higher rates of preterm birth and perinatal mortality; however, women without proteinuria had a higher frequency of thrombocytopenia or liver dysfunction (17). Women with gestational hypertension who present with severe-range blood pressures should be managed with the same approach as for women with severe preeclampsia. Gestational hypertension and preeclampsia may also be undistinguishable in terms of long-term cardiovascular risks, including chronic hypertension (32).

Hemolysis, Elevated Liver Enzymes, and Low Platelet Count Syndrome

The clinical presentation of hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome is one of the more severe forms of preeclampsia because it has been associated with increased rates of maternal morbidity and mortality (33). Although different diagnostic benchmarks have been proposed (34), many clinicians use the following criteria (35) to make the diagnosis: lactate dehydrogenase (LDH) elevated to 600 IU/L or more, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) elevated more than twice the upper limit of normal, and the platelets count less than 100,000 $\times$ 10^9/L. Although HELLP syndrome is mostly a third-trimester condition, in 30% of cases it is

first expressed or progresses postpartum. Furthermore, HELLP syndrome may have an insidious and atypical onset, with up to 15% of the patients lacking either hypertension or proteinuria (36). In HELLP syndrome, the main presenting symptoms are right upper quadrant pain and generalized malaise in up to 90% of cases and nausea and vomiting in 50% of cases (35, 37).

Eclampsia

Eclampsia is the convulsive manifestation of the hypertensive disorders of pregnancy and is among the more severe manifestations of the disease. Eclampsia is defined by new-onset tonic-clonic, focal, or multifocal seizures in the absence of other causative conditions such as epilepsy, cerebral arterial ischemia and infarction, intracranial hemorrhage, or drug use. Some of these alternative diagnoses may be more likely in cases in which new-onset seizures occur after 48–72 hours postpartum (38) or when seizures occur during administration of magnesium sulfate.

Eclampsia is a significant cause of maternal death, particularly in low-resource settings. Seizures may lead to severe maternal hypoxia, trauma, and aspiration pneumonia. Although residual neurologic damage is rare, some women may have short-term and long-term consequences such as impaired memory and cognitive function, especially after recurrent seizures or uncorrected severe hypertension leading to cytotoxic edema or infarction (39). Permanent white matter loss has been documented on magnetic resonance imaging (MRI) after eclampsia in up to one fourth of women, however, this does not translate into significant neurologic deficits (39).

Eclampsia often (78–83% of cases) is preceded by premonitory signs of cerebral irritation such as severe and persistent occipital or frontal headaches, blurred vision, photophobia, and altered mental status. However, eclampsia can occur in the absence of warning signs or symptoms (40, 41). Eclampsia can occur before, during, or after labor. Of note, a significant proportion of women (20–38%) do not demonstrate the classic signs of preeclampsia (hypertension or proteinuria) before the seizure episode (42). Headaches are believed to reflect the development of elevated cerebral perfusion pressure, cerebral edema, and hypertensive encephalopathy (43).

The term preeclampsia implies that the natural history of patients with persistent hypertension and significant proteinuria during pregnancy is to have tonic–clonic seizures if no prophylaxis if instituted. However, the results of two randomized placebo-controlled trials indicate that seizure occurred in only a small proportion of patients with preeclampsia (1.9%) (44) or severe preeclampsia (3.2%) (45) allocated to the placebo arm of both studies. It is also noteworthy that there is a significant proportion of patients who had abrupt-onset eclampsia without warning signs or symptoms (40). In a nationwide analysis of cases of eclampsia in the United Kingdom, it was noted that in 38% of eclamptic cases the seizure occurred without any prior documentation of either hypertension or proteinuria in the hospital setting (46). Thus, the notion that preeclampsia has a natural linear progression from preeclampsia without severe features to preeclampsia with severe features and eventually to eclamptic convulsions is inaccurate.

Nervous system manifestations frequently encountered in preeclampsia are headache, blurred vision, scotomata, and hyperreflexia. Although uncommon, temporary blindness (lasting a few hours to as long as a week) also may accompany preeclampsia with severe features and eclampsia (47). Posterior reversible encephalopathy syndrome (PRES) is a constellation of a range of clinical neurologic signs and symptoms such as vision loss or deficit, seizure, headache, and altered sensorium or confusion (48). Although suspicion for PRES is increased in the setting of these clinical features, the diagnosis of PRES is made by the presence of vasogenic edema and hyperintensities in the posterior aspects of the brain on magnetic resonance imaging. Women are particularly at risk of PRES in the settings of eclampsia and preeclampsia with headache, altered consciousness, or visual abnormalities (49). Another condition that may be confused with eclampsia or preeclampsia is reversible cerebral vasoconstriction syndrome (50). Reversible cerebral vasoconstriction syndrome is characterized by reversible multifocal narrowing of the arteries of the brain with signs and symptoms that typically include thunderclap headache and, less commonly, focal neurologic deficits related to brain edema, stroke, or seizure. Treatment of women with PRES and reversible cerebral vasoconstriction syndrome may include medical control of hypertension, antiepileptic medication and long-term neurologic follow-up.

Pathophysiology

Several mechanisms of disease have been proposed in preeclampsia (1, 51, 52) including the following: chronic uteroplacental ischemia (53), immune maladaptation (53), very low-density lipoprotein toxicity (53), genetic imprinting (53), increased trophoblast apoptosis or necrosis (54, 55), and an exaggerated maternal inflammatory response to deported trophoblasts (56, 57). More recent observations suggest a possible role for imbalances of angiogenic factors in the pathogenesis of preeclampsia (58). It is possible that a combination of some of these purported mechanisms may be responsible

for triggering the clinical spectrum of preeclampsia. For example, there is clinical (59, 60) and experimental evidence (61, 62) suggesting that uteroplacental ischemia leads to increased circulating concentrations of antiangiogenic factors and angiogenic imbalances (63).

Vascular Changes

In addition to hypertension, women with preeclampsia or eclampsia typically lack the hypervolemia associated with normal pregnancy; thus, hemoconcentration is a frequent finding (64). In addition, the interaction of various vasoactive agents, such as prostacyclin (vasodilator), thromboxane A_2 (potent vasoconstrictor), nitric oxide (potent vasodilator), and endothelins (potent vasoconstrictors) results in another significant change described in preeclampsia: intense vasospasm. Attempts to correct the contraction of the intravascular space in preeclampsia with vigorous fluid therapy are likely to be ineffective and could be dangerous because of the frequent capillary leak and decreased colloid oncotic pressure often associated with preeclampsia. Aggressive fluid therapy may result in elevation of the pulmonary capillary wedge pressure and increased risk of pulmonary edema. A study using invasive hemodynamic monitoring in women with preeclampsia found that before intravenous fluid therapy, women with preeclampsia had hyperdynamic ventricular function with low pulmonary capillary wedge pressure (65). However, after aggressive fluid therapy, the pulmonary capillary wedge pressure increased significantly above normal levels (65) with increased risk of pulmonary edema.

Hematologic Changes

Various hematologic changes also may occur in women with preeclampsia, especially in preeclampsia with severe features. Thrombocytopenia and hemolysis may occur and may reach severe levels as part of HELLP syndrome. Thrombocytopenia results from increased platelet activation, aggregation, and consumption (66) and is a marker of disease severity. A platelet count less than 150,000 $\times$ 10^9/L is found in approximately 20% of patients with preeclampsia, varying from 7% in cases without severe manifestations to 50% in cases with severe manifestations (67). However, reduced platelet counts significant liver dysfunction, or there is suspected are not found in all cases of preeclampsia or eclampsia (68). Interpretation of hematocrit levels in preeclampsia should take into consideration that hemolysis and hemoconcentration may occur (69). In some cases, the hematocrit may not appear decreased despite hemolysis because of baseline hemoconcentration. Lactate dehydrogenase is present in erythrocytes in high concentration. High serum concentrations of LDH (more than 600 IU/L) may be a sign of hemolysis (34, 35).

Hepatic Changes

Hepatic function may be significantly altered in women with preeclampsia with severe features. Alanine aminotransferase and AST may be elevated. Aspartate aminotransferase is the dominant transaminase released into the peripheral circulation in liver dysfunction due to preeclampsia and is related to periportal necrosis. The fact that AST is increased to a greater extent than ALT, at least initially, may help in distinguishing preeclampsia from other potential causes of parenchymal liver disease in which ALT usually is higher than AST. Increased serum levels of LDH in preeclampsia are caused by hepatic dysfunction (LDH derived from ischemic, or necrotic tissues, or both) and hemolysis (LDH from red blood cell destruction). Increase in bilirubin secondary to significant hemolysis may develop only in the late stages of the disease. Similarly, alterations in hepatic synthetic function, as reflected by abnormalities of prothrombin time, partial prothrombin time, and fibrinogen, usually develop in advanced preeclampsia. Evaluation of these coagulation parameters is probably only useful when the platelet count is below 150,000 $\times$ 10^9/L, there is significant liver dysfunction, or there is suspected placental abruption (70).

Renal Changes

The histopathologic renal changes classically described in preeclampsia as glomerular endotheliosis consist of swollen, vacuolated endothelial cells with fibrils, swollen mesangial cells, subendothelial deposits of protein reabsorbed from the glomerular filtrate, and tubular casts (71, 72). Proteinuria in preeclampsia is nonselective, as a result of increased tubular permeability to most large-molecular-weight proteins (albumin, globulin, transferrin, and hemoglobin). Urinary calcium decreases because of an increased tubular reabsorption of calcium.

In women with preeclampsia, contraction of the intravascular space secondary to vasospasm leads to worsening renal sodium and water retention (73). The normal increase in renal blood flow and glomerular filtration rate and the expected decrease in serum creatinine may not occur in women with preeclampsia, especially if the disease is severe. Preeclampsia with severe features may include acute renal deterioration as part of the clinical spectrum. Oliguria in severe preeclampsia is a consequence of intrarenal vasospasm with an approximate 25% reduction in glomerular filtration rate. In these patients, transient oliguria (less than 100 mL over 4 hours) is a common observation in labor or the first 24 hours of the postpartum period. Plasma concentrations of uric acid normally increase in late pregnancy, and this is thought to be due to increased rates of fetal or placental

production, or both, decreased binding to albumin, and a decrease in uric acid clearance. The serum uric acid concentration increases to a greater extent in preeclampsia (74). The most commonly accepted explanation for hyperuricemia in preeclampsia, besides increased production, is the increased reabsorption and decreased excretion of uric acid in the proximal renal tubules.

Fetal Consequences

As a result of impaired uteroplacental blood flow secondary to failure of physiologic transformation of the spiral arteries or placental vascular insults, or both, manifestations of preeclampsia also may be seen in the fetal–placental unit (63). Abnormalities in the placental bed and subsequent failure of physiologic transformation of the spiral arteries in the first or early second trimester (75, 76) limit the blood flow to the uteroplacental unit. Additional mechanisms for chronic uteroplacental ischemia include placental vascular insults (77, 78). Among women with preeclampsia, clinical manifestations that follow from this uteroplacental ischemia include fetal growth restriction, oligohydramnios, placental abruption, and nonreassuring fetal status demonstrated on antepartum surveillance. Consequently, fetuses of women with preeclampsia are at increased risk of spontaneous or indicated preterm delivery.

Clinical Considerations and Recommendations

▶ ***Are there screening methods that are useful to identify women at risk of developing hypertensive disorders of pregnancy?***

Several studies have evaluated the role of biochemical markers or a combination of biochemical and biophysical markers in the prediction of preeclampsia in the first and second trimesters of pregnancy (79). Regardless of the parameters used, screening for preeclampsia in low-risk women is associated with very low positive predictive values ranging from 8% to 33% (79). Thus, most screen–positive patients will not develop the disease and any prophylactic intervention in the screen-positive group would unnecessarily expose a large number of patients who would not benefit from these interventions.

In general, the sensitivity and specificity for the prediction of early-onset preeclampsia using first-trimester (80–82) and second-trimester biochemical (81, 83) or biophysical parameters (84–87) are better than for late-onset preeclampsia. The reason for this is still unclear but it is possible that the timing of the insults to the fetal supply line or the fetal response to these insults may be different between early-onset and late-onset preeclampsia. Even so, there is limited evidence that an accurate prediction of early-onset preeclampsia can be followed by interventions that improve maternal or fetal outcome.

Regardless of the index or combinations of indices used, uterine artery Doppler studies alone have a low predictive value for the development of early-onset preeclampsia and an even lower value for late-onset preeclampsia (88). Extensive work has identified some angiogenic factors (soluble fms-like tyrosine kinase-[sFlt-1], placental growth factor [PlGF], and soluble endoglin) in the second trimester as likely tools for the prediction of early-onset preeclampsia. However, no single test reliably predicts preeclampsia and further prospective investigation is required to demonstrate clinical utility. In the first trimester of pregnancy, it has been reported that a combination of low maternal serum concentrations of PlGF, high uterine artery pulsatility index, and other maternal parameters, identified 93.1% of patients who would develop preeclampsia requiring delivery before 34 weeks of gestation (82). However, the results of this study are based on mathematical modeling derived from a nested case−control study applied to a large cohort of almost 7,800 patients in which PlGF was measured only in the case−control group. The calculated positive predictive value was only 21.2%, indicating that approximately 79% of the women in the screen-positive group would not develop hypertensive disorders during pregnancy (82). Of note, a similar algorithm underperformed in a subsequent randomized trial performed by the same research group (89). Thus, biomarkers and ultrasonography cannot accurately predict preeclampsia and should remain investigational.

▶ ***Are there prevention strategies for reducing the risk of hypertensive disorders of pregnancy?***

Strategies to prevent preeclampsia have been studied extensively over the past 30 years. To date, no intervention has been proved unequivocally effective at eliminating the risk of preeclampsia. With regard to nutritional interventions, evidence is insufficient to demonstrate effectiveness for vitamins C and E (90), fish oil (91), garlic supplementation (92), vitamin D (93), folic acid (94) or sodium restriction (95) for reducing the risk of preeclampsia. A meta-analysis of 13 trials (15,730 women) reported a significant reduction in preeclampsia with calcium supplementation, with the greatest effect among women with low-baseline calcium intake (96). Yet, this is not the case in the United States or other developed countries. Likewise, data do not support

effectiveness of bed rest and, thus, it should not routinely be recommended (97).

Investigators hypothesized that an imbalance in prostacyclin and thromboxane A_2 metabolism was involved in the pathogenesis of preeclampsia, leading to the initial studies of aspirin for preeclampsia prevention because of its preferential inhibition of thromboxane A_2 at lower doses (98, 99). In a recent meta-analysis of aggregate data from 45 randomized trials, only a modest reduction in preeclampsia was noted when low-dose aspirin was started after 16 weeks of gestation (relative risk [RR], 0.81; 95% CI, 0.66–0.99) but a more significant reduction in severe preeclampsia (RR, 0.47; 95% CI, 0.26–0.83) and fetal growth restriction (RR, 0.56; 95% CI, 0.44–0.70) was demonstrated when low-dose aspirin was started before 16 weeks of gestation (100). In contrast, in pooled individual data from 31 high-quality randomized trials, the beneficial effects of low-dose aspirin were consistent, whether treatment was started before or after 16 weeks of gestation (101). Women with any of the high-risk factors for preeclampsia (previous pregnancy with preeclampsia, multifetal gestation, renal disease, autoimmune disease, type 1 or type 2 diabetes mellitus, and chronic hypertension) and those with more than one of the moderate-risk factors (first pregnancy, maternal age of 35 years or older, a body mass index [BMI; calculated as weight in kilograms divided by height in meters squared] of more than 30, family history of preeclampsia, sociodemographic characteristics, and personal history factors) should receive low-dose (81 mg/day) aspirin for preeclampsia prophylaxis initiated between 12 weeks and 28 weeks of gestation (optimally before 16 weeks of gestation) and continuing until delivery (Table 1).

In a recent multicenter, double blind, placebo-controlled trial, pregnant women at increased risk of preterm preeclampsia (less than 37 weeks of gestation) were randomly assigned to receive aspirin, at a higher dose (150 mg/day), or placebo from 11 weeks to 14 weeks of gestation until 36 weeks of gestation (89). Preterm preeclampsia occurred in 1.6% of the participants in the aspirin group, as compared with 4.3% in the placebo group (odds ratio, 0.38; 95% CI, 0.20−0.74; P=.004). The authors also reported that there were no significant differences in the incidence of neonatal adverse outcomes between groups. The authors concluded that low-dose aspirin in women at high risk of preeclampsia was associated with a lower incidence for preterm preeclampsia. However, there were no differences in the rates of term preeclampsia between study groups. Of note, as a possible study limitation, the prevalence of preterm preeclampsia in the placebo group was one half of that expected for a high-risk population based on first-trimester parameters (89).

The use of metformin for the prevention of preeclampsia has been suggested. In a meta-analysis of five randomized controlled trials comparing metformin treatment (n=611) with placebo and control (n=609), no difference in the risk of preeclampsia was found (combined/pooled risk ratio, 0.86; 95% CI, 0.33–2.26); P=.76; I^2=66%) (102). Because preeclampsia was a secondary outcome in most studies in this meta-analysis, the effect of metformin needs to be assessed by a study designed to evaluate the reduction in the prevalence of preeclampsia as a primary endpoint. In the meantime, the use of metformin for the prevention of preeclampsia remains investigational, as is the use of sildenafil and statins (103–105). These drugs are not recommended for this indication outside of the context of clinical trials.

▶ ***What is the optimal treatment for women with gestational hypertension or preeclampsia?***

Delivery Versus Expectant Management

At the initial evaluation, a complete blood count with platelet estimate, serum creatinine, LDH, AST, ALT, and testing for proteinuria should be obtained in parallel with a comprehensive clinical maternal and fetal evaluation. In the settings of diagnostic dilemmas, such as in the evaluation of possible preeclampsia superimposed upon chronic hypertension, a uric acid test may be considered. Fetal evaluation should include ultrasonographic evaluation for estimated fetal weight and amount of amniotic fluid, as well as fetal antepartum testing. Subsequent management will depend on the results of the evaluation and gestational age. The decision to deliver must balance the maternal and fetal risks.

Continued observation is appropriate for a woman with a preterm fetus if she has gestational hypertension or preeclampsia without severe features (21). There are no randomized controlled trials in this population, but retrospective data suggest that without severe features, the balance should be in favor of continued monitoring until delivery at 37 0/7 weeks of gestation in the absence of abnormal antepartum testing, preterm labor, preterm prelabor rupture of membranes (also referred to as premature rupture of membranes) or vaginal bleeding, for neonatal benefit (106). The risks associated with expectant management in the late preterm period include the development of severe hypertension, eclampsia, HELLP syndrome, placental abruption, fetal growth restriction and fetal death; however, these risks are small and counterbalanced by the increased rates of admission to the neonatal intensive care unit, neonatal respiratory complications and neonatal death that would be associated with delivery before 37 0/7 weeks of gestation (39). In the

Table 1. Clinical Risk Factors and Aspirin Use*

Level of Risk	Risk Factors	Recommendation
High†	• History of preeclampsia, especially when accompanied by an adverse outcome • Multifetal gestation • Chronic hypertension • Type 1 or 2 diabetes • Renal disease • Autoimmune disease (ie, systemic lupus erythematosus, the antiphospholipid syndrome)	Recommend low-dose aspirin if the patient has one or more of these high-risk factors
Moderate‡	• Nulliparity • Obesity (body mass index greater than 30) • Family history of preeclampsia (mother or sister) • Sociodemographic characteristics (African American race, low socioeconomic status) • Age 35 years or older • Personal history factors (eg, low birth weight or small for gestational age, previous adverse pregnancy outcome, more than 10-year pregnancy interval)	Consider low-dose aspirin if the patient has more than one of these moderate-risk factors§
Low	• Previous uncomplicated full-term delivery	Do not recommend low-dose aspirin

*Includes only risk factors that can be obtained from the patient's medical history. Clinical measures, such as uterine artery Doppler ultrasonography, are not included.

†Single risk factors that are consistently associated with the greatest risk of preeclampsia. The preeclampsia incidence rate would be approximately 8% or more in a pregnant woman with one or more of these risk factors.

‡A combination of multiple moderate-risk factors may be used by clinicians to identify women at high risk of preeclampsia. These risk factors are independently associated with moderate risk of preeclampsia, some more consistently than others.

§Moderate-risk factors vary in their association with increased risk of preeclampsia.

Modified from LeFevre, ML. U.S. Preventive Services Task Force. Low-dose aspirin use for the prevention of morbidity and mortality from preeclampsia: U.S. Preventive Services Task Force Recommendation Statement. Ann Intern Med 2014;161(11):819–26.

HYPITAT trial, women with gestational hypertension and preeclampsia without severe features after 36 weeks of gestation were allocated to expectant management or induction of labor. The latter option was associated with a significant reduction in a composite of adverse maternal outcome including new-onset severe preeclampsia, HELLP syndrome, eclampsia, pulmonary edema, or placental abruption (RR, 0.71; 95% CI, 0.59–0.86) (107). In addition, no differences in rates of neonatal complications or cesarean delivery were reported by the authors (107).

Continued monitoring of women with gestational hypertension or preeclampsia without severe features consists of serial ultrasonography to determine fetal growth, weekly antepartum testing, close monitoring of blood pressure, and weekly laboratory tests for preeclampsia. The frequency of these tests may be modified based on clinical findings and patient symptoms. Following the initial documentation of proteinuria and the establishment of the diagnosis of preeclampsia, additional quantifications of proteinuria are no longer necessary. Although the amount of proteinuria is expected to increase over time with expectant management, this change is not predictive of perinatal outcome and should not influence the management of preeclampsia (108, 109). Women should be advised to immediately report any persistent, concerning, or unusual symptoms. In women with gestational hypertension without severe features, when there is progression to preeclampsia with severe features, this progression usually takes 1–3 weeks after diagnosis, whereas in women with preeclampsia without severe features, the progression to severe

preeclampsia could happen within days (72). Gestational hypertension and preeclampsia are known risk factors for fetal death and antenatal testing is indicated. However, limited-to-no data exist regarding when to start testing, the frequency of testing, and which test to use. In women with gestational hypertension or preeclampsia without severe features at or beyond 37 0/7 weeks of gestation, delivery rather than expectant management upon diagnosis is recommended.

Preeclampsia with severe features can result in acute and long-term complications for the woman and her newborn. Maternal complications include pulmonary edema, myocardial infarction, stroke, acute respiratory distress syndrome, coagulopathy, renal failure, and retinal injury. These complications are more likely to occur in the presence of preexistent medical disorders. The clinical course of preeclampsia with severe features is characterized by progressive deterioration of maternal and fetal condition. Therefore, delivery is recommended when gestational hypertension or preeclampsia with severe features (Box 3) is diagnosed at or beyond 34 0/7 weeks of gestation, after maternal stabilization or with labor or prelabor rupture of membranes. Delivery should not be delayed for the administration of steroids in the late preterm period.

In women with preeclampsia with severe features at less than 34 0/7 weeks of gestation, with stable maternal and fetal condition, expectant management may be considered. Two randomized controlled trials of delivery versus expectant management of preterm preeclampsia with severe features demonstrated that expectant management is associated with higher gestational age at delivery and improved neonatal outcomes (110, 111). These observations were reiterated by a Cochrane systematic review (112). The limited available randomized data are consistent with observational evidence suggesting that expectant management of early preeclampsia with severe features prolongs pregnancy by 1–2 weeks, has low maternal risk, and improves neonatal outcomes (113). In contrast, in a multicenter randomized controlled trial in Latin America, the authors found no neonatal benefit with expectant management of preeclampsia with severe features from 28 weeks to 34 weeks of gestation (114). These different results may reflect the limitations in neonatal intensive care in low-resource settings.

Embarking on a course of expectant management necessitates adherence to principles of shared decision making with discussions of maternal and fetal risks and benefits, appropriate resources (levels of care), and ongoing vigilant surveillance. Close maternal and fetal clinical monitoring is necessary, and laboratory testing (complete blood count including platelets, liver enzymes, and serum creatinine) should be performed serially (115).

The expectant management of preeclampsia with severe features before 34 0/7 weeks of gestation is based on strict selection criteria of those appropriate candidates and is best accomplished in a setting with resources appropriate for maternal and neonatal care (116). Because expectant management is intended to provide neonatal benefit at the expense of maternal risk, expectant management is not advised when neonatal survival is not anticipated. During expectant management, delivery is recommended at any time in the case of deterioration of maternal or fetal condition, which may include some of the criteria in Box 4. Indications for expedited delivery irrespective of gestational age after maternal stabilization are described in Box 4 (115).

If delivery is indicated at less than 34 0/7 weeks of gestation, administration of corticosteroids for fetal lung maturation is recommended (115); however, delaying delivery for optimal corticosteroid exposure may not always be advisable. Maternal or fetal deterioration may preclude completion of the course of steroid treatment. Previously, fetal growth restriction was considered an indication for delivery. In the setting of normal fetal parameters (eg, amniotic fluid volume, Doppler findings, antenatal fetal testing), continuation of expectant management may be reasonable in the absence of other, aforementioned maternal and fetal criteria.

Inpatient Versus Outpatient Management

Ambulatory management at home is an option only for women with gestational hypertension or preeclampsia without severe features and requires frequent fetal and maternal evaluation. Hospitalization is appropriate for women with severe features and for women in whom adherence to frequent monitoring is a concern. Because assessment of blood pressure is essential for this clinical condition, health care providers are encouraged to follow the recommendations from regulatory bodies regarding the proper technique for blood pressure measurement. Having a blood pressure cuff that is too small or too large may result in erroneous evaluations. To reduce inaccurate readings, an appropriate size cuff should be used (length 1.5 times upper arm circumference or a cuff with a bladder that encircles 80% or more of the arm). The blood pressure level should be taken with an appropriately-sized cuff with the patient in an upright position after a 10-minute or longer rest period. For patients in the hospital, the blood pressure can be taken with either the patient sitting up or in the left lateral recumbent position with the patient's arm at the level of the heart (117). The patient should not use tobacco or caffeine for 30 minutes preceding the measurement

Box 4. Conditions Precluding Expectant Management

Maternal

- Uncontrolled severe-range blood pressures (persistent systolic blood pressure 160 mm Hg or more or diastolic blood pressure 110 mm Hg or more not responsive to antihypertensive medication
- Persistent headaches, refractory to treatment
- Epigastric pain or right upper pain unresponsive to repeat analgesics
- Visual disturbances, motor deficit or altered sensorium
- Stroke
- Myocardial infarction
- HELLP syndrome
- New or worsening renal dysfunction (serum creatinine greater than 1.1 mg/dL or twice baseline)
- Pulmonary edema
- Eclampsia
- Suspected acute placental abruption or vaginal bleeding in the absence of placenta previa

Fetal

- Abnormal fetal testing
- Fetal death
- Fetus without expectation for survival at the time of maternal diagnosis (eg, lethal anomaly, extreme prematurity)
- Persistent reversed end-diastolic flow in the umbilical artery

Abbreviation: HELLP, hemolysis, elevated liver enzymes, and low platelet count.
In some cases, a course of antenatal steroids can be considered depending on gestational age and maternal severity of illness.
Data from Balogun OA, Sibai BM. Counseling, management, and outcome in women with severe preeclampsia at 23 to 28 weeks' gestation. Clin Obstet Gynecol 2017;60:183–9.

because these agents can temporarily lead to increased blood pressure (118).

If home management is selected, frequent fetal and maternal evaluation are required. No randomized trials have determined the best tests for fetal or maternal evaluation. Among women with gestational hypertension or preeclampsia without severe features, expectant management up to 37 0/7 weeks of gestation is recommended, during which frequent fetal and maternal evaluation is recommended. Fetal monitoring consists of ultrasonography to determine fetal growth every 3–4 weeks of gestation and amniotic fluid volume assessment at least once weekly. In addition, an antenatal test one-to-two times per week for patients with gestational hypertension or preeclampsia without severe features is recommended.

Maternal evaluation consists primarily of frequent evaluation for either the development of or worsening of preeclampsia. In women with gestational hypertension or preeclampsia without severe features, weekly evaluation of platelet count, serum creatinine, and liver enzyme levels is recommended. In addition, for women with gestational hypertension, once weekly assessment of proteinuria is recommended. However, these tests should be repeated sooner if disease progression is a concern. In addition, women should be asked about symptoms of preeclampsia with severe features (eg, severe headaches, visual changes, epigastric pain, and shortness of breath). Blood pressure measurements and symptom assessment are recommended serially, using a combination of in-clinic and ambulatory approaches, with at least one visit per week in-clinic.

Intrapartum Management

In addition to appropriate management of labor and delivery, the two main goals of management of women with preeclampsia during labor and delivery are 1) prevention of seizures and 2) control of hypertension.

Seizure Prophylaxis

The prevention of eclampsia is empirically based on the concept of timely delivery, as previously discussed, once preeclampsia has been diagnosed. A significant body of evidence attests to the efficacy of magnesium sulfate to prevent seizures in women with preeclampsia with severe features and eclampsia. In the Magpie study, a randomized placebo-controlled trial with 10,110 participants (two thirds originating from developing countries), the seizure rate was reduced overall by more than one half with this treatment. It is interesting to note that the reduction in the rate of eclampsia was not statistically significant in the subset of women enrolled in high-resource countries in the Western world (RR, 0.67; 95% CI, 0.19–2.37) (44). In a subsequent systematic review that included the Magpie study and five other studies, magnesium sulfate compared with placebo more than halved the risk of eclampsia (RR, 0.41; 95% CI, 0.29–0.58), reduced the risk of placental abruption (RR, 0.64; 95% CI, 0.50–0.83), and reduced the risk of maternal mortality albeit nonsignificantly (RR, 0.54; 95% CI, 0.26–1.10). There were no differences in maternal morbidity or perinatal mortality. A quarter of women reported adverse effects with magnesium sulfate, primarily hot flushes, and the rate of cesarean delivery was increased by 5% when magnesium sulfate was used (119).

There is no consensus regarding the prophylactic use of magnesium sulfate for the prevention of seizures in women with gestational hypertension or preeclampsia without severe features. Two small randomized trials (total n=357) allocated women with preeclampsia without severe features to either placebo or magnesium sulfate and reported no cases of eclampsia among women allocated to placebo and no significant differences in the proportion of women that progressed to severe preeclampsia (120, 121). However, given the small sample size, the results of these studies cannot be used for clinical guidance (122, 123).

The rate of seizures in preeclampsia with severe features without magnesium sulfate prophylaxis is four times higher than in those without severe features (4 in 200 versus 1 in 200). It has been calculated that 129 women need to be treated to prevent one case of eclampsia in asymptomatic cases, whereas in symptomatic cases (severe headache, blurred vision, photophobia, hyperreflexia, epigastric pain), the number needed to treat is 36 (124). The evidence regarding the benefit-to-risk ratio of magnesium sulfate prophylaxis is less supportive of routine use in preeclampsia without severe features (122). The clinical decision of whether to use magnesium sulfate for seizure prophylaxis in patients with preeclampsia without severe features should be determined by the physician or institution, considering patient values or preferences, and the unique risk-benefit trade-off of each strategy. Although the benefit-to-risk ratio for routine prophylaxis is less compelling for patients in high resource settings, it is recommended that magnesium sulfate should be used for the prevention and treatment of seizures in women with gestational hypertension with severe features and preeclampsia with severe features or eclampsia (124, 125).

Magnesium sulfate is more effective than phenytoin, diazepam, or nimodipine (a calcium-channel blocker used in clinical neurology to reduce cerebral vasospasm) in reducing eclampsia and should be considered the drug of choice in the prevention of eclampsia in the intrapartum and postpartum periods (119, 126, 127). Benzodiazepines and phenytoin are justified only in the context of antiepileptic treatment or when magnesium sulfate is contraindicated or unavailable (myasthenia gravis, hypocalcemia, moderate-to-severe renal failure, cardiac ischemia, heart block, or myocarditis).

There are still sparse data regarding the ideal dosage of magnesium sulfate. Even the therapeutic range of 4.8–9.6 mg/dL (4–8 mEq/L) quoted in the literature is questionable (128, 129). Although there is a relationship between toxicity and plasma concentration of magnesium, with higher infusion rates increasing the potential for toxicity, the accurate magnesium concentration clinically effective in prevention of eclampsia has not been established. Seizures occur even with magnesium at a therapeutic level, whereas several trials using infusion rates of 1 g/hour, frequently associated with subtherapeutic magnesium levels, were able to significantly reduce the rate of eclampsia or recurrent convulsions (44, 130). Further complicating aspects are that steady magnesium levels are reached more slowly during the antepartum period than postpartum period. Larger volume of distribution and higher BMI also affect the dosage and duration needed to reach adequate circulating levels. It has been reported in patients with a high BMI (especially greater than 35) that the antepartum level of magnesium may remain subtherapeutic for as long as 18 hours after infusion initiation when an intravenous loading dose of 4.5 g followed by 1.8 g/hour is used (131). However, infusion rates in excess of 2 g/hour have been associated with increased perinatal mortality in a systematic review of randomized studies of magnesium sulfate used for tocolysis (132). These data may be considered supportive for the regimen generally preferred in the United States (intravenous [IV] administration of a 4–6 g loading dose over 20–30 minutes, followed by a maintenance dose of 1–2 g/hour). For women requiring cesarean delivery (before onset of labor), the infusion should ideally begin before surgery and continue during surgery, as well as for 24 hours afterwards. For women who deliver vaginally, the infusion should continue for 24 hours after delivery. In case of difficulties with establishing venous access, magnesium sulfate can be administered by intramuscular (IM) injection, 10 g initially as a loading dose (5 g IM in each buttock), followed by 5 g every 4 hours. The medication can be mixed with 1 mL of xylocaine 2% solution because the intramuscular administration is painful. The rate of adverse effects is also higher with the intramuscular administration (44). The adverse effects of magnesium sulfate (respiratory depression and cardiac arrest) come largely from its action as a smooth muscle relaxant. Deep tendon reflexes are lost at a serum magnesium level of 9 mg/dL (7 mEq/L), respiratory depression occurs at 12 mg/dL (10 mEq/L), and cardiac arrest at 30 mg/dL (25 mEq/L). Accordingly, provided deep tendon reflexes are present, more serious toxicity is avoided. (Table 2) Because magnesium sulfate is excreted almost exclusively in the urine, measuring urine output should be part of the clinical monitoring, in addition to monitoring of respiration status and tendon reflexes. If renal function is impaired, serum magnesium levels will increase quickly, which places the patient at risk of significant adverse effects. In patients with mild renal failure (serum creatinine 1.0–1.5 mg/dL) or oliguria (less than 30 mL urine output per hour for more than 4 hours), the loading dose of 4–6 g should be followed by

Table 2. Serum Magnesium Concentration and Toxicities

Serum Magnesium Concentration			
mmol/L	mEq/L	mg/dL	Effect
2–3.5	4–7	5–9	Therapeutic range
>3.5	>7	>9	Loss of patellar reflexes
>5	>10	>12	Respiratory paralysis
>12.5	>25	>30	Cardiac arrest

Data from Duley L. Magnesium sulphate regimens for women with eclampsia: messages from the Collaborative Eclampsia Trial. Br J Obstet Gynaecol 1996;103:103–5 *and* Lu JF, Nightingale CH. Magnesium sulfate in eclampsia and pre-eclampsia: pharmacokinetic principles. Clin Pharmacokinet 2000;38:305–14.

a maintenance dose of only 1 gm/hour. Using a lower loading dose, such as 4 g, may be associated with subtherapeutic levels for at least 4 hours after loading (133). In cases with renal dysfunction, laboratory determination of serum magnesium levels every 4 hours becomes necessary. If the serum level exceeds 9.6 mg/dL (8 mEq/L), the infusion should be stopped and serum magnesium levels should be determined at 2-hour intervals. The infusion can be restarted at a lower rate when the serum level decreases to less than 8.4 mg/dL (7 mEq/L) (133). The serum concentration of magnesium is related to the occurrence of adverse effects and toxicities (see Table 2) (128, 134). Patients at risk of impending respiratory depression may require tracheal intubation and emergency correction with calcium gluconate 10% solution, 10 mL IV over 3 minutes, along with furosemide intravenously to accelerate the rate of urinary excretion.

Antihypertensive Approach: Drugs and Thresholds for Treatment

The objectives of treating severe hypertension are to prevent congestive heart failure, myocardial ischemia, renal injury or failure, and ischemic or hemorrhagic stroke. Antihypertensive treatment should be initiated expeditiously for acute-onset severe hypertension (systolic blood pressure of 160 mm Hg or more or diastolic blood pressure of 110 mm Hg or more, or both) that is confirmed as persistent (15 minutes or more). The available literature suggests that antihypertensive agents should be administered within 30–60 minutes. However, it is recommended to administer antihypertensive therapy as soon as reasonably possible after the criteria for acute-onset severe hypertension are met. Intravenous hydralazine or labetalol and oral nifedipine are the three agents most commonly used for this purpose (see Table 3). A recent Cochrane systematic review that involved 3,573 women found no significant differences regarding either efficacy or safety between hydralazine and labetalol or between hydralazine and calcium channel blockers (135). Thus, any of these agents can be used to treat acute severe hypertension in pregnancy (135, 136). Although parenteral antihypertensive therapy may be needed initially for acute control of blood pressure, oral medications can be used as expectant management is continued. Oral labetalol and calcium channel blockers have been commonly used. One approach is to begin an initial regimen of labetalol at 200 mg orally every 12 hours and increase the dose up to 800 mg orally every 8–12 hours as needed (maximum total 2,400 mg/d). If the maximum dose is inadequate to achieve the desired blood pressure goal, or the dosage is limited by adverse effect, then short-acting oral nifedipine can be added gradually.

Monitoring for Disease Progression

Because the clinical course of gestational hypertension or preeclampsia without severe features can evolve during labor, all women with gestational hypertension or preeclampsia without severe features who are in labor must be monitored for early detection of progression to severe disease. This should include monitoring of blood pressure and symptoms during labor and delivery as well as immediately after delivery. Magnesium sulfate therapy should be initiated if there is progression to preeclampsia with severe features. The evidence regarding the benefit-to-risk ratio of magnesium sulfate prophylaxis is less supportive of routine use in preeclampsia without severe features (122). The clinical decision of whether to use magnesium sulfate for seizure prophylaxis in patients with preeclampsia without severe features should be determined by the physician or institution, considering patient values or preferences and the unique risk-benefit trade-off of each strategy.

Mode of Delivery

The mode of delivery in women with gestational hypertension or preeclampsia (with or without severe features) should be determined by routine obstetric considerations. Vaginal delivery often can be accomplished, but with labor induction in preeclampsia with severe features this is less likely with decreasing gestational age at diagnosis. The likelihood of cesarean delivery at less than 28 weeks of gestation could be as high as 97%, and at 28–32 weeks of gestation as high as 65% (137–139). For gestational hypertension or preeclampsia without severe features, vaginal delivery is preferred (137–139). Retrospective studies comparing induction of labor with cesarean delivery in women with preeclampsia with severe features remote from term concluded that induction of labor was reasonable and was not harmful to low-birth-weight infants (140, 141). The decision to perform cesarean delivery should be

Table 3. Antihypertensive Agents Used for Urgent Blood Pressure Control in Pregnancy

Drug	Dose	Comments	Onset of Action
Labetalol	10–20 mg IV, then 20–80 mg every 10–30 minutes to a maximum cumulative dosage of 300 mg; or constant infusion 1–2 mg/min IV	Tachycardia is less common with fewer adverse effects. Avoid in women with asthma, preexisting myocardial disease, decompensated cardiac function, and heart block and bradycardia.	1–2 minutes
Hydralazine	5 mg IV or IM, then 5–10 mg IV every 20–40 minutes to a maximum cumulative dosage of 20 mg; or constant infusion of 0.5–10 mg/hr	Higher or frequent dosage associated with maternal hypotension, headaches, and abnormal fetal heart rate tracings; may be more common than other agents.	10–20 minutes
Nifedipine (immediate release)	10–20 mg orally, repeat in 20 minutes if needed; then 10–20 mg every 2–6 hours; maximum daily dose is 180 mg	May observe reflex tachycardia and headaches	5–10 minutes

Abbreviations: IM, intramuscularly; IV, intravenously.

individualized, based on anticipated probability of vaginal delivery and on the nature and progression of preeclampsia disease state.

Anesthesia Considerations

With improved techniques over the past decades, regional anesthesia has become the preferred technique for women with preeclampsia with severe features and eclampsia for labor and delivery. A secondary analysis of women with preeclampsia with severe features in a randomized trial of low-dose aspirin reported that epidural anesthesia was not associated with an increased rate of cesarean delivery, pulmonary edema, or renal failure (142). Also, in a prospective study, the incidence and severity of hypotension did not appear to be increased with spinal anesthesia for cesarean delivery in women with preeclampsia with severe features (n=65) compared with women without preeclampsia (143).

When the use of spinal or epidural anesthesia in women with preeclampsia with severe features was compared in a randomized trial (144), the incidence of hypotension was higher in the spinal group (51% versus 23%) but was easily treated and of short duration (less than 1 minute). General anesthesia carries more risk to pregnant women than regional anesthesia does because of the risk of aspiration, failed intubation because of pharyngolaryngeal edema, and stroke secondary to increased systemic and intracranial pressures during intubation and extubation (145, 146). However, neuraxial anesthesia and analgesia are contraindicated in the presence of a coagulopathy because of the potential for hemorrhagic complications (147). Thrombocytopenia also increases the risk of epidural hematoma. There is no consensus in regard to the safe lower-limit for platelet count and neuraxial anesthesia. The literature offers only limited and retrospective data to address this issue, but a recent retrospective cohort study of 84,471 obstetric patients from 19 institutions combined with a systematic review of the medical literature support the assertion that the risk of epidural hematoma from neuraxial anesthetics in a parturient patient with a platelet count of more than 70×10^9/L is exceptionally low (less than 0.2%) (148). Extrapolating this expanded data to previous recommendations (149) would suggest that epidural or spinal anesthesia is considered acceptable, and the risk of epidural hematoma is exceptionally low, in patients with platelet counts of 70×10^9/L or more provided that the platelet level is stable, there is no other acquired or congenital coagulopathy, the platelet function is normal, and the patient is not on any antiplatelet or anticoagulant therapy (148, 149).

Magnesium sulfate has significant anesthetic implications because it prolongs the duration of nondepolarizing muscle relaxants. However, women with preeclampsia who require cesarean delivery should

continue magnesium sulfate infusion during the delivery. This recommendation is based on the observation that magnesium sulfate half-life is 5 hours and that discontinuation of the infusion of magnesium sulfate before cesarean delivery would only minimally reduce magnesium concentration at the time of delivery while possibly increasing the risk of seizure (150). Women with preeclampsia with severe features undergoing cesarean delivery remain at risk of developing eclampsia. The induction of general anesthesia and the stress of delivery may even reduce the seizure threshold and increase the likelihood of eclampsia in the immediate postpartum period if the infusion of magnesium sulfate is stopped during delivery.

Postpartum Hypertension and Postpartum Headache

Postpartum hypertension and preeclampsia are either persistent or exacerbated hypertension in women with previous hypertensive disorders of pregnancy or a new-onset condition. It is important to increase the awareness among health care providers and to empower patients to seek medical advice if symptoms that precede eclampsia, hypertensive encephalopathy, pulmonary edema, or stroke are noted in the postpartum period. Most women who present with eclampsia and stroke in the postpartum period have these symptoms for hours or days before presentation (151–154). Some common medications and substances used in the postpartum period may potentially aggravate hypertension through three major mechanisms: volume retention, sympathomimetic activation, and direct vasoconstriction. Of particular interest are nonsteroidal antiinflammatory drugs (NSAIDs), which are frequently prescribed as postpartum analgesics. These medications decrease prostaglandins leading to a lack of vasodilation and increased sodium retention. Nonsteroidal anti-inflammatory medications should continue to be used preferentially over opioid analgesics; however, women with chronic hypertension may theoretically require intensification of blood pressure monitoring and regimen adjustments when on these medications. Overall, data support the safe use of NSAIDs in postpartum patients with blood pressure issues. In a randomized trial comparing use of ibuprofen to acetaminophen in postpartum patients with preeclampsia with severe features, ibuprofen did not lengthen the duration of severe-range blood pressures (155). In a cohort of 399 patients with preeclampsia with severe features, there was no association of NSAID use with postpartum blood pressure elevations (156). Further, another cohort study of postpartum patients on magnesium for seizure prophylaxis for preeclampsia did not show differences in blood pressure, antihypertensive requirements, or other adverse events for patients managed with NSAIDs in the postpartum period (157, 158).

▶ *What is the optimal treatment for eclampsia?*

The initial steps in the management of a woman with eclampsia are basic supportive measures such as calling for help, prevention of maternal injury, placement in lateral decubitus position, prevention of aspiration, administration of oxygen, and monitoring vital signs including oxygen saturation. Only subsequently is attention directed to the administration of magnesium sulfate. Most eclamptic seizures are self-limited. Magnesium sulfate is not necessary to arrest the seizure but to prevent recurrent convulsions.

During eclamptic seizures, there are usually prolonged fetal heart rate decelerations, even fetal bradycardia, and sometimes an increase in uterine contractility and baseline tone. After a seizure, because of maternal hypoxia and hypercarbia, the fetal heart rate tracing may show recurrent decelerations, tachycardia, and reduced variability. However, only after maternal hemodynamic stabilization should one proceed with delivery. Furthermore, maternal resuscitation is usually followed by normalization of the fetal tracing.

Cochrane reviews, including data originating from developing countries, indicate a significant reduction in recurrent seizures and eclampsia-related maternal mortality with the use of magnesium sulfate. Magnesium sulfate administered intramuscularly or intravenously is superior to phenytoin, diazepam, or lytic cocktail (usually chlorpromazine, promethazine, and pethidine) and also is associated with less maternal and neonatal morbidity (126, 159, 160). Thus, these data support the use of magnesium sulfate as the drug of choice to prevent recurrent seizures in women with eclampsia. In the rare cases of an extremely agitated patient, IV clonazepam 1 mg, diazepam 10 mg, or midazolam may be used for sedation to facilitate the placement of the IV lines and Foley catheter, and the collection of blood specimens. These drugs should be used cautiously and only if absolutely necessary because they inhibit laryngeal reflexes, increasing the risk of aspiration and also may depress the central respiratory centers leading to apnea.

Women with eclampsia should be delivered in a timely fashion. However, eclampsia by itself is not an indication for cesarean delivery. Once the patient is stabilized, the method of delivery should depend, in part, on factors such as gestational age, fetal presentation, and the findings of the cervical examination. A high rate of failure may be anticipated with induction or augmentation in pregnancies less than 30 weeks of gestation if the

patient is not in active labor and the Bishop score is unfavorable. In these cases, it may be preferable to opt for cesarean delivery without further delay. However, patients that adequately progress in labor could be allowed to continue labor even after an eclamptic seizure.

It has been proposed that when convulsions recur, a further 2–4 grams of magnesium sulfate could be administered IV over 5 minutes (130). In cases refractory to magnesium sulfate (still seizing at 20 minutes after the bolus or more than two recurrences), a health care provider can use sodium amobarbital (250 mg IV in 3 minutes), thiopental, or phenytoin (1,250 mg IV at a rate of 50 mg/minute). Endotracheal intubation and assisted ventilation in the intensive care unit are appropriate in these circumstances. Head imaging should also be considered because most of cases refractory to magnesium sulfate therapy may prove to have abnormal findings on brain imaging (161).

▶ *What is the management of acute complications for preeclampsia with HELLP?*

The clinical course of HELLP syndrome often is characterized by progressive and sometimes sudden deterioration in maternal and fetal condition. Considering the serious nature of this entity, with increased rates of maternal morbidity and mortality, many authors have concluded that women with HELLP syndrome should be delivered regardless of their gestational age. Because the management of patients with HELLP syndrome requires the availability of neonatal and obstetric intensive care units and personnel with special expertise, patients with HELLP syndrome who are remote from term should receive care at a tertiary care center (116, 162).

It has been hypothesized that the antiinflammatory and immunosuppressive effects of corticosteroids may modify some of the proinflammatory features of preeclampsia with severe features and favorably affect the clinical course. Several randomized controlled trials of high-dose corticosteroid treatment for antepartum or postpartum stabilization of HELLP syndrome have been conducted. The use of corticoids in the management of HELLP syndrome compared with placebo or no treatment was reviewed in a Cochrane Database Systematic Review, which included 11 randomized trials (550 women) (163). There was no difference in the risk of maternal death, severe maternal morbidity, or perinatal or infant death. The only effect of treatment on individual outcomes was improved platelet count (standardized mean difference [SMD] 0.67; 95% CI, 0.24−1.10). The authors concluded that the evidence is insufficient to support the use of corticosteroids for attenuation of the disease process in HELLP syndrome (163).

Very close monitoring is required in HELLP syndrome until delivery and in the postpartum period, with laboratory testing at least at 12-hour intervals. Aspartate aminotransferase levels more than 2,000 IU/L or LDH more than 3,000 IU/L suggest an increased mortality risk. In the natural history of HELLP syndrome there is an inverse relationship between the trends in platelet values and liver enzymes level. During the aggravation slope in the disease evolution, platelet count usually decreases at an average rate of approximately 40% per day, whereas the liver enzymes values tend to increase. The lowest observed platelet count occurs at a mean of 23 hours after delivery. The disease may achieve peak intensity during the first 2 days after delivery, including a downward trend in hematocrit. If the platelet count continues to drop and liver enzymes to increase after 4 days postpartum, the validity of the initial diagnosis of HELLP syndrome should be reassessed. With supportive care alone, 90% of patients with HELLP syndrome will have platelet count more than 100~~,000~~ $\times$ 10^9/L and reversed trend (decrease) in liver enzymes values within 7 days after delivery. Not infrequently, a rebound phenomenon in platelet count follows reaching values of 400~~,000~~–871~~,000~~ $\times$ 10^9/L (164). Women with HELLP syndrome are also at increased risk of pulmonary edema, acute respiratory distress syndrome and renal failure (165).

▶ *What are the risks of subsequent cardiovascular disease among women with hypertensive disorders of pregnancy and are there prevention strategies that modify this risk?*

Women with a history of preeclampsia continue to have an elevated risk of cardiovascular disease in subsequent years. Several systematic reviews and meta-analyses have linked preeclampsia with an increased risk of cardiovascular disease (hypertension, myocardial infarction, congestive heart failure), cerebrovascular events (stroke), peripheral arterial disease, and cardiovascular mortality later in life, with an estimated doubling of odds compared with women unaffected by preeclampsia (166–168). Meta-regression analysis reveals a graded relationship between the severity of preeclampsia or eclampsia and the risk of cardiac disease (mild: RR, 2.00; 95% CI, 1.83–2.19; moderate: RR, 2.99; 95% CI, 2.51–3.58; severe: RR, 5.36; 95% CI, 3.96–7.27, $P<.0001$) (169). The risk is even higher (4–8 times the risk for women with normal pregnancies) in women with recurrent preeclampsia (170) and women with early-onset preeclampsia or preeclampsia requiring preterm delivery (171). More recent evidence suggests that all hypertensive conditions in pregnancy are associated with later cardiovascular disease with an approximately doubling of the rate of incident cardiovascular disease and a five times higher rate of hypertension (172).

The mechanisms that account for an increased risk of cardiovascular disease in women with a history of preeclampsia are not yet well understood, but endothelial dysfunction, which has been linked to atherosclerosis, persists in women with a history of preeclampsia many years after an affected pregnancy (173). A study of cardiovascular risk factors present before and after pregnancy suggested that nearly one half of the elevated risk of future hypertension after preeclampsia can be explained by prepregnancy risk factors (174). Yet, it may be possible that the stress incurred to the cardiovascular system during gestation triggers a biological response that would otherwise not have occurred despite any genetic predisposition or risk factors (172). It remains unclear if cardiovascular changes associated with preeclampsia during pregnancy causally lead to cardiovascular remodeling increasing the risk of cardiovascular disease later in life or if preeclampsia is a manifestation of an underlying increased risk of cardiovascular disease (for example, a common genetic–environmental risk factor(s) interaction [such as hyperlipidemia, obesity, diabetes mellitus, or renal disease] that predisposes women to develop preeclampsia during pregnancy and cardiovascular diseases later in life) (175). Preventive strategies to be considered by patients and health care providers may warrant closer long-term follow-up and lifestyle modifications to better manage risk factors for cardiovascular disease (eg, achieving healthful weight, exercise, diet, smoking cessation), for which women and their primary care providers may maintain ongoing care and vigilance.

Summary of Recommendations

The following recommendations are based on good and consistent scientific evidence (Level A):

- Women with any of the high-risk factors for preeclampsia (previous pregnancy with preeclampsia, multifetal gestation, renal disease, autoimmune disease, type 1 or type 2 diabetes mellitus, and chronic hypertension) and those with more than one of the moderate-risk factors (first pregnancy, maternal age of 35 years or older, a body mass index of more than 30, family history of preeclampsia, sociodemographic characteristics, and personal history factors) should receive low-dose (81 mg/day) aspirin for preeclampsia prophylaxis, initiated between 12 weeks and 28 weeks of gestation (optimally before 16 weeks of gestation) and continuing until delivery.
- In women with gestational hypertension or preeclampsia without severe features at or beyond 37 0/7 weeks of gestation, delivery rather than expectant management upon diagnosis is recommended.
- Magnesium sulfate should be used for the prevention and treatment of seizures in women with gestational hypertension and preeclampsia with severe features or eclampsia.
- Nonsteroidal anti-inflammatory medications should continue to be used preferentially over opioid analgesics. Postpartum patients on magnesium for seizure prophylaxis for preeclampsia did not show differences in blood pressure, antihypertensive requirements, or other adverse events for patients managed with NSAIDs in the postpartum period.

The following recommendations are based on limited or inconsistent scientific evidence (Level B):

- Delivery is recommended when gestational hypertension or preeclampsia with severe features is diagnosed at or beyond 34 0/7 weeks of gestation, after maternal stabilization or with labor or prelabor rupture of membranes. Delivery should not be delayed for the administration of steroids in the late preterm period.
- The expectant management of preeclampsia with severe features before 34 0/7 weeks of gestation is based on strict selection criteria of those appropriate candidates and is best accomplished in a setting with resources appropriate for maternal and neonatal care. Because expectant management is intended to provide neonatal benefit at the expense of maternal risk, expectant management is not advised when neonatal survival is not anticipated. During expectant management, delivery is recommended at any time in the case of deterioration of maternal or fetal condition.
- Antihypertensive treatment should be initiated expeditiously for acute-onset severe hypertension (systolic blood pressure of 160 mm Hg or more or diastolic blood pressure of 110 mm Hg or more, or both) that is confirmed as persistent (15 minutes or more). The available literature suggests that antihypertensive agents should be administered within 30–60 minutes. However, it is recommended to administer antihypertensive therapy as soon as reasonably possible after the criteria for acute-onset severe hypertension are met.

The following recommendations are based primarily on consensus and expert opinion (Level C):

- It is recommended that women with gestational hypertension in the absence of proteinuria are

diagnosed with preeclampsia if they present with any of the following severe features: thrombocytopenia (platelet count less than 100,000 × 10^9/L); impaired liver function as indicated by abnormally elevated blood concentrations of liver enzymes (to twice the upper limit of normal concentration); severe persistent right upper quadrant or epigastric pain and not accounted for by alternative diagnoses; renal insufficiency (serum creatinine concentration more than 1.1 mg/dL or a doubling of the serum creatinine concentration in the absence of other renal disease); pulmonary edema, or new-onset headache unresponsive to acetaminophen and not accounted for by alternative diagnoses, or visual disturbances.

- Women with gestational hypertension who present with severe-range blood pressures should be managed with the same approach as for women with severe preeclampsia.
- Among women with gestational hypertension or preeclampsia without severe features, expectant management up to 37 0/7 weeks of gestation is recommended, during which frequent fetal and maternal evaluation is recommended. Fetal monitoring consists of ultrasonography to determine fetal growth every 3–4 weeks of gestation, and amniotic fluid volume assessment at least once weekly. In addition, an antenatal test one-to-two times per week for patients with gestational hypertension or preeclampsia without severe features is recommended.
- Epidural or spinal anesthesia is considered acceptable, and the risk of epidural hematoma is exceptionally low, in patients with platelet counts 70 × 10^9/L or more provided that the platelet level is stable, there is no other acquired or congenital coagulopathy, the platelet function is normal, and the patient is not on any antiplatelet or anticoagulant therapy.

References

1. Steegers EA, von Dadelszen P, Duvekot JJ, Pijnenborg R. Pre-eclampsia. Lancet 2010;376:631–44. (Level III)
2. Khan KS, Wojdyla D, Say L, Gülmezoglu AM, Van Look PF. WHO analysis of causes of maternal death: a systematic review. Lancet 2006;367:1066–74. (Systematic Review)
3. Wallis AB, Saftlas AF, Hsia J, Atrash HK. Secular trends in the rates of preeclampsia, eclampsia, and gestational hypertension, United States, 1987-2004. Am J Hypertens 2008;21:521–6. (Level II-3)
4. Ananth CV, Keyes KM, Wapner RJ. Pre-eclampsia rates in the United States, 1980-2010: age-period-cohort analysis. BMJ 2013;347:f6564. (Level II-3)
5. Stevens W, Shih T, Incerti D, Ton TGN, Lee HC, Peneva D, et al. Short-term costs of preeclampsia to the United States health care system. Am J Obstet Gynecol 2017; 217:237–48.e16. (Level III)
6. Conde-Agudelo A, Belizan JM. Risk factors for pre-eclampsia in a large cohort of Latin American and Caribbean women. BJOG 2000;107:75–83. (Level II-3)
7. Sibai BM, Hauth J, Caritis S, Lindheimer MD, MacPherson C, Klebanoff M, et al. Hypertensive disorders in twin versus singleton gestations. National Institute of Child Health and Human Development Network of Maternal– Fetal Medicine Units. Am J Obstet Gynecol 2000;182: 938–42. (Level II-3)
8. Bartsch E, Medcalf KE, Park AL, Ray JG. Clinical risk factors for pre-eclampsia determined in early pregnancy: systematic review and meta-analysis of large cohort studies. High Risk of Preeclampsia Identification Group. BMJ 2016;353:i1753. (Systematic Review and Meta-Analysis)
9. Ostlund I, Haglund B, Hanson U. Gestational diabetes and preeclampsia. Eur J Obstet Gynecol Reprod Biol 2004;113:12–6. (Level II-3)
10. Alfirevic Z, Roberts D, Martlew V. How strong is the association between maternal thrombophilia and adverse pregnancy outcome? A systematic review. Eur J Obstet Gynecol Reprod Biol 2002;101:6–14. (Systematic Review)
11. Smyth A, Oliveira GH, Lahr BD, Bailey KR, Norby SM, Garovic VD. A systematic review and meta-analysis of pregnancy outcomes in patients with systemic lupus erythematosus and lupus nephritis. Clin J Am Soc Nephrol 2010;5:2060–8. (Systematic Review and Meta-analysis)
12. Zhang JJ, Ma XX, Hao L, Liu LJ, Lv JC, Zhang H. A systematic review and meta-analysis of outcomes of pregnancy in CKD and CKD outcomes in pregnancy. Clin J Am Soc Nephrol 2015;10:1964–78. (Systematic Review and Meta-Analysis)
13. Chesley LC, Cooper DW. Genetics of hypertension in pregnancy: possible single gene control of pre-eclampsia and eclampsia in the descendants of eclamptic women. Br J Obstet Gynaecol 1986;93:898–908. (Level III)
14. Morgan T, Craven C, Lalouel JM, Ward K. Angiotensinogen Thr235 variant is associated with abnormal physiologic change of the uterine spiral arteries in first-trimester decidua. Am J Obstet Gynecol 1999;180:95–102. (Level III)
15. Ward K, Hata A, Jeunemaitre X, Helin C, Nelson L, Namikawa C, et al. A molecular variant of angiotensinogen associated with preeclampsia. Nat Genet 1993;4:59–61. (Level III)
16. Williams PJ, Broughton Pipkin F. The genetics of pre-eclampsia and other hypertensive disorders of pregnancy. Best Pract Res Clin Obstet Gynaecol 2011;25:405–17. (Level III)
17. Homer CS, Brown MA, Mangos G, Davis GK. Non-proteinuric pre-eclampsia: a novel risk indicator in women with gestational hypertension. J Hypertens 2008;26:295–302. (Level II-3)

18. Barton JR, Riely CA, Adamec TA, Shanklin DR, Khoury AD, Sibai BM. Hepatic histopathologic condition does not correlate with laboratory abnormalities in HELLP syndrome (hemolysis, elevated liver enzymes, and low platelet count). Am J Obstet Gynecol 1992; 167:1538–43. (Level III)

19. Sperling JD, Dahlke JD, Huber WJ, Sibai BM. The role of headache in the classification and management of hypertensive disorders in pregnancy. Obstet Gynecol 2015;126: 297–302. (Level III)

20. Thangaratinam S, Gallos ID, Meah N, Usman S, Ismail KM, Khan KS. How accurate are maternal symptoms in predicting impending complications in women with pre- eclampsia? A systematic review and meta-analysis. TIPPS (Tests in Prediction of Preeclampsia's Severity) Review Group. Acta Obstet Gynecol Scand 2011;90:564–73. (Systematic Review and Meta-Analysis)

21. Report of the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy. Am J Obstet Gynecol 2000;183:S1–22. (Level III)

22. von Dadelszen P, Payne B, Li J, Ansermino JM, Broughton Pipkin F, Cote AM, et al. Prediction of adverse maternal outcomes in pre-eclampsia: development and validation of the fullPIERS model. PIERS Study Group. Lancet 2011;377:219–27. (Level II-2)

23. Kuo VS, Koumantakis G, Gallery ED. Proteinuria and its assessment in normal and hypertensive pregnancy. Am J Obstet Gynecol 1992;167:723–8. (Level II-3)

24. Morris RK, Riley RD, Doug M, Deeks JJ, Kilby MD. Diagnostic accuracy of spot urinary protein and albumin to creatinine ratios for detection of significant proteinuria or adverse pregnancy outcome in patients with suspected pre-eclampsia: systematic review and meta-analysis. BMJ 2012;345:e4342. (Systematic Review and Meta-Analysis)

25. Phelan LK, Brown MA, Davis GK, Mangos G. A prospective study of the impact of automated dipstick urinalysis on the diagnosis of preeclampsia. Hypertens Pregnancy 2004;23:135–42. (Level II-3)

26. North RA, Taylor RS, Schellenberg JC. Evaluation of a definition of pre-eclampsia. Br J Obstet Gynaecol 1999;106:767–73 (Level II-2)

27. Bernstein PS, Martin JN Jr, Barton JR, Shields LE, Dru- zin ML, Scavone BM, et al. National Partnership for Maternal Safety: consensus bundle on severe hypertension during pregnancy and the postpartum period. Obstet Gynecol 2017;130:347–57. (Level III)

28. Pettit F, Brown MA. The management of pre-eclampsia: what we think we know. Eur J Obstet Gynecol Reprod Biol 2012;160:6–12. (Level III)

29. Sibai BM, Stella CL. Diagnosis and management of atypical preeclampsia-eclampsia. Am J Obstet Gynecol 2009; 200:481.e1–7. (Level III)

30. Magee LA, von Dadelszen P, Bohun CM, Rey E, El- Zibdeh M, Stalker S, et al. Serious perinatal complications of non-proteinuric hypertension: an international, multicentre, retrospective cohort study. J Obstet Gynaecol Can 2003;25:372–82. (Level II-3)

31. Thornton CE, Makris A, Ogle RF, Tooher JM, Hennessy A. Role of proteinuria in defining pre-eclampsia: clinical outcomes for women and babies. Clin Exp Pharmacol Physiol 2010;37:466–70. (Level II-3)

32. Williams D. Long-term complications of preeclampsia. Semin Nephrol 2011;31:111–22. (Level III)

33. Barton JR, Sibai BM. Diagnosis and management of hemolysis, elevated liver enzymes, and low platelets syndrome. Clin Perinatol 2004;31:807–33, vii. (Level III)

34. Martin JN Jr, Blake PG, Perry KG Jr, McCaul JF, Hess LW, Martin RW. The natural history of HELLP syndrome: patterns of disease progression and regression. Am J Obstet Gynecol 1991;164:1500–9; discussion 1509–13. (Level II-3)

35. Sibai BM. The HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets): much ado about nothing? Am J Obstet Gynecol 1990;162:311–6. (Level III)

36. Martin JN Jr, Rinehart BK, May WL, Magann EF, Terrone DA, Blake PG. The spectrum of severe preeclampsia: comparative analysis by HELLP (hemolysis, elevated liver enzyme levels, and low platelet count) syndrome classification. Am J Obstet Gynecol 1999;180: 1373–84. (Level II-3)

37. Tomsen TR. HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets) presenting as generalized malaise. Am J Obstet Gynecol 1995;172:1876–8; discussion 1878–80. (Level III)

38. Brown CE, Cunningham FG, Pritchard JA. Convulsions in hypertensive, proteinuric primiparas more than 24 hours after delivery. Eclampsia or some other cause? J Reprod Med 1987;32:499–503. (Level III)

39. Zeeman GG. Neurologic complications of pre-eclampsia. Semin Perinatol 2009;33:166–72. (Level III)

40. Sibai BM. Diagnosis, prevention, and management of eclampsia. Obstet Gynecol 2005;105:402–10. (Level III)

41. Cooray SD, Edmonds SM, Tong S, Samarasekera SP, Whitehead CL. Characterization of symptoms immediately preceding eclampsia. Obstet Gynecol 2011;118: 995–9. (Level III)

42. Noraihan MN, Sharda P, Jammal AB. Report of 50 cases of eclampsia. J Obstet Gynaecol Res 2005;31:302–9. (Level III)

43. Belfort MA, Saade GR, Grunewald C, Dildy GA, Abedejos P, Herd JA, et al. Association of cerebral perfusion pressure with headache in women with pre-eclampsia. Br J Obstet Gynaecol 1999;106:814–21. (Level II-3)

44. Altman D, Carroli G, Duley L, Farrell B, Moodley J, Neilson J, et al. Do women with preeclampsia, and their babies, benefit from magnesium sulphate? The Magpie Trial: a randomised placebo-controlled trial. Magpie Trial Collaboration Group. Lancet 2002;359:1877–90. (Level I)

45. Coetzee EJ, Dommisse J, Anthony J. A randomised controlled trial of intravenous magnesium sulphate versus placebo in the management of women with severe pre- eclampsia. Br J Obstet Gynaecol 1998;105:300–3. (Level I)

46. Douglas KA, Redman CW. Eclampsia in the United Kingdom. BMJ 1994;309:1395–400. (Level II-3)

47. Cunningham FG, Fernandez CO, Hernandez C. Blindness associated with preeclampsia and eclampsia. Am J Obstet Gynecol 1995;172:1291–8. (Level III)

48. Hinchey J, Chaves C, Appignani B, Breen J, Pao L, Wang A, et al. A reversible posterior leukoencephalopathy syn- drome. N Engl J Med 1996;334:494–500. (Level III)

49. Wagner SJ, Acquah LA, Lindell EP, Craici IM, Wingo MT, Rose CH, et al. Posterior reversible encephalopathy syndrome and eclampsia: pressing the case for more aggressive blood pressure control. Mayo Clin Proc 2011;86:851–6. (Level II-2)

50. Singhal AB, Bernstein RA. Postpartum angiopathy and other cerebral vasoconstriction syndromes. Neurocrit Care 2005;3:91–7. (Level III)

51. Redman CW, Sargent IL. Latest advances in understanding preeclampsia. Science 2005;308:1592–4. (Level III)

52. von Dadelszen P, Magee LA, Roberts JM. Subclassification of preeclampsia. Hypertens Pregnancy 2003;22:143–8. (Level III)

53. Dekker GA, Sibai BM. Etiology and pathogenesis of preeclampsia: current concepts. Am J Obstet Gynecol 1998; 179:1359–75. (Level III)

54. Crocker IP, Cooper S, Ong SC, Baker PN. Differences in apoptotic susceptibility of cytotrophoblasts and syncytiotrophoblasts in normal pregnancy to those complicated with preeclampsia and intrauterine growth restriction. Am J Pathol 2003;162:637–43. (Level III)

55. Leung DN, Smith SC, To KF, Sahota DS, Baker PN. Increased placental apoptosis in pregnancies complicated by preeclampsia. Am J Obstet Gynecol 2001;184:1249–50. (Level III)

56. Sargent IL, Germain SJ, Sacks GP, Kumar S, Redman CW. Trophoblast deportation and the maternal inflammatory response in pre-eclampsia. J Reprod Immunol 2003; 59: 153–60. (Level III)

57. Chua S, Wilkins T, Sargent I, Redman C. Trophoblast deportation in pre-eclamptic pregnancy. Br J Obstet Gynaecol 1991;98:973–9. (Level III)

58. Levine RJ, Lam C, Qian C, Yu KF, Maynard SE, Sachs BP, et al. Soluble endoglin and other circulating antiangiogenic factors in preeclampsia. CPEP Study Group [published erratum appears in N Engl J Med 2006;355: 1840]. N Engl J Med 2006;355:992–1005. (Level II-2)

59. Chaiworapongsa T, Espinoza J, Gotsch F, Kim YM, Kim GJ, Goncalves LF, et al. The maternal plasma soluble vascular endothelial growth factor receptor-1 concentration is elevated in SGA and the magnitude of the increase relates to Doppler abnormalities in the maternal and fetal circulation. J Matern Fetal Neonatal Med 2008; 21:25–40. (Level II-3)

60. Crispi F, Dominguez C, Llurba E, Martin-Gallan P, Ca- bero L, Gratacos E. Placental angiogenic growth factors and uterine artery Doppler findings for characterization of different subsets in preeclampsia and in isolated intrauterine growth restriction. Am J Obstet Gynecol 2006;195: 201–7. (Level II-3)

61. Nagamatsu T, Fujii T, Kusumi M, Zou L, Yamashita T, Osuga Y, et al. Cytotrophoblasts up-regulate soluble fms-like tyrosine kinase-1 expression under reduced oxygen: an implication for the placental vascular development and the pathophysiology of preeclampsia. Endocrinology 2004;145:4838–45. (Level III)

62. Nevo O, Soleymanlou N, Wu Y, Xu J, Kingdom J, Many A, et al. Increased expression of sFlt-1 in in vivo and in vitro models of human placental hypoxia is mediated by HIF-1. Am J Physiol Regul Integr Comp Physiol 2006;291:R1085–93. (Level III)

63. Espinoza J. Uteroplacental ischemia in early- and late-onset pre-eclampsia: a role for the fetus? Ultrasound Obstet Gynecol 2012;40:373–82. (Level III)

64. Pritchard JA, Cunningham FG, Pritchard SA. The Parkland Memorial Hospital protocol for treatment of eclampsia: evaluation of 245 cases. Am J Obstet Gynecol 1984; 148:951–63. (Level III)

65. Hankins GD, Wendel GD Jr, Cunningham FG, Leveno KJ. Longitudinal evaluation of hemodynamic changes in eclampsia. Am J Obstet Gynecol 1984;150:506–12. (Level III)

66. Burrows RF, Kelton JG. Thrombocytopenia at delivery: a prospective survey of 6715 deliveries. Am J Obstet Gynecol 1990;162:731–4. (Level II-3)

67. Giles C, Inglis TC. Thrombocytopenia and macrothrombocytosis in gestational hypertension. Br J Obstet Gynaecol 1981;88:1115–9. (Level II-3)

68. Sibai BM, Anderson GD, McCubbin JH. Eclampsia II. Clinical significance of laboratory findings. Obstet Gynecol 1982;59:153–7. (Level III)

69. Gant NF, Cunningham FG. Management of preeclampsia. Semin Perinatol 1994;18:94–102. (Level III)

70. Leduc L, Wheeler JM, Kirshon B, Mitchell P, Cotton DB. Coagulation profile in severe preeclampsia. Obstet Gynecol 1992;79:14–8. (Level III)

71. Spargo B, McCartney CP, Winemiller R. Glomerular capillary endotheliosis in toxemia of pregnancy. Arch Pathol 1959;68:593–9. (Level III)

72. Hennessy A, Makris A. Preeclamptic nephropathy. Nephrology (Carlton) 2011;16:134–43. (Level III)

73. Svenningsen P, Friis UG, Versland JB, Buhl KB, Moller Frederiksen B, Andersen H, et al. Mechanisms of renal NaCl retention in proteinuric disease. Acta Physiol (Oxf) 2013;207:536–45. (Level III)

74. Sagen N, Haram K, Nilsen ST. Serum urate as a predictor of fetal outcome in severe pre-eclampsia. Acta Obstet Gynecol Scand 1984;63:71–5. (Level III)

75. Espinoza J, Romero R, Mee Kim Y, Kusanovic JP, Has- san S, Erez O, et al. Normal and abnormal transformation of the spiral arteries during pregnancy. J Perinat Med 2006;34:447–58. (Level III)

76. Pijnenborg R, Vercruysse L, Hanssens M. The uterine spiral arteries in human pregnancy: facts and controversies. Placenta 2006;27:939–58. (Level III)

77. Moldenhauer JS, Stanek J, Warshak C, Khoury J, Sibai B. The frequency and severity of placental findings in women with preeclampsia are gestational age dependent. Am J Obstet Gynecol 2003;189:1173–7. (Level II-3)

78. Ogge G, Chaiworapongsa T, Romero R, Hussein Y, Kusanovic JP, Yeo L, et al. Placental lesions associated with maternal underperfusion are more frequent in early-onset than in late-onset preeclampsia. J Perinat Med 2011;39: 641–52. (Level II-2)

79. Espinoza J. Recent biomarkers for the identification of patients at risk for preeclampsia: the role of uteroplacental ischemia. Expert Opin Med Diagn 2012;6:121–30. (Level III)

80. Bolin M, Wiberg-Itzel E, Wikstrom AK, Goop M, Larsson A, Olovsson M, et al. Angiopoietin-1/angiopoietin-2 ratio for prediction of preeclampsia. Am J Hypertens 2009;22:891–5. (Level II-2)

81. Kusanovic JP, Romero R, Chaiworapongsa T, Erez O, Mittal P, Vaisbuch E, et al. A prospective cohort study of the value of maternal plasma concentrations of angiogenic and anti-angiogenic factors in early pregnancy and midtrimester in the identification of patients destined to develop preeclampsia. J Matern Fetal Neonatal Med 2009;22:1021–38. (Level II-2)

82. Poon LC, Kametas NA, Maiz N, Akolekar R, Nicolaides KH. First-trimester prediction of hypertensive disorders in pregnancy. Hypertension 2009;53:812–8. (Level II-2)

83. Espinoza J, Romero R, Nien JK, Gomez R, Kusanovic JP, Goncalves LF, et al. Identification of patients at risk for early onset and/or severe preeclampsia with the use of uterine artery Doppler velocimetry and placental growth factor [published erratum appears in Am J Obstet Gynecol 2007;196: 614]. Am J Obstet Gynecol 2007;196:326.13. (Level II-2)

84. Harrington K, Cooper D, Lees C, Hecher K, Campbell S. Doppler ultrasound of the uterine arteries: the importance of bilateral notching in the prediction of pre-eclampsia, placental abruption or delivery of a small-for-gestational-age baby. Ultrasound Obstet Gynecol 1996;7:182–8. (Level II-3)

85. Albaiges G, Missfelder-Lobos H, Lees C, Parra M, Nicolaides KH. One-stage screening for pregnancy complications by color Doppler assessment of the uterine arteries at 23 weeks' gestation. Obstet Gynecol 2000;96: 559–64. (Level II-3)

86. Papageorghiou AT, Yu CK, Cicero S, Bower S, Nicolaides KH. Second-trimester uterine artery Doppler screening in unselected populations: a review. J Matern Fetal Neonatal Med 2002;12:78–88. (Level III)

87. Papageorghiou AT, Yu CK, Bindra R, Pandis G, Nicolaides KH. Multicenter screening for pre-eclampsia and fetal growth restriction by transvaginal uterine artery Doppler at 23 weeks of gestation. Fetal Medicine Foundation Second Trimester Screening Group. Ultrasound Obstet Gynecol 2001;18:441–9. (Level II-3)

88. Cnossen JS, Morris RK, Ter Riet G, Mol BW, van der Post JA, Coomarasamy A, et al. Use of uterine artery Doppler ultrasonography to predict preeclampsia and intrauterine growth restriction: a systematic review and bivariable meta-analysis. CMAJ 2008;178:701–11. (Systematic Review and Meta-Analysis)

89. Rolnik DL, Wright D, Poon LC, O'Gorman N, Syngelaki A, de Paco Matallana C, et al. Aspirin versus placebo in pregnancies at high risk for preterm preeclampsia. N Engl J Med 2017;377:613–22. (Level I)

90. Rumbold A, Duley L, Crowther CA, Haslam RR. Antioxidants for preventing pre-eclampsia. Cochrane Database of Systematic Reviews 2008, Issue 1. Art. No.: CD004227. (Systematic Review and Meta-Analysis)

91. Zhou SJ, Yelland L, McPhee AJ, Quinlivan J, Gibson RA, Makrides M. Fish-oil supplementation in pregnancy does not reduce the risk of gestational diabetes or preeclampsia. Am J Clin Nutr 2012;95:1378–84. (Level I)

92. Meher S, Duley L. Garlic for preventing pre-eclampsia and its complications. Cochrane Database of Systematic Reviews 2006, Issue 3. Art. No.: CD006065 (Systematic Review)

93. Bodnar LM, Catoy JM, Simhan HN, Holick MF, Powers RW, Roberts JM. Maternal vitamin D deficiency increases the risk of preeclampsia. J Clin Endocrinol Metab 2007;92:3517–22. (Level II-2)

94. Wen SW, White RR, Rybak N, Gaudet LM, Robson S, Hague W, et al. Effect of high dose folic acid supplementation in pregnancy on preeclampsia (FACT): double blind, phase III, randomised controlled, international, multicentre trial. FACT Collaborating Group. BMJ 2018;362:k3478. (Level I)

95. Duley L, Henderson-Smart David J. Reduced salt intake compared to normal dietary salt, or high intake, in pregnancy. Cochrane Database of Systematic Reviews 1999, Issue 3. Art. No.: CD001687. (Level III)

96. Hofmeyr GJ, Lawrie TA, Atallah AN, Torloni MR. Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. Cochrane Database of Systematic Reviews 2018, Issue 10. Art. No.: CD001059. DOI: 10.1002/14651858.CD001059.pub5. (Systematic Review)

97. Meher S, Abalos E, Carroli G. Bed rest with or without hospitalisation for hypertension during pregnancy. Cochrane Database of Systematic Reviews 2005, Issue 4. Art. No.: CD003514. (Systematic Review and Meta-Analysis)

98. Benigni A, Gregorini G, Frusca T, Chiabrando C, Ballerini S, Valcamonico A, et al. Effect of low-dose aspirin on fetal and maternal generation of thromboxane by platelets in women at risk for pregnancy-induced hypertension. N Engl J Med 1989;321:357–62. (Level I)

99. Schiff E, Peleg E, Goldenberg M, Rosenthal T, Ruppin E, Tamarkin M, et al. The use of aspirin to prevent pregnancy-induced hypertension and lower the ratio of thromboxane A2 to prostacyclin in relatively high risk pregnancies. N Engl J Med 1989;321:351–6. (Level I)

100. Roberge S, Nicolaides K, Demers S, Hyett J, Chaillet N, Bujold E. The role of aspirin dose on the prevention of preeclampsia and fetal growth restriction: systematic review and meta-analysis. Am J Obstet Gynecol 2017; 216:110–20.e6. (Systematic Review and Meta-Analysis)

101. Meher S, Duley L, Hunter K, Askie L. Antiplatelet therapy before or after 16 weeks' gestation for preventing preeclampsia: an individual participant data meta-analysis. Am J Obstet Gynecol 2017;216:121–8.e2. (Systematic Review and Meta-Analysis)

102. Alqudah A, McKinley MC, McNally R, Graham U, Watson CJ, Lyons TJ, et al. Risk of pre-eclampsia in women taking metformin: a systematic review and meta-analysis. Diabet Med 2018;35:160–72. (Systematic Review and Meta-Analysis)

103. George EM, Granger JP. Mechanisms and potential therapies for preeclampsia. Curr Hypertens Rep 2011;13:269–75. (Level III)

104. Samangaya RA, Mires G, Shennan A, Skillern L, Howe D, McLeod A, et al. A randomised, double-blinded, placebo-controlled study of the phosphodiesterase type 5 inhibitor sildenafil for the treatment of preeclampsia. Hypertens Pregnancy 2009;28:369–82. (Level I)

105. Trapani A Jr, Goncalves LF, Trapani TF, Vieira S, Pires M, Pires MM. Perinatal and hemodynamic evaluation of sildenafil citrate for preeclampsia treatment: a randomized controlled trial. Obstet Gynecol 2016; 128:253–9. (Level I)

106. Sibai BM. Management of late preterm and early-term pregnancies complicated by mild gestational hypertension/pre-eclampsia. Semin Perinatol 2011;35:292–6. (Level III)

107. Koopmans CM, Bijlenga D, Groen H, Vijgen SM, Aarnoudse JG, Bekedam DJ, et al. Induction of labour versus expectant monitoring for gestational hypertension or mild pre-eclampsia after 36 weeks' gestation (HYPITAT): a multicentre, open-label randomised controlled trial. HY- PITAT study group. Lancet 2009;374:979–88. (Level I)

108. Schiff E, Friedman SA, Kao L, Sibai BM. The importance of urinary protein excretion during conservative management of severe preeclampsia. Am J Obstet Gynecol 1996; 175:1313–6. (Level II)

109. Newman MG, Robichaux AG, Stedman CM, Jaekle RK, Fontenot MT, Dotson T, et al. Perinatal outcomes in preeclampsia that is complicated by massive proteinuria. Am J Obstet Gynecol 2003;188:264–8. (Level II-3)

110. Odendaal HJ, Pattinson RC, Bam R, Grove D, Kotze TJ. Aggressive or expectant management for patients with severe preeclampsia between 28–34 weeks' gestation: a randomized controlled trial. Obstet Gynecol 1990;76: 1070–5. (Level I)

111. Sibai BM, Mercer BM, Schiff E, Friedman SA. Aggressive versus expectant management of severe preeclampsia at 28 to 32 weeks' gestation: a randomized controlled trial. Am J Obstet Gynecol 1994;171:818–22. (Level I)

112. Churchill D, Duley L, Thornton JG, Jones L. Interventionist versus expectant care for severe pre-eclampsia between 24 and 34 weeks' gestation. Cochrane Database of Systematic Reviews 2013, Issue 7. Art. No.: CD003106. (Systematic Review and Meta-Analysis)

113. Magee LA, Yong PJ, Espinosa V, Cote AM, Chen I, von Dadelszen P. Expectant management of severe preeclampsia remote from term: a structured systematic review. Hypertens Pregnancy 2009;28:312–47. (Systematic Review)

114. Vigil-De Gracia P, Reyes Tejada O, Calle Minaca A, Tellez G, Chon VY, Herrarte E, et al. Expectant management of severe preeclampsia remote from term: the MEXPRE Latin Study, a randomized, multicenter clinical trial. Am J Obstet Gynecol 2013;209:425.e1–8. (Level I)

115. Balogun OA, Sibai BM. Counseling, management, and outcome in women with severe preeclampsia at 23 to 28 weeks' gestation. Clin Obstet Gynecol 2017;60:183–9. (Level III)

116. Levels of maternal care. Obstetric Care Consensus No. 9. American College of Obstetricians and Gynecologists. Obstet Gynecol 2019;134:e41–55. (Level III)

117. Garovic VD. Hypertension in pregnancy: diagnosis and treatment. Mayo Clin Proc 2000;75:1071–6. (Level III)

118. Pickering TG, Hall JE, Appel LJ, Falkner BE, Graves J, Hill MN, et al. Recommendations for blood pressure measurement in humans and experimental animals: part 1: blood pressure measurement in humans: a statement for professionals from the Subcommittee of Professional and Public Education of the American Heart Association Council on High Blood Pressure Research. Circulation 2005;111:697–716. (Level III)

119. Duley L, Gülmezoglu AM, Henderson-Smart DJ, Chou D. Magnesium sulphate and other anticonvulsants for women with pre-eclampsia. Cochrane Database of Systematic Reviews 2010, Issue 11. Art. No.: CD000025. (Systematic Review and Meta-Analysis)

120. Witlin AG, Friedman SA, Egerman RS, Frangieh AY, Sibai BM. Cerebrovascular disorders complicating pregnancy—beyond eclampsia. Am J Obstet Gynecol 1997; 176:1139–45; discussion 1145–8. (Level III)

121. Livingston JC, Livingston LW, Ramsey R, Mabie BC, Sibai BM. Magnesium sulfate in women with mild preeclampsia: a randomized controlled trial. Obstet Gynecol 2003;101:217–20. (Level I)

122. Cahill AG, Macones GA, Odibo AO, Stamilio DM. Magnesium for seizure prophylaxis in patients with mild preeclampsia. Obstet Gynecol 2007;110:601–7. (Level III)

123. Sibai BM. Magnesium sulfate prophylaxis in preeclampsia: lessons learned from recent trials. Am J Obstet Gynecol 2004;190:1520–6. (Level III)

124. Schrier RW. Body fluid volume regulation in health and disease: a unifying hypothesis. Ann Intern Med 1990;113: 155–9. (Level III)

125. Chien PF, Khan KS, Arnott N. Magnesium sulphate in the treatment of eclampsia and pre-eclampsia: an overview of the evidence from randomised trials. Br J Obstet Gynaecol 1996;103:1085–91. (Meta-Analysis)

126. Duley L, Henderson-Smart DJ, Walker GJA, Chou D. Magnesium sulphate versus diazepam for eclampsia. Cochrane Database of Systematic Reviews 2010, Issue 12. Art. No.: CD000127. (Systematic Review and Meta-Analysis)

127. Belfort MA, Anthony J, Saade GR, Allen JC Jr. A comparison of magnesium sulfate and nimodipine for the prevention of eclampsia. Nimodipine Study Group. N Engl J Med 2003;348:304–11. (Level I)

128. Lu JF, Nightingale CH. Magnesium sulfate in eclampsia and preeclampsia: pharmacokinetic principles. Clin Pharmacokinet 2000;38:305–14. (Level III)

129. Okusanya BO, Oladapo OT, Long Q, Lumbiganon P, Carroli G, Qureshi Z, et al. Clinical pharmacokinetic properties of magnesium sulphate in women with pre-eclampsia and eclampsia. BJOG 2016;123:356–66. (Systematic Review)

130. Which anticonvulsant for women with eclampsia? Evidence from the Collaborative Eclampsia Trial [published erratum appears in Lancet 1995;346:258]. Lancet 1995; 345:1455–63. (Level I)

131. Dayicioglu V, Sahinoglu Z, Kol E, Kucukbas M. The use of standard dose of magnesium sulphate in prophylaxis of eclamptic seizures: do body mass index alterations have any effect on success? Hypertens Pregnancy 2003;22: 257–65. (Level II-3)

132. Crowther CA, Brown J, McKinlay CJD, Middleton P. Magnesium sulphate for preventing preterm birth in threatened preterm labour. Cochrane Database of Systematic Reviews 2014, Issue 8. Art. No.: CD001060. (Systematic Review)

133. Alexander JM, McIntire DD, Leveno KJ, Cunningham FG. Selective magnesium sulfate prophylaxis for the prevention of eclampsia in women with gestational hypertension. Obstet Gynecol 2006;108:826–32. (Level II-3)

134. Duley L. Magnesium sulphate regimens for women with eclampsia: messages from the Collaborative Eclampsia Trial. Br J Obstet Gynaecol 1996;103:103–5. (Level III)

135. Duley L, Meher S, Jones L. Drugs for treatment of very high blood pressure during pregnancy. Cochrane Database of Systematic Reviews 2013, Issue 7. Art. No.: CD001449. (Systematic Review and Meta-Analysis)

136. Emergent therapy for acute-onset, severe hypertension during pregnancy and the postpartum period. ACOG Committee Opinion No. 767. American College of Obstetricians and Gynecologists. Obstet Gynecol 2019;133: e174–80. (Level III)

137. Alanis MC, Robinson CJ, Hulsey TC, Ebeling M, Johnson DD. Early-onset severe preeclampsia: induction of labor vs elective cesarean delivery and neonatal outcomes. Am J Obstet Gynecol 2008;199:262.e1–6. (Level II-3)

138. Blackwell SC, Redman ME, Tomlinson M, Landwehr JB Jr, Tuynman M, Gonik B, et al. Labor induction for the preterm severe pre-eclamptic patient: is it worth the effort? J Matern Fetal Med 2001;10:305–11. (Level II-3)

139. Sibai BM. Evaluation and management of severe pre-eclampsia before 34 weeks' gestation. Publications Committee, Society for Maternal–Fetal Medicine. Am J Obstet Gynecol 2011;205:191–8. (Level III)

140. Alexander JM, Bloom SL, McIntire DD, Leveno KJ. Severe preeclampsia and the very low birth weight infant: is induction of labor harmful? Obstet Gynecol 1999;93: 485–8. (Level II-3)

141. Nassar AH, Adra AM, Chakhtoura N, Gomez-Marin O, Beydoun S. Severe preeclampsia remote from term: labor induction or elective cesarean delivery? Am J Obstet Gynecol 1998;179:1210–3. (Level II-3)

142. Hogg B, Hauth JC, Caritis SN, Sibai BM, Lindheimer M, Van Dorsten JP, et al. Safety of labor epidural anesthesia for women with severe hypertensive disease. National Institute of Child Health and Human Development Maternal–Fetal Medicine Units Network. Am J Obstet Gynecol 1999;181:1096–101. (Level II-2)

143. Aya AG, Vialles N, Tanoubi I, Mangin R, Ferrer JM, Robert C, et al. Spinal anesthesia-induced hypotension: a risk comparison between patients with severe pre-eclampsia and healthy women undergoing preterm cesarean delivery. Anesth Analg 2005;101:869–75. (Level II-2)

144. Visalyaputra S, Rodanant O, Somboonviboon W, Tantivitayatan K, Thienthong S, Saengchote W. Spinal versus epidural anesthesia for cesarean delivery in severe preeclampsia: a prospective randomized, multicenter study. Anesth Analg 2005;101:862–8. (Level I)

145. Hawkins JL, Koonin LM, Palmer SK, Gibbs CP. Anesthesia-related deaths during obstetric delivery in the United States, 1979-1990. Anesthesiology 1997;86:277–84. (Level III)

146. Huang CJ, Fan YC, Tsai PS. Differential impacts of modes of anaesthesia on the risk of stroke among pre-eclamptic women who undergo Caesarean delivery: a population-based study. Br J Anaesth 2010;105:818–26. (Level II-3)

147. Vandermeulen EP, Van Aken H, Vermylen J. Anticoagulants and spinal-epidural anesthesia. Anesth Analg 1994; 79:1165–77. (Level III)

148. Lee LO, Bateman BT, Kheterpal S, Klumpner TT, Housey M, Aziz MF, et al. Risk of epidural hematoma after neuraxial techniques in thrombocytopenic parturients: a report from the Multicenter Perioperative Outcomes Group. Multicenter Perioperative Outcomes Group Investigators. Anesthesiology 2017;126:1053–63. (Systematic Review)

149. van Veen JJ, Nokes TJ, Makris M. The risk of spinal haematoma following neuraxial anaesthesia or lumbar puncture in thrombocytopenic individuals. Br J Haematol 2010;148:15–25. (Level III)

150. Taber EB, Tan L, Chao CR, Beall MH, Ross MG. Pharmacokinetics of ionized versus total magnesium in subjects with preterm labor and preeclampsia. Am J Obstet Gynecol 2002;186:1017–21. (Level III)

151. Al-Safi Z, Imudia AN, Filetti LC, Hobson DT, Bahado-Singh RO, Awonuga AO. Delayed postpartum preeclampsia and eclampsia: demographics, clinical course, and complications. Obstet Gynecol 2011;118: 1102–7. (Level II-3)

152. Chames MC, Livingston JC, Ivester TS, Barton JR, Sibai BM. Late postpartum eclampsia: a preventable disease? Am J Obstet Gynecol 2002;186:1174–7. (Level III)

153. Filetti LC, Imudia AN, Al-Safi Z, Hobson DT, Awonuga AO, Bahado-Singh RO. New onset delayed postpartum preeclampsia: different disorders? J Matern Fetal Neonatal Med 2012;25:957–60. (Level II-3)

154. Matthys LA, Coppage KH, Lambers DS, Barton JR, Sibai BM. Delayed postpartum preeclampsia: an experience of 151 cases. Am J Obstet Gynecol 2004;190:1464–6. (Level II-3)

155. Blue NR, Murray-Krezan C, Drake-Lavelle S, Weinberg D, Holbrook BD, Katukuri VR, et al. Effect of ibuprofen vs acetaminophen on postpartum hypertension in preeclampsia with severe features: a double-masked, randomized controlled trial. Am J Obstet Gynecol 2018;218:616.e1–8. (Level I)

156. Viteri OA, England JA, Alrais MA, Lash KA, Villegas MI, Ashimi Balogun OA, et al. Association of nonsteroidal antiinflammatory drugs and postpartum hypertension in women with preeclampsia with severe features. Obstet Gynecol 2017;130:830–5. (Level II-3)

157. Wasden SW, Ragsdale ES, Chasen ST, Skupski DW. Impact of non-steroidal anti-inflammatory drugs on hypertensive disorders of pregnancy. Pregnancy Hypertens 2014;4:259–63. (Level II-3)

158. Anastasio HB, Campbell LE, Buermeyer A, Saccone G, Moreno S, Cruz Y, et al. Nonsteroidal antiinflammatory drug administration and postpartum blood pressure in women with hypertensive disorders of pregnancy. Obstet Gynecol 2018;132:1471–6. (Level II–2)

159. Duley L, Henderson-Smart DJ, Chou D. Magnesium sulphate versus phenytoin for eclampsia. Cochrane Database of Systematic Reviews 2010, Issue 10. Art. No.: CD000128. (Systematic Review and Meta-Analysis)

160. Duley L, Gülmezoglu AM, Chou D. Magnesium sulphate versus lytic cocktail for eclampsia. Cochrane Database of Systematic Reviews 2010, Issue 9. Art. No.: CD002960. (Systematic Review and Meta-Analysis)

161. Dunn R, Lee W, Cotton DB. Evaluation by computerized axial tomography of eclamptic women with seizures refractory to magnesium sulfate therapy. Am J Obstet Gynecol 1986;155:267–8. (Level III)

162. Sibai BM. Diagnosis, controversies, and management of the syndrome of hemolysis, elevated liver enzymes, and low platelet count. Obstet Gynecol 2004;103:981–91. (Level III)

163. Woudstra DM, Chandra S, Hofmeyr GJ, Dowswell T. Corticosteroids for HELLP (hemolysis, elevated liver enzymes, low platelets) syndrome in pregnancy. Cochrane Database of Systematic Reviews 2010, Issue 9. Art. No.: CD008148. (Systematic Review and Meta-Analysis)

164. Neiger R, Contag SA, Coustan DR. The resolution of preeclampsia-related thrombocytopenia. Obstet Gynecol 1991;77:692–5. (Level III)

165. Sibai BM, Ramadan MK. Acute renal failure in pregnancies complicated by hemolysis, elevated liver enzymes, and low platelets. Am J Obstet Gynecol 1993;168:1682–7; discussion 1687–90. (Level III)

166. Behrens I, Basit S, Melbye M, Lykke JA, Wohlfahrt J, Bundgaard H, et al. Risk of post-pregnancy hypertension in women with a history of hypertensive disorders of pregnancy: nationwide cohort study. BMJ 2017;358:j3078. (Level II–2)

167. Stuart JJ, Tanz LJ, Missmer SA, Rimm EB, Spiegelman D, James-Todd TM, et al. Hypertensive disorders of pregnancy and maternal cardiovascular disease risk factor development: an observational cohort study. Ann Intern Med 2018;169:224–32. (Level II–2)

168. Brown MC, Best KE, Pearce MS, Waugh J, Robson SC, Bell R. Cardiovascular disease risk in women with pre-eclampsia: systematic review and meta-analysis. Eur J Epidemiol 2013;28:1–19. (Systematic Review and Meta-Analysis)

169. McDonald SD, Malinowski A, Zhou Q, Yusuf S, Devereaux PJ. Cardiovascular sequelae of preeclampsia/eclampsia: a systematic review and meta-analyses. Am Heart J 2008;156:918–30. (Systematic Review and Meta-Analysis)

170. Funai EF, Paltiel OB, Malaspina D, Friedlander Y, Deutsch L, Harlap S. Risk factors for pre-eclampsia in nulliparous and parous women: the Jerusalem perinatal study. Paediatr Perinat Epidemiol 2005;19:59–68. (Level II–2)

171. Ray JG, Vermeulen MJ, Schull MJ, Redelmeier DA. Cardiovascular health after maternal placental syndromes (CHAMPS): population-based retrospective cohort study. Lancet 2005;366:1797–803. (Level II–3)

172. Grandi SM, Vallee-Pouliot K, Reynier P, Eberg M, Platt RW, Arel R, et al. Hypertensive disorders in pregnancy and the risk of subsequent cardiovascular disease. Paediatr Perinat Epidemiol 2017;31:412–21. (Level II–3)

173. Powe CE, Levine RJ, Karumanchi SA. Preeclampsia, a disease of the maternal endothelium: the role of antiangiogenic factors and implications for later cardiovascular disease. Circulation 2011;123:2856–69. (Level III)

174. Romundstad PR, Magnussen EB, Smith GD, Vatten LJ. Hypertension in pregnancy and later cardiovascular risk: common antecedents? Circulation 2010;122:579–84. (Level II–2)

175. Ahmed R, Dunford J, Mehran R, Robson S, Kunadian V. Pre-eclampsia and future cardiovascular risk among women: a review. J Am Coll Cardiol 2014;63:1815–22. (Level III)

The MEDLINE database, the Cochrane Library, and the American College of Obstetricians and Gynecologists' own internal resources and documents were used to locate relevant articles published between January 1985–June 2018. Studies were reviewed and evaluated for quality according to the method outlined by the U.S. Preventive Services Task Force:

- I Evidence obtained from at least one properly designed randomized controlled trial.
- II-1 Evidence obtained from well-designed controlled trials without randomization.
- II-2 Evidence obtained from well-designed cohort or case–control analytic studies, preferably from more than one center or research group.
- II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.
- III Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Based on the highest level of evidence found in the data, recommendations are provided and graded according to the following categories:

Level A—Recommendations are based on good and consistent scientific evidence.

Level B—Recommendations are based on limited or inconsistent scientific evidence.

Level C—Recommendations are based primarily on consensus and expert opinion.

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Pregnancy and Heart Disease

Maternal heart disease has emerged as a major threat to safe motherhood and women's long-term cardiovascular health. In the United States, disease and dysfunction of the heart and vascular system as "cardiovascular disease" is now the leading cause of death in pregnant women and women in the postpartum period (1, 2) accounting for 4.23 deaths per 100,000 live births, a rate almost twice that of the United Kingdom (3, 4). The most recent data indicate that cardiovascular diseases constitute 26.5% of U.S. pregnancy-related deaths (5). Of further concern are the disparities in cardiovascular disease outcomes, with higher rates of morbidity and mortality among nonwhite and lower-income women. Contributing factors include barriers to prepregnancy cardiovascular disease assessment, missed opportunities to identify cardiovascular disease risk factors during prenatal care, gaps in high-risk intrapartum care, and delays in recognition of cardiovascular disease symptoms during the puerperium. The purpose of this document is to 1) describe the prevalence and effect of heart disease among pregnant and postpartum women; 2) provide guidance for early antepartum and postpartum risk factor identification and modification; 3) outline common cardiovascular disorders that cause morbidity and mortality during pregnancy and the puerperium; 4) describe recommendations for care for pregnant and postpartum women with preexisting or new-onset acquired heart disease; and 5) present a comprehensive interpregnancy care plan for women with heart disease.

Background

Emerging Trends in Cardiovascular Disease

Cardiovascular disease affects approximately 1–4% of the nearly 4 million pregnancies in the United States each year. The incidence of pregnancy in women with congenital heart disease and acquired heart disease is on the rise (6). In developed countries, maternal morbidity and mortality secondary to congenital heart disease have remained relatively stable at 11% and 0.5% (7), respectively; however, the United States experienced a significant linear increase in maternal congenital heart disease (6.4 to 9.0 per 10,000 delivery hospitalizations) from 2000 to 2010 (8), and maternal deaths due to acquired heart disease remain high. From 2002 to 2011, 22.2% of maternal deaths in Illinois were due to cardiovascular disease, 97.1% of which were related to acquired heart disease (9). This rising trend in maternal deaths related to cardiovascular disease appears to be due to acquired heart disease (10).

The most common presentations of maternal acquired heart disease during pregnancy and the postpartum periods are heart failure, myocardial infarction, arrhythmia, or aortic dissection (11, 12). Diagnosis can be challenging because the overlap of cardiovascular symptoms with those of normal pregnancy may lead to delays in diagnosis and subsequent care (10). If cardiovascular disease were to be considered in the differential diagnosis by treating health care providers, it is estimated that a quarter or more of maternal deaths could be prevented (10, 13, 14). A recent study of maternal cardiovascular mortality in Illinois found that 28.1% of maternal cardiac deaths were potentially deemed preventable due to health care provider issues, patient features (eg, nonadherence, obesity) (9), and health care system factors related to access. In the United Kingdom, a 2015 report on maternal mortality concluded that substandard health care accounted for more than 50% of cardiac deaths, half of which were considered avoidable (15).

Risk Factors for Cardiovascular Disease Across the Maternity Care Continuum

There are four key risk factors linked to cardiovascular disease-related maternal mortality:

1. Race/Ethnicity: Non-Hispanic black women have a 3.4 times higher risk of dying from cardiovascular disease-related pregnancy complications compared with non-Hispanic white women independent of other variables (5). Between 2011 and 2013, there were 43.5 pregnancy-related deaths per 100,000 live births for non-Hispanic black women compared with 11.0 and 12.7 pregnancy-related deaths per 100,000 live births for Hispanic and non-Hispanic white women, respectively (5). This disparity can be explained in part by exposure to structural, institutional, and systemic barriers that contribute to a higher rate of comorbidities.
2. Age: Age older than 40 years increases the risk of heart disease-related maternal death 30 times the risk for women younger than 20 years (16, 17).
3. Hypertension: Hypertensive disorders affect up to 10% of pregnancies and can lead to maternal morbidity and mortality. Severe and early-onset hypertension during pregnancy put women at an increased risk of cardiac compromise during or following delivery (18–20). In pregnancies complicated by hypertension, the incidence of myocardial infarction and heart failure is 13-fold and 8-fold higher, respectively, than in healthy pregnancies (18).
4. Obesity: Prepregnancy obesity increases maternal death risk due to a cardiac cause (21), especially if associated with moderate-to-severe obstructive sleep apnea (22). In the United Kingdom from 2006 to 2008, 60% of maternal deaths in which the body mass index (BMI, calculated as weight in kilograms divided by height in meters squared) was known were in overweight or obese women (15).

The presence of one or more of these risk factors should raise the threshold for suspicion that a patient is at-risk for maternal heart disease and pregnancy-related morbidity and mortality (23).

Social Determinants of Disparities in Cardiovascular Disease in Health and Health Care

Increased rates of cardiovascular disease-related complications among women of color are explained, in part, by racial and ethnic bias in the provision of health care and health system processes (24). Patient, physician, and health system-level factors can affect outcomes. Physician implicit and explicit bias and overt racism often can result in missed diagnoses or inappropriate treatment. Health system barriers to efficient triage based on symptom severity, language barriers, and differences in cultural humility are important factors that must be investigated to understand fully the pervasiveness of disparities that women of color face when encountering the health care system (25). Moreover, women of color may have experienced injustice in health care processes, leading to mistrust of the medical system. These factors contribute to a disproportionately higher rate of pregnancy-associated complications among women of color which, in turn, places these women not only at a greater risk of cardiovascular events in the postpartum period but also increase their lifetime risk of cardiovascular disease. Thus, it is important to improve education for these women and their trusted lay sources of information by emphasizing the value of medical care and the importance of healthy dietary habits and regular exercise. Non-Hispanic black women are more likely to develop gestational diabetes mellitus, preeclampsia, and have a preterm delivery or low-birthweight infant compared with non-Hispanic white women (23, 26). These health disparities often are amplified by missed opportunities to identify cardiovascular disease risk factors before pregnancy and limited access to cardiac-related care algorithms during intrapartum and postpartum care (23, 27). Additionally, the higher rate of obesity among racial and ethnic nonwhite groups independently contributes to disparities in the development of adverse pregnancy outcomes leading to long-term risk of cardiovascular disease. A higher prevalence of postpartum weight retention and persistence of high-glucose levels among women with gestational diabetes mellitus places them at increased risk of cardiovascular disease (28, 29).

Physiologic Changes in Pregnancy That Affect Cardiovascular Stress

Pregnancy is a natural stress test because the cardiovascular system undergoes structural and hemodynamic adaptations to sustain a high-volume load. An understanding of these physiologic changes is essential for health care providers.

Hemodynamic Changes

Antepartum. Because of increases in estrogen and progesterone and the activation of the renin-angiotensin-aldosterone system, pregnancy causes a continuous increase in cardiac output and plasma volume and a decrease in maternal systemic vascular resistance (30). Blood pressure initially decreases but increases in the third trimester (31, 32) (Table 1). Uterine mechanical compression of the inferior vena cava can occur during the second and third trimesters, potentially reducing venous return to the right ventricle, causing a postural hypotensive syndrome (33) and exacerbating lower-extremity edema. These changes are amplified in women with multiple gestations.

Intrapartum and Postpartum. During labor and after delivery, there are dramatic changes in cardiac output, heart rate, blood pressure, and plasma volume (34, 35). Although heart rate and blood pressure normally decrease within 48 hours postpartum, blood pressure may increase again between days 3–6 due to fluid shifts (36) (Table 1). During this period, clinicians should monitor patients for hypertensive complications and those related to fluid overload (37). Increased hydrostatic pressure and decreased colloid osmotic pressure render women with cardiovascular disease susceptible to pulmonary edema at the time of delivery and immediately postpartum, particularly in women with severe cardiovascular disease and excessive intravenous fluid administration or preeclampsia, or both. Increased maternal plasma atrial natriuretic peptide levels in the first week postpartum allow for postpartum diuresis (38). Maternal hemodynamics generally return to a prepregnancy state 3–6 months after delivery.

Structural Changes

The heart ventricles adapt to the plasma volume increase during pregnancy. Left ventricular end diastolic volume increases by approximately 10% (39) and left and right ventricular mass increase by approximately 50% and 40%, respectively (40). Reports of ejection fraction during pregnancy are varied. Ejection fractions in some women show no change, (39) although others decrease

Table 1. Cardiovascular Changes in a Normal Pregnancy*

	First Trimester	Second Trimester	Third Trimester	Stage 1 Labor	Stage 2 Labor	Early Postpartum	3–6 months Postpartum
Cardiac output	↑5–10%	↑↑35–45%		↑30%	↑↑50%	↑↑↑60–80% immediately, then rapidly decreases within the first hour	Return to prepregnancy values
Heart rate	↑3–5%	↑10–15%	↑15–20%	During uterine contractions: ↑40–50%		↓5–10% within 24 hours; continues to decrease throughout the first 6 weeks	Return to prepregnancy values
Blood pressure	↓10%	↓5%	↑5%	During uterine contractions: ↑SBP 15–25% ↑DBP 10–15%		↓SBP 5–10% within 48 hours; may increase again between days 3–6 due to fluid shifts	Return to prepregnancy values
Plasma volume	↑	↑↑40–50%		↑	↑↑	↑↑↑500 mL due to autotransfusion	Return to prepregnancy values

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure.

*Hemodynamic changes that occur during pregnancy, labor, and postpartum (compared with prepregnancy) should be understood to identify early interventions (such as blood pressure control and diuresis) that may be needed to prevent clinical deterioration in a woman with cardiovascular disease.

Data from Kuhn JC, Falk RS, Langesaeter E. Haemodynamic changes during labour: continuous minimally invasive monitoring in 20 healthy parturients. Int J Obstet Anesth 2017;31:74–83; Ouzounian JG, Elkayam U. Physiologic changes during normal pregnancy and delivery. Cardiol Clin 2012;30:317–29; Sanghavi M, Rutherford JD. Cardiovascular physiology of pregnancy. Circulation 2014;130:1003–8; Shen M, Tan H, Zhou S, Smith GN, Walker MC, Wen SW. Trajectory of blood pressure change during pregnancy and the role of pre-gravid blood pressure: a functional data analysis approach. Sci Rep 2017;7:6227; Sohnchen N, Melzer K, Tejada BM, Jastrow-Meyer N, Othenin-Girard V, Irion O, et al. Maternal heart rate changes during labour. Eur J Obstet Gynecol Reprod Biol 2011;158:173–8; and Walters BN, Walters T. Hypertension in the puerperium [letter]. Lancet 1987;2:330.

(41, 42). Importantly, approximately 20% of women have diastolic dysfunction at term, which may be associated with dyspnea on exertion (41, 43). Structural changes of the maternal heart return to baseline before 1 year postpartum.

Hematologic, Coagulation, and Metabolic Changes

Hematologic, coagulation, and metabolic changes in pregnancy are important contributors to cardiovascular risk. Although intensified erythropoiesis in pregnancy increases red blood cell mass by 20–30%, this increase is proportionally lower than the increase in plasma volume, resulting in physiologic anemia from hemodilution. Because severe anemia may be associated with heart failure and myocardial ischemia, hemoglobin or hematocrit levels should be checked each trimester in women with cardiovascular disease. Pregnancy is associated with physiologic and anatomic changes that increase the risk of thromboembolism, including hypercoagulability, venous stasis, decreased venous outflow, compression of the inferior vena cava and pelvic veins by the enlarging uterus, and decreased mobility (44). Pregnancy also alters the levels of coagulation factors normally responsible for hemostasis. The overall effect of these changes is an amplified thrombogenic state with an increased risk of thromboembolism. Certain disorders, such as antiphospholipid antibody syndrome and high-risk thrombophilia and smoking, further increase the risk of thrombosis and embolism during pregnancy. From a metabolic standpoint, pregnancy is a catabolic state that leads to insulin resistance and an atherogenic lipid profile with elevated serum fatty acids.

Signs and Symptoms of Heart Disease

Normal pregnancy and postpartum symptoms and signs can overlap with findings reflective of underlying heart disease (Table 2). Health care providers should become familiar with the signs and symptoms of cardiovascular disease as an important step toward improving maternal outcomes.

Clinical Considerations and Recommendations

▶ ***What are the prerequisites of pregnancy preparation and prepregnancy counseling for patients with known heart disease?***

Whenever possible, optimization of maternal health status should be attempted and achieved before pregnancy. Risk to a woman's heart and cardiovascular system engendered by pregnancy depends upon the specific type of heart disease and clinical status of the patient. Women with known cardiovascular disease (Table 3) should be evaluated by a cardiologist ideally before pregnancy or as early as possible during the pregnancy for an accurate diagnosis and assessment of the effect pregnancy will have on the underlying cardiovascular disease, to assess the potential risks to the woman and fetus, and to optimize the underlying cardiac condition. A detailed history, including family history and any current cardiovascular symptoms, physical examination, and review of medical records, including prior cardiovascular testing and interventions, should be obtained (45–48). A comprehensive cardiovascular family history should include inquiry about structural, vascular, or rhythm disorders and sudden unexpected death. Clues to a familial cardiac condition may include prior cardiac surgery, myocardial infarction, stroke, aortic dissection, and sudden death. Upon confirmation of family history of cardiovascular disease, health care providers should ask whether genetic testing has been performed. A known gene mutation, such as *MYH7* for cardiomyopathy, may have implications for a patient's individual risk of developing cardiomyopathy and may alert the patient and care team to plan postpartum surveillance and to screen offspring (49).

Patients with moderate and high-risk cardiovascular disease should be managed during pregnancy, delivery, and the postpartum period in medical centers with a multidisciplinary Pregnancy Heart Team (Table 4) that includes obstetric providers, maternal–fetal medicine subspecialists, cardiologists, and an anesthesiologist at a minimum. Ad hoc members may include cardiac surgeons, interventional cardiologists, cardiac imaging specialists, electrophysiologists, pulmonary hypertension and heart failure specialists, adult congenital cardiologists, emergency physicians, intensivists, neonatologists, geneticists, mental health specialists, primary care physicians, other medical specialists, advanced practice providers and specialized nurses, midwives, or pharmacists. The members of the Pregnancy Heart Team (Table 4) should work together to assess and counsel the patient regarding the individualized risks of her underlying cardiac condition should she become pregnant, the potential risk of transmission of congenital heart or genetic disease to the child, and the need for increased medical surveillance during the antepartum, parturition, and postpartum phases of pregnancy (Table 3).

A triad of cardiovascular risk screening, patient education, and multidisciplinary team planning has been suggested to optimize outcomes in women with known cardiovascular disease (50). It is imperative to

Table 2. How to Differentiate Common Signs and Symptoms of Normal Pregnancy Versus Those That Are Abnormal and Indicative of Underlying Cardiac Disease

	ROUTINE CARE	CAUTION*†	STOP†‡
	Reassurance	Nonemergent Evaluation	Prompt Evaluation Pregnancy Heart Team
History of CVD	None	None	Yes
Self-reported symptoms	None or mild	Yes	Yes
Shortness of breath	No interference with activities of daily living; with heavy exertion only	With moderate exertion, new-onset asthma, persistent cough, or moderate or severe OSA§	At rest; paroxysmal nocturnal dyspnea or orthopnea; bilateral chest infiltrates on CXR or refractory pneumonia
Chest pain	Reflux related that resolves with treatment	Atypical	At rest or with minimal exertion
Palpitations	Few seconds, self-limited	Brief, self-limited episodes; no lightheadedness or syncope	Associated with near syncope
Syncope	Dizziness only with prolonged standing or dehydration	Vasovagal	Exertional or unprovoked
Fatigue	Mild	Mild or moderate	Extreme
Vital signs	Normal		
HR (beats per minute)	<90	90–119	≥120
Systolic BP (mm Hg)	120–139	140–159	≥160 (or symptomatic low BP)
RR (per minute)	12–15	16–25	≥25
Oxygen saturation	>97%	95–97%	<95% (unless chronic)
Physical examination	Normal		
JVP	Not visible	Not visible	Visible >2 cm above clavicle
Heart	S3, barely audible soft systolic murmur	S3, systolic murmur	Loud systolic murmur, diastolic murmur, S4
Lungs	Clear	Clear	Wheezing, crackles, effusion
Edema	Mild	Moderate	Marked

Abbreviations: BP, blood pressure; CVD, cardiovascular disease; CXR, chest x-ray; HR, heart rate; JVP, jugular venous pressure; OSA, obstructive sleep apnea; RR, respiratory rate.

*If unclear, any combination of factors in the yellow column that add up to 4 or more should prompt further evaluation.

†Data in this column from Afshan B. Hameed, Christine H. Morton, and Allana Moore. Improving Health Care Response to Cardiovascular Disease in Pregnancy and Postpartum. Developed under contract #11-10006 with the California Department of Public Health, Maternal, Child and Adolescent Health Division. Published by the California Department of Public Health, 2017. Available at https://www.cmqcc.org/resources-toolkits/toolkits/improving-health-care-response-cardiovascular-disease-pregnancy-and.

‡History of CVD or signs and symptoms in the red column should lead to urgent evaluation by the Pregnancy Heart Team.

§Should raise concern about heart failure and should promptly be evaluated.

Modified from Thorne S. Pregnancy and native heart valve disease. Heart 2016;102:1410–7.

Table 3. Modified World Health Organization Pregnancy Risk Classification for Women With Preexisting Cardiovascular Disease

Modified WHO Pregnancy Risk Classification (Risk of Pregnancy by medical condition) Suggested follow-up	Specific Cardiac Lesions	Pregnancy Care Delivery Location

mWHO Risk Class I
No detectable increased risk of maternal mortality and no or mild increase in morbidity
(2–5% risk of maternal cardiac event rate)
Follow-up: Cardiology evaluation once or twice during pregnancy
	• Uncomplicated, small, or mild
	  ○ Pulmonary stenosis
	  ○ Patient ductus arteriosus
	  ○ Mitral valve prolapse
	• Successfully repaired simple lesions (atrial or ventricular septal defect, patent ductus arteriosus, anomalous pulmonary venous drainage)
	• Atrial or ventricular ectopic beats, isolated
		• Prepregnancy/pregnancy counseling
		• Care at local hospital
		• Delivery at local hospital*

mWHO Risk Class II Small increased risk of maternal mortality or moderate increase in morbidity (6–10% maternal cardiac event rate) Follow-up: Cardiology, every trimester	• Unoperated atrial or ventricular septal defect • Repaired Tetralogy of Fallot or aortic coarctation • Most arrhythmias (supraventricular arrhythmias) • Turner syndrome without congenital cardiac disease	• Prepregnancy/pregnancy counseling • Pregnancy Heart Team* consultation/ counseling • Care at local hospital • Delivery at local hospital*
mWHO Risk Classes II and III Intermediate increased risk of maternal mortality or moderate to severe increase in morbidity (11–19% maternal cardiac event rate) Follow-up: Cardiology, every trimester	• Mild left ventricular impairment (EF >45%) • Hypertrophic cardiomyopathy • Native or bioprosthetic valve disease not considered mWHO Risk Class I or IV (mild mitral stenosis, moderate aortic stenosis) • Marfan or other HTAD syndrome without aortic dilation • Aorta <45 mm in bicuspid aortic valve pathology • Repaired coarctation without residua (non-Turner) • Atrioventricular septal defect	• Prepregnancy/pregnancy counseling • Pregnancy heart team* consultation/ counseling • Care at an appropriate level hospital (critical members of the Pregnancy Heart Team* available depending on cardiac disease) • Delivery at an appropriate level hospital*†
Pre-mWHO Risk Class III Significantly increased risk of maternal mortality or severe morbidity (20–27% maternal cardiac event rate) Follow-up: Cardiology, every 1–2 months	• Moderate left ventricular impairment (EF 30–45%) • Previous peripartum cardiomyopathy without any residual left ventricular impairment • Mechanical valve • Systemic right ventricle with good or mildly decreased ventricular function • Uncomplicated Fontan circulation, • Unrepaired cyanotic heart disease • Other complex heart disease • Moderate mitral stenosis • Severe asymptomatic aortic stenosis • Moderate aortic dilation (40–45 mm in Marfan syndrome or other HTAD; 45–50 mm in bicuspid aortic valve; Turner syndrome ASI 20–25 mm/m^2; Tetralogy of Fallot <50 mm) • Ventricular tachycardia	• Prepregnancy/pregnancy counseling • Pregnancy Heart Team* consultation/ counseling • Care at an appropriate level hospital† • Delivery at an appropriate level hospital*†

(*continued*)

Table 3. Modified World Health Organization Pregnancy Risk Classification for Women With Preexisting Cardiovascular Disease (*continued*)

Modified WHO Pregnancy Risk Classification (Risk of Pregnancy by medical condition) Suggested follow-up	Specific Cardiac Lesions	Pregnancy Care Delivery Location
mWHO Risk Class IV Pregnancy contraindicated Discuss induced abortion Extremely high risk of maternal mortality or severe morbidity (>27% maternal cardiac event rate) Follow-up: Cardiology follow-up every month (minimum)	▪ Pulmonary arterial hypertension ▪ Severe systemic ventricular dysfunction (EF <30%, NYHA III-IV) ▪ Previous peripartum cardiomyopathy with any residual left ventricular dysfunction ▪ Severe mitral stenosis ▪ Severe symptomatic aortic stenosis ▪ Systemic right ventricle with moderate to severely decreased ventricular function ▪ Severe aortic dilation (>45 mm in Marfan syndrome or other HTAD; >50 mm in bicuspid aortic valve; Turner syndrome ASI >25 mm/m^2; Tetralogy of Fallot >50 mm) ▪ Vascular Ehlers-Danlos ▪ Severe (re)coarctation ▪ Fontan circulation with any complication	▪ Pregnancy Heart Team* consultation/ counseling ▪ Care at an appropriate level hospital† (critical members of the Pregnancy Heart Team* available depending on cardiac disease) ▪ Delivery at an appropriate level hospital*‡

Abbreviations: ASI, aortic size index; EF, ejection fraction; HTAD, hereditary thoracic aortic disease; mWHO, modified World Health Organization; NYHA, New York Heart Association.

*Pregnant women with a positive cardiac history or findings, or both, should receive prenatal, intrapartum, and postpartum care in a hospital setting that represents an appropriate maternal level of care that is at Level II or higher depending upon the specific cardiac lesion(s) that are present. "The goal of regionalized maternal care is for pregnant women at high risk to receive care in facilities that are prepared to provide the required level of specialized care, thereby reducing maternal morbidity and mortality in the United States." (Levels of maternal care. Obstetric Care Consensus No. 2. American College of Obstetricians and Gynecologists. Obstet Gynecol 2015;125:502–15).

†**mWHO Risk Class III.** Critical members of the Pregnancy Heart Team available depending on cardiac disease. For example: A mechanical valve patient requires care at a center with cardiologist/maternal–fetal medicine team who monitor and adjust anticoagulation weekly, delivery at a center with obstetric anesthesia, and advance cardiac care options including access to emergency cardiac surgery should acute prosthetic valve thrombosis necessitate emergency intervention.

‡**mWHO Risk Class IV.** For example, a severe pulmonary hypertension patient requires care and delivery at a center with maternal–fetal medicine, obstetric and cardiac anesthesia, a pulmonary hypertension specialist, and advanced heart failure care options, such as ventricular assist device and extracorporeal membrane oxygenator management.

Adapted from Thorne S, MacGregor A, Nelson-Piercy C. Risks of contraception and pregnancy in heart disease. Heart 2006;92:1520–5).

identify cardiac conditions associated with significantly increased maternal mortality or severe morbidity. Pregnancy is not recommended for women in modified World Health Organization (WHO) pregnancy risk category IV (Table 3) (51–53). Discussion of cardiovascular disease with the woman should include the possibilities that 1) pregnancy can contribute to a decline in cardiac status that may not return to baseline after the pregnancy; 2) maternal morbidity or mortality is possible; and 3) fetal risk of congenital heart or genetic conditions, fetal growth restriction, preterm birth, intrauterine fetal demise, and perinatal mortality is higher when compared with risk when cardiovascular disease is not present (54–56).

Approximately one third of cardiac patients will require medication during pregnancy (57), and special emphasis should be placed on agents to be avoided, and when feasible, switching to safer alternatives before pregnancy (see Table 5). Certain medications, such as angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and aldosterone antagonists should be avoided if possible because of the risk of potential fetal adverse effects (58). However, there may be cardiac conditions that are controlled only by medications or interventions that have potential teratogenic effects that must be used during pregnancy despite known risk to the fetus, such as warfarin in a patient with a mechanical valve prosthesis (57). In these circumstances, the

Table 4. The Pregnancy Heart Team

	Modified WHO Pregnancy Risk Classification I	Modified WHO Pregnancy Risk Classification II	Modified WHO Pregnancy Risk Classifications III and IV
Pregnancy Heart Team Members	Obstetrician, family medicine practitioner, internist	Obstetrician, family medicine practitioner, internist	Obstetrician, family medicine practitioner, maternal–fetal medicine subspecialist, internist, obstetric anesthesiologist, cardiology subspecialists in adult congenital/aortopathy*, heart rhythm*, heart failure*, pulmonary hypertension*, and cardiac imaging*
		Maternal–fetal medicine subspecialist	
	Cardiologist consultation	Cardiologist consultation	Interventional cardiologist*
			Cardiac surgeon*
			Neonatologist*
			Geneticist*
			Mental health specialist*
			Pharmacist*

Abbreviation: WHO, World Health Organization.

*Ad Hoc members of a Pregnancy Heart Team

specialists who constitute the Pregnancy Heart Team (Table 4) should review the risks, benefits, and alternative therapeutic options with the patient and document in the medical record a summary of what is discussed and recommended. Patients should be encouraged not to stop any medications until they have reviewed management options with their care team.

Although the goal of prepregnancy counseling is to identify and modify risks to improve pregnancy outcome, the individual's choices will be conditional upon her values and preferences, and patient autonomy must be ensured. A collaborative discussion with shared decision making should take place between the Pregnancy Heart Team (Table 4), the patient, and her family. A personalized approach estimating the maternal and fetal hazards related to the patient's specific cardiac disorder and the patient's pregnancy plans can provide anticipatory guidance to help support her decision making. For some patients, the prepregnancy evaluation may suggest a pregnancy risk that is unacceptable (Table 3). For those women, reproductive alternatives, such as surrogacy or adoption, and effective contraceptive methods should be discussed (58).

▶ ***Why is risk assessment indicated, what types are recommended, and which patients should be referred to centers with a high level of care?***

A key area of competence and expertise for obstetric care providers is the ability to differentiate between common symptoms of pregnancy and those suggestive of cardiovascular disease. Maternal mortality reviews indicate that most women who die from cardiovascular disease had either undiagnosed cardiovascular disease or new-onset cardiovascular disease of pregnancy, specifically peripartum cardiomyopathy. Therefore, all women should be assessed for cardiovascular disease in the antepartum and postpartum periods using the California Improving Health Care Response to Cardiovascular Disease in Pregnancy and Postpartum toolkit algorithm (Fig. 1). Use of this algorithm could have identified individuals as high risk requiring further cardiac evaluation and referral in 88% of maternal deaths (50). Patients with concerning symptoms or signs of cardiovascular disease should undergo consultation with a Pregnancy Heart Team (Table 4).

Risk Assessment of the Pregnant or Postpartum Patient With Known Cardiovascular Disease

Risk assessment can be accomplished using one of the several available risk stratification models, such as the Canadian Cardiac Disease in Pregnancy risk index (CARPREG II) (a comprehensive scoring system that incorporates general cardiac factors, specific cardiac lesions, and process of care factors), the Zwangerschap bij Aangeboren HARtAfwijkingen (ZAHARA) (a weighted risk score for congenital heart disease patients), and the modified World Health Organization (WHO) classification of maternal cardiovascular risk (54–56, 59). Among these, the modified WHO

Table 5. Cardiac Medications With Potential Pregnancy and Lactation Influence

Drug	Teratogenic	Fetal Effects	Breastfeeding
Inotropic Agents			
Dopamine	No	No adverse fetal effects	Probably compatible, may inhibit prolactin release
Dobutamine	No	No adverse fetal effects	Probably compatible
Epinephrine	No	No adverse fetal effects when used acutely	Probably compatible
Vasodilators			
Nitroprusside	No	Potential for fetal cyanide toxicity with high doses	Possibly hazardous
Hydralazine	No	Relatively safe for the fetus	Probably compatible
Nitroglycerin	No	No adverse fetal effects Observe for risks of methemoglobinemia	Possibly hazardous
Ephedrine sulfate	No	No adverse fetal effects when used acutely	Possibly hazardous with chronic use
Angiotensin Converting Enzyme Inhibitors and Angiotensin Receptor Blockers			
	Yes	Contraindicated Associated with fetal renal failure, growth restriction, malformations and death	Probably compatible No published information
Beta-blockers			
Propranolol	No	May increase risk of growth restriction	Probably compatible
Labetalol	No	No adverse fetal effects	Probably compatible
Atenolol	No	May increase risk of growth restriction	Probably compatible Limited information
Metoprolol	No	May increase risk of growth restriction	Probably compatible
Esmolol	No	May cause beta blockage in fetus	Probably compatible No published information
Carvedilol	Limited Information	May increase risk of growth restriction	Probably compatible No published information
Calcium Channel Blockers			
Verapamil	No	No adverse fetal effects	Probably compatible
Nifedipine	No	No adverse fetal effects	Probably compatible
Diltiazem	No	No adverse fetal effects	Probably compatible Limited information
Amlodipine	No	No adverse fetal effects Limited human information, animal data suggest risk	Probably compatible Limited information
Antiarrhythmic Agents			
Lidocaine	No	No adverse fetal effects	Probably compatible
Procainamide	No Limited human information	Limited human information	Probably compatible Limited information
Phenytoin	Yes	Potential for early hemorrhagic disease of the newborn	Probably compatible

(*continued*)

Table 5. Cardiac Medications With Potential Pregnancy and Lactation Influence (*continued*)

Drug	Teratogenic	Fetal Effects	Breastfeeding
Amiodarone	No	May be associated with fetal thyroid toxicity	Hazardous
Flecainide	Yes	Limited human information	Probably compatible
	Limited human information		Limited information
Sotalol	No	Human data suggest fetal risk	Possibly hazardous
	Limited human information		
AV Node Blocking Agents			
Adenosine	No Information	No adverse fetal effects	Probably compatible
			No published information
Digoxin	No	No adverse fetal effects	Probably Compatible
Anticoagulants and Anti-Thrombotics			
Warfarin	Yes	Risk of fetal hemorrhage	Probably compatible
Low-molecular-weight heparin	No	No adverse fetal effects	Probably compatible
		Does not cross placenta	
Unfractionated heparin	No	No adverse fetal effects	Probably compatible
		Does not cross placenta	
Clopidogrel	No	Limited human information	Probably compatible
	Limited human information		No published information
Direct Factor Xa Inhibitors (rivaroxaban or apixaban)			
	No	Product labeling warns about abnormal bleeding risk	Possibly hazardous
		Crosses placenta	No published information
Diuretics			
Hydrochlorothiazide	No	No adverse fetal effects	Probably compatible
Furosemide	No	No adverse fetal effects	Probably compatible
			No published information

* For additional information on an individual medication's risk with breastfeeding, see https://toxnet.nlm.nih.gov/lactmed.htm.

Data from Hale TW. Hale's medications and mothers' milk: a manual of lactational pharmacology. 18th ed. New York (NY): Springer; 2019 and Briggs GG, Freeman RK, Towers CV, Forinash AB. Drugs in pregnancy and lactation. 11th ed. Philadelphia (PA): Wolters Kluwer; 2017.

risk assessment model is most widely accepted and validated in pregnant women with known cardiovascular disease (Table 3). The modified WHO pregnancy risk classification stratifies cardiovascular disease into 5 groups and informs the health care provider of the frequency of cardiology evaluation recommended. All pregnant and postpartum women with known or suspected cardiovascular disease should proceed with further evaluation by a Pregnancy Heart Team (Table 4) consisting of a cardiologist and maternal–fetal medicine subspecialist, or both, and other subspecialists as necessary. The goal is to establish a multidisciplinary comprehensive plan of care for the pregnancy, delivery, and postpartum periods. A mechanism for local, regional, and high-level facility referral should be in place for all labor and delivery units, particularly those with limited resources, in the event the need for consultation or emergency transfer arises. Referral to a hospital setting that represents an appropriate maternal level of care dependent upon the specific cardiac lesion (Table 3) is recommended for all pregnant patients with moderate- to high-risk cardiac conditions (modified WHO risk classes III and IV) because outcomes are

significantly better for women in these facilities (8, 60). Complex congenital heart disease patients should be managed, to the extent possible, at advanced care centers with congenital heart disease expertise.

▶ ***What are the indicated tests and how should these tests be interpreted for the pregnant patient with possible heart disease?***

Testing of maternal cardiac status is warranted during pregnancy or postpartum in women who present with symptoms such as shortness of breath, chest pain, or palpitations and known cardiovascular disease whether symptomatic or asymptomatic, or both. Factors linked to cardiovascular disease, such as family history and underlying medical conditions, play an important role in assessing the risk of cardiovascular disease (Fig. 1). The type of testing and urgency of evaluation depends on the underlying cardiac condition and symptoms at the time of presentation (Table 2; Fig. 1).

Natriuretic Peptides

Brain natriuretic peptide (BNP) and N-terminal pro-brain natriuretic peptide (NT-proBNP) are natriuretic peptides (referred to collectively as BNP in this document). Elevated levels can be suggestive of heart failure. Although BNP reference ranges vary among laboratories, assays, age, gender, and BMI, in general a BNP level of greater than 100 pg/mL and an NT-proBNP level greater than 450 pg/mL suggest the diagnosis of heart failure in nonpregnant patients (61). Brain natriuretic peptide levels in healthy women increase twofold during pregnancy (62) with a further increase early after delivery, (63) but values remain within normal range. Levels of BNP increase significantly in pregnant women with shortness of breath related to heart failure from left ventricular systolic dysfunction, (64) diastolic dysfunction, (65) and hypertensive disorders, including preeclampsia. (66)

Natriuretic peptides should be measured in the presence of new clinical symptoms or suggestive signs of heart failure to prevent delayed diagnosis. It may be helpful to obtain a baseline BNP level during pregnancy in women at high risk of or with known heart disease, such as dilated cardiomyopathy and congenital heart disease (Fig. 1). Serial determinations of BNP levels throughout each trimester and in the early postpartum period may assist in clinical decision making. Normal or low BNP levels are useful in excluding cardiac decompensation during pregnancy (67–69), and increasing BNP levels from the second trimester of pregnancy appear to predict adverse events (67, 70).

Cardiac Troponin I, Troponin T, and "High-Sensitivity" Troponin

Cardiac troponin I, troponin T, and "high-sensitivity" troponin are specific and sensitive biomarkers of myocardial injury (71). The diagnosis of acute coronary syndrome associated with pregnancy is similar to that in the general adult population, including comparable symptoms, electrocardiogram abnormalities, and elevations in biomarkers such as troponin (72). All pregnant and postpartum patients with chest pain should undergo standard troponin testing and an electrocardiogram to evaluate for acute coronary syndrome. Cardiology consultation should be obtained as clinically indicated. It should be noted that troponin I may be mildly elevated in the early postpartum period (73) in women with preeclampsia with severe features and in other noncardiac conditions, such as acute pulmonary embolisms or chronic renal disease (74).

Electrocardiogram

An electrocardiogram should be performed in pregnant women presenting with chest pain, shortness of breath, or palpitations to assess for features of ischemia, infarction, or arrhythmias. Normal pregnancy-related physiologic changes in maternal heart rate and chest wall shape cause benign nonpathologic electrocardiogram changes (75). Nonspecific ST-wave and T-wave abnormalities are found in up to 14% of pregnancies, usually occur in the left precordial leads, resolve after delivery, and may recur with subsequent pregnancies. Any rhythm abnormalities noted on electrocardiogram should prompt further evaluation.

Chest Radiograph

A chest radiograph with abdominal shield (76) should be considered as an important early test in pregnant or postpartum women presenting with shortness of breath to evaluate cardiac or pulmonary etiology.

Echocardiogram

An echocardiogram should be performed in pregnant or postpartum women with known or suspected congenital heart disease (including presumed corrected cardiac malformations), valvular and aortic disease, cardiomyopathies, and those with a history of exposure to cardiotoxic chemotherapy (eg, doxorubicin hydrochloride). Women with pulmonary hypertension or unexplained oxygen desaturation should have an echocardiogram before pregnancy, when pregnancy is confirmed, and during and after pregnancy. If there is doubt about the etiology as well as presence and severity of pulmonary hypertension, cardiac catheterization should be performed (52). The frequency of clinical and echocardiographic follow-up during pregnancy and postpartum is individualized. Cardiac chamber enlargement,

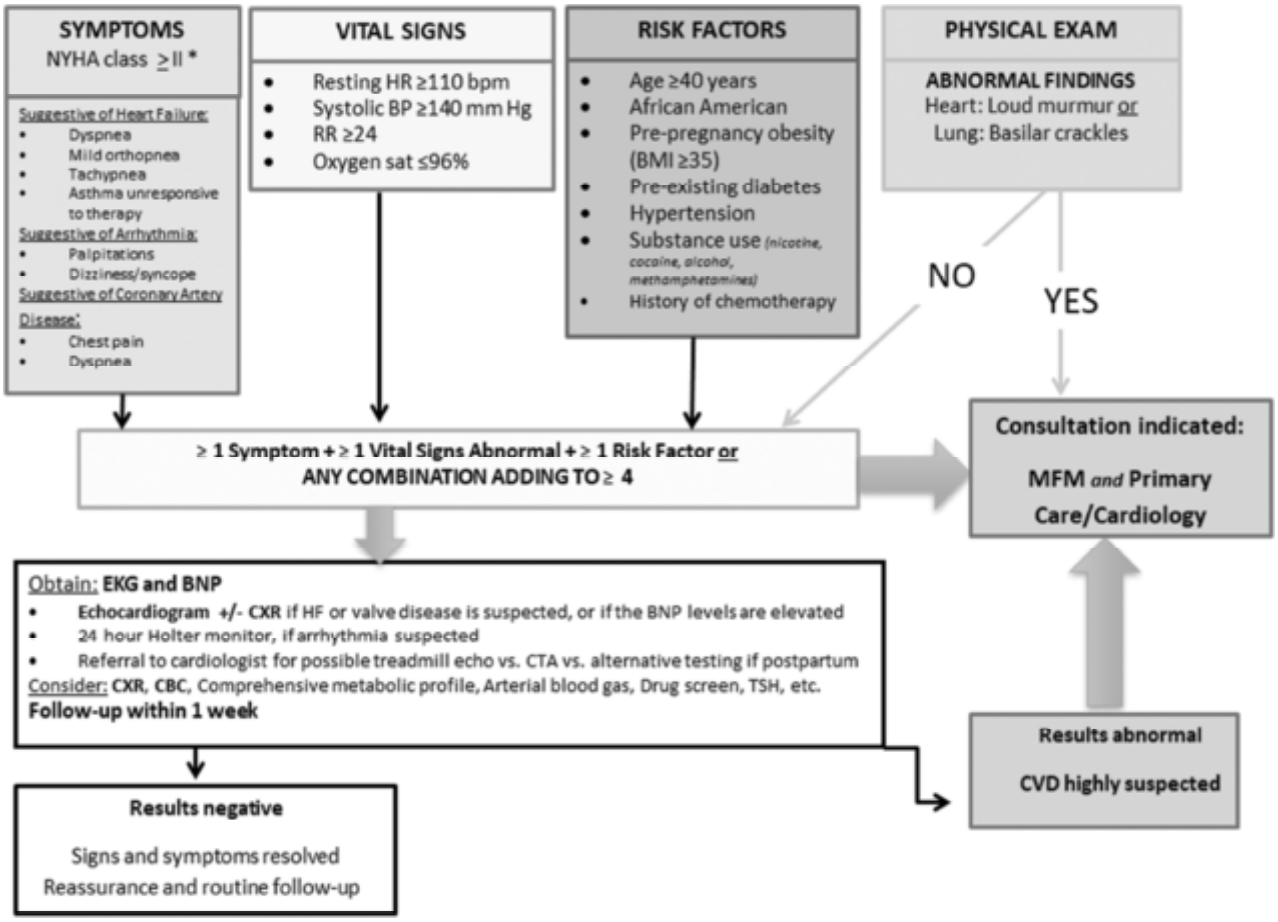

Figure 1. Cardiovascular Disease Assessment in Pregnant and Postpartum Women. *The NYHA Functional Classification is available at http://www.heart.org/HEARTORG/Conditions/HeartFailure/AboutHeartFailure/Classes-of-Heart-Failure_UCM_306328_Article.jsp. Abbreviations: BMI, body mass index; BNP, brain natriuretic peptide; BP, blood pressure; CBC, complete blood count; CVD, cardiovascular disease; CXR, chest x-ray; EKG, electrocardiogram; HR, heart rate; MFM, maternal–fetal medicine; TSH, thyroid stimulating hormone; NYHA, New York Heart Association; RR, respiratory rate. (Modified from California Department of Public Health, 2017; supported by Title V funds. Developed in partnership with California Maternal Quality Care Collaborative Cardiovascular Disease in Pregnancy and Postpartum Taskforce. Visit www.CMQCC.org for details.)

concentric cardiac remodeling, diastolic dysfunction, valvular annular dilatation with regurgitation, and small asymptomatic pericardial effusion are frequent normal echocardiogram findings during late gestation. (41, 77–79)

Exercise Stress Test

An exercise stress test is an important predictor of a woman's ability to tolerate pregnancy. An exercise stress test provides an objective assessment of maternal functional capacity and facilitates the identification of exercise-induced arrhythmias (52). An exercise stress test should be performed in patients with known heart disease who plan pregnancy (80). International guidelines recommend submaximal exercise testing (80% of predicted maximal heart rate) in asymptomatic patients with suspected heart disease if already pregnant (80).

Computed Tomography

Computed tomography should be performed in pregnant or postpartum women presenting with chest pain when pulmonary embolism or acute aortic dissection is suspected. Iodinated contrast materials are not teratogenic or carcinogenic but cross the placenta and can produce transient depressive effects on the developing fetal thyroid gland. It is recommended that contrast agents be used only when absolutely required to obtain additional diagnostic information that will affect care. Less than 1% of iodinated contrast administered to a lactating woman is excreted into breast milk and absorbed through the infant's gastrointestinal tract. Therefore, breastfeeding can be continued without interruption after administration of iodinated contrast (81).

Magnetic Resonance Imaging

Magnetic resonance imaging is used rarely in the urgent or emergent evaluation of cardiovascular concerns during pregnancy because imaging is less available and is more time consuming than computerized tomography. However, it is the preferred imaging modality in pregnant women to assess aortic dimension and for assessment of ventricular function and wall motion when echocardiography is nondiagnostic. When elective cross-sectional imaging is needed during pregnancy, a discussion with a cardiac imaging specialist to assist with choosing the most appropriate study and protocol is recommended to evaluate the patient optimally. There are no reported adverse maternal or fetal effects from magnetic resonance imaging during pregnancy (82). Reference values for cardiac magnetic resonance imaging indices during normal pregnancy and the postpartum state have been reported (40). Gadolinium, the contrast agent used for magnetic resonance imaging, should be limited in pregnant patients. It may be used as a contrast agent only if it significantly improves diagnostic performance and is expected to improve fetal or maternal outcome. Breastfeeding should not be interrupted after gadolinium contrast is administered (81).

Holter Monitor or Prolonged Cardiac Monitoring Device

A Holter monitor (24-hour to 48-hour ambulatory electrocardiogram monitoring) or a prolonged cardiac monitoring device (such as wireless patch cardiac monitor) is helpful for assessing symptoms of palpitations, lightheadedness, and syncope during pregnancy (83).

D-dimer

D-dimer is not recommended as part of routine evaluation of cardiac disease in pregnancy or the postpartum period (44).

▶ *Which types of preexisting maternal cardiac disease have the greatest effect on pregnancy and the postpartum period?*

Evidence of underlying or overt cardiovascular disease can present initially either during pregnancy or in the first days, weeks, and months postpartum. Women with any high-risk cardiovascular disease, such as pulmonary hypertension, congenital heart disease, noncongenital valvular disease, dilated hypertrophic or peripartum cardiomyopathy, aortic disorders, or coronary artery disease should be monitored during pregnancy and the postpartum period by a cardiologist with expertise in the management of such patients or a Pregnancy Heart Team (Table 4) if institutionally available. A plan for management during pregnancy, labor, and postpartum should be decided and recorded in the medical and prenatal records.

Pulmonary Arterial Hypertension

Pulmonary arterial hypertension is defined as a mean pulmonary arterial pressure more than 25 mm Hg at rest. It can be either idiopathic or caused by various disorders. Pulmonary arterial hypertension carries an increased risk of maternal mortality, reported to range from 9% to 28% (84–86). Despite improved prognosis in women with pulmonary arterial hypertension, low-risk patients might not be identified easily. Therefore, all women with severe pulmonary arterial hypertension should be advised against pregnancy. Health professionals caring for women with pulmonary arterial hypertension should ensure that women who are at risk of pregnancy understand these hazards and receive effective contraception. Induced abortion should be discussed if pregnancy occurs (80, 87). If a woman with severe pulmonary hypertension elects to proceed with or continue pregnancy, medical therapy for pulmonary hypertension can be initiated or modified during pregnancy (Table 5).

Congenital Heart Disease

Congenital heart disease encompasses multiple cardiac structural lesions. Many patients with congenital heart disease require additional specialized care while pregnant. Regular follow-up is required, the frequency of which depends on the type of the disease and the patient response to pregnancy (Table 3). Patients with high-risk lesions, such as those associated with pulmonary hypertension (eg, Eisenmenger syndrome), severe left-sided heart obstruction, severe ventricular dysfunction, cyanosis, failing Fontan circulation, and lesions associated with complex arrhythmias are counseled to avoid pregnancy or to proceed with surgical correction before pregnancy to allow for a lower-risk future pregnancy. The implications of maternal congenital heart disease on the fetus, including potential inheritance, should be discussed. In addition, certain genetic disorders are associated with congenital heart disease (eg, Noonan syndrome, Down syndrome, Holt-Oram syndrome, 22q11 microdeletion) and, therefore, prepregnancy genetic consultation and testing is recommended. Congenital heart disease in the woman should prompt fetal echocardiography, and conversely, identification of congenital heart disease in a fetus or neonate may prompt screening for parental congenital heart disease.

Noncongenital Valvular Disease

Noncongenital valvular disease, (examples include rheumatic valvular disease, mitral valve prolapse, bioprosthetic valve prosthesis, or valve disease related to infective endocarditis), requires specialized evaluation. A transthoracic echocardiogram and an exercise stress test generally are recommended for patients with moderate-to-severe valve disease (such as valve stenosis or severe regurgitation), associated ventricular dysfunction, or pulmonary hypertension. Women with asymptomatic valve disease should be monitored by a cardiologist and may require additional testing or care during pregnancy. The frequency of monitoring necessary is indicated in the patient's modified WHO classification (Table 3). Ideally, symptomatic severe valve disease should be treated before pregnancy.

Mechanical Valve Prostheses

During pregnancy, mechanical valve prostheses and some cardiac lesions require therapeutic anticoagulation, which carries an increased risk for the woman and fetus. A detailed discussion about anticoagulation options and risks, frequency, and type of monitoring is best performed and documented before pregnancy. Regular monitoring and medication adjustment to confirm therapeutic levels is required (80, 88, 89). All pregnant patients with mechanical and bioprosthetic valves should be maintained on daily low-dose (81 mg) aspirin during pregnancy (90). Endocarditis prophylaxis should be administered around the time of delivery in high-risk patients (see "Intrapartum Management Principles") (88, 91).

Preexisting Dilated Cardiomyopathy

Prepregnancy assessment will include a baseline BNP level, transthoracic echocardiogram to assess ejection fraction, and hemodynamics, as well as an exercise stress test to assess functional capacity. The cause of the cardiomyopathy should be evaluated. Prepregnancy genetic consultation is recommended for patients with familial dilated cardiomyopathy. Cardiomyopathy related to prior unrecognized peripartum cardiomyopathy also should be considered. Women with preexisting dilated cardiomyopathy have a high rate (25–40%) of major adverse cardiovascular events, mainly heart failure, during pregnancy (92, 93). Patients should be counseled to avoid pregnancy or consider induced abortion if they have severe heart disease, including an ejection fraction less than 30% or class III/IV heart failure, severe valvular stenosis, Marfan syndrome with aortic diameter more than 45 mm, bicuspid aortic valve with aortic diameter more than 50 mm, or pulmonary arterial hypertension (Table 3) (80). Furthermore, women with ejection fractions between 30% and 45% also should be counseled regarding an increased risk of adverse cardiac events during pregnancy, such as heart failure or arrhythmia (94). Once pregnancy occurs, medication changes (Table 5) and follow-up frequency are dependent on cardiac and functional status.

Hypertrophic Cardiomyopathy

Hypertrophic cardiomyopathy is the most common genetic cardiac disease, with a prevalence of 2%. An analysis of pregnancy outcomes in such patients reported that cardiovascular complications are common and can be predicted by prepregnancy status, facilitating prepregnancy counseling and targeted antenatal care (95). Prepregnancy cardiovascular and genetic consultations are recommended for patients with hypertrophic cardiomyopathy.

Aortic Aneurysmal Disease and Dissection

Aortic aneurysmal disease and dissection in women of childbearing age generally are triggered genetically and are familial, syndromic, congenital, or inflammatory. Before pregnancy, a thorough cardiovascular specialty consultation to assess the cause, size, and location of the aneurysm is recommended. This consultation should include imaging with echocardiography and either computerized tomography or magnetic resonance imaging to evaluate the entire aorta. Although most dissections in young patients occur in the ascending aorta, the descending thoracic or abdominal aorta also can be affected. The cause, location, and size of the aortic aneurysm will influence counseling before and management during pregnancy. For example, all patients with vascular Ehlers-Danlos syndrome are advised to avoid pregnancy. The risk of aortic dissection associated with these conditions is increased during pregnancy and postpartum because of hormonal and hemodynamic changes on the aorta. No aortic dimension guarantees a safe pregnancy in a patient with aortopathy. The aortic size threshold for intervention before pregnancy depends on the cause of aortic aneurysmal disease (Table 6) (6, 80, 96). Even after ascending aorta replacement, aortic dissection can affect the remaining native aorta, so patients with prior operative intervention also should be monitored closely. During pregnancy, patients with aortic aneurysmal disease often are treated with beta-blocker therapy and should be seen regularly with repeat aortic imaging. The frequency of follow-up and imaging depends on the underlying disorder and aortic aneurysm location and dimension (Table 6). Surgical or percutaneous intervention for aortic aneurysm or dissection during

pregnancy or postpartum rarely is needed and should occur only for an aortic emergency. Type and timing of invasive maternal interventions and the preferred mode of delivery should be made by the Pregnancy Heart Team (Table 4).

Atrial Arrhythmias

Atrial arrhythmias that cause palpitations are a common indication for cardiac evaluation during pregnancy. Any pregnant woman who presents with an arrhythmia should undergo evaluation to assess the cause and the possibility of underlying structural heart disease. The most common arrhythmias during pregnancy are premature atrial beats and paroxysmal supraventricular tachycardia, usually atrioventricular-nodal reentrant tachycardia that can be successfully treated with medication. Atrial fibrillation and flutter during pregnancy often occur in women with structural heart disease. Management is individualized depending on the effect of the arrhythmia and the presence of underlying cardiac disease (55).

Ventricular Arrhythmias

Ventricular arrhythmias are rarely encountered during pregnancy. If detected, a search for a cause and underlying structural heart disease is appropriate. The most common type of ventricular tachycardia that occurs in the absence of structural heart disease is right ventricular outflow tract ventricular tachycardia. This form of ventricular tachycardia initially may be identified during pregnancy because it is catecholamine sensitive, and it often can be treated successfully with beta-blockers or verapamil. Women with the long QT syndrome are at risk of ventricular tachycardia, especially in the postpartum period. Treatment with beta-blocker therapy throughout pregnancy and postpartum is appropriate. Acute treatment of sustained ventricular arrhythmias in pregnant women is similar to that in nonpregnant women. In women with structural heart disease and ventricular tachycardia, the risk versus benefit of antiarrhythmic drug therapy, an implantable cardioverter-defibrillator, and ablation should be reviewed with a Pregnancy Heart Team (Table 4) in conjunction with an electrophysiologist with expertise in managing patients with arrhythmias during pregnancy (80, 97).

▶ *How should women at high risk of peripartum cardiomyopathy be identified, assessed, and managed?*

Peripartum cardiomyopathy occurs in 25–100 per 100,000 live births in the United States (98). It is characterized as a nonischemic cardiomyopathy presenting late in pregnancy or the first few months postpartum (99, 100) with a decrease in the left ventricular ejection fraction to less than 45% and no previous history of

Table 6. Management Strategies in Pregnant Women With Aortopathy

Marfan Syndrome	Surveillance Frequency	Suggested Mode of Delivery
Normal-sized aorta	Each trimester	Vaginal
Dilated ascending aorta <40 mm	4–6 weeks	Vaginal
Ascending aorta 40–45 mm	4 weeks	Cesarean
Ascending aorta >45 mm	Prophylactic aortic surgery before or during pregnancy for rapid growth	Cesarean

Bicuspid Aortic Valve	Surveillance Frequency	Suggested Mode of Delivery
Ascending aorta <45 mm	4–6 weeks	Vaginal
Ascending aorta 45–50 mm	4 weeks	Cesarean
Ascending aorta >50 mm	Aortic surgery before or during pregnancy for rapid growth	Cesarean

Modified from Elkayam U, Goland S, Pieper PG, Silversides CK. High-risk cardiac disease in pregnancy: part II. J Am Coll Cardiol 2016;68:502–16.

cardiac disease. The etiology remains uncertain. Although an autoimmune pathogenesis has been postulated (101), recent work has focused on vascular (102) and genetic etiologies (103).

Most women eventually recover myocardial function. For the remainder, chronic cardiomyopathy and heart failure persist. The overall rate of death or cardiac transplantation for women presenting with peripartum cardiomyopathy is 5–10% by 1 year postpartum (104, 105). Peripartum cardiomyopathy disproportionately affects non-Hispanic black women as evidenced by an increased incidence (106) and a lower rate of complete myocardial recovery (104, 107–110). Other risk factors for peripartum cardiomyopathy include increased maternal age, multifetal pregnancies, gestational hypertension, and preeclampsia. Women with a history of peripartum cardiomyopathy have a risk as high as 20% of experiencing a recurrence during subsequent pregnancies (111–113).

Pregnant or postpartum women who present with shortness of breath, chest discomfort, palpitations, arrhythmias, or fluid retention should be evaluated for peripartum cardiomyopathy. An echocardiogram is generally the most important diagnostic test. This evaluation also applies to women who are thought to have a hypertensive disorder of pregnancy. Consultation with a cardiologist is recommended to assist in management of peripartum cardiomyopathy, and referral to an appropriate level facility should be considered to allow multidisciplinary care by a Pregnancy Heart Team (Table 4). Medical management of peripartum cardiomyopathy follows the same general principles as management of heart failure with a reduced ejection fraction. Treatment with bromocriptine to improve myocardial recovery in peripartum cardiomyopathy remains investigational and requires further study (98, 114, 115). Breastfeeding should not be discouraged in women with peripartum cardiomyopathy because there are no data to suggest it negatively affects maternal cardiac status.

For women with peripartum cardiomyopathy who are pregnant at the time of peripartum cardiomyopathy diagnosis, timing and mode of delivery should be individualized, weighing the maternal risks of continuing pregnancy against the perinatal morbidity and mortality associated with preterm birth, and documented by a Pregnancy Heart Team (Table 4). Women presenting with shock (hypotension, tachycardia, or end-organ compromise) should be transferred to an appropriate level facility for consideration of a ventricular assist device support and transplant options. Vaginal delivery is a reasonable consideration for many women with peripartum cardiomyopathy because vaginal delivery results in less maternal morbidity and improved neonatal outcomes (116).

Predicted outcomes of women with peripartum cardiomyopathy can be stratified by the severity of left ventricular dysfunction at presentation because women with a lower left ventricular ejection fraction have poorer outcomes (117). In the North American Registry Investigations of Pregnancy-Associated Cardiomyopathy (104), women with an initial ejection fraction less than 30% had less myocardial recovery and higher rates of left ventricular assist device implantation, cardiac transplantation, and death. In contrast, nearly 90% of women with an initial ejection fraction of more than 30% had complete myocardial recovery.

▶ ***How should acute coronary events, including maternal cardiac arrest, be managed during pregnancy?***

Acute Myocardial Infarction and Acute Coronary Syndrome

Ischemic heart disease complicates 8 per 100,000 hospitalizations for pregnancy and postpartum care (118). Maternal death occurs in 5–11% of affected patients with the highest risk in the peripartum period, a rate that is 3–4 times more than that of nonpregnant age-matched women (17, 119).

Acute coronary syndrome implies suspicion of myocardial oxygen deprivation culminating in myocardial injury and necrosis. The spectrum of myocardial ischemia includes stable angina, unstable angina, and myocardial infarction. Increased cardiac output, enhanced stroke volume, and hypercoagulability favor the development or unmasking of underlying coronary artery disease. Risk factors for acute coronary syndrome during pregnancy (120) include traditional and pregnancy-specific features (see Box 1).

Box 1. Risk Factors for Acute Coronary Syndrome During Pregnancy

- Maternal age more than 30 years
- Non-Hispanic black race
- Elevated body mass index
- Diabetes mellitus
- Tobacco use
- Hyperlipidemia
- Strong family history of cardiovascular disease
- Hypertensive disorders of pregnancy
- History of coronary artery dissection
- Blood transfusion
- Peripartum infection

Acute coronary syndrome can be caused by coronary atherosclerosis, dissection, embolism, spasm, arteritis, and coronary artery occlusion related to aortic dissection. The differential diagnosis also should include takotsubo (stress) cardiomyopathy (119, 120). Coronary artery dissection is the most common cause of pregnancy-associated acute coronary syndrome and, although it can happen at any time during pregnancy, typically occurs in the early postpartum period (119, 121, 122). Coronary angiography remains the standard for diagnosis in patients with ST-segment elevation myocardial infarction. The noninvasive approach, however, is preferred in stable patients with preserved global left ventricular function because of the risk of complications, such as iatrogenic coronary dissection associated with coronary angiography and other interventions (119, 122, 123).

Every pregnant or postpartum patient with chest pain or cardiac symptoms should have consideration of acute coronary syndrome. Patients who have an acute coronary syndrome can present with typical (chest pain or shortness of breath) or atypical (vomiting, reflux, or diaphoresis) symptoms that mimic physiological changes of pregnancy or a pregnancy-related condition such as preeclampsia, or both. Some patients present with hemodynamic compromise, arrhythmia, or cardiogenic shock. Elevated troponins have sensitivity and specificity for myocardial damage. Electrocardiographic changes revealing ST-segment elevations or depression are pathological and suggest acute myocardial infarction or ischemia. The differential diagnosis includes pericarditis, pulmonary embolism, and electrolyte abnormalities.

Acute coronary syndrome during pregnancy is best managed by a medical team such as a Pregnancy Heart Team (Table 4). Management of the maternal condition should receive priority. While maternal evaluation and initial therapy are proceeding, an unstable patient should be placed in a left lateral tilt ranging from 30–90 degrees. Fetal monitoring and corticosteroids to enhance fetal lung maturation are recommended for appropriate gestational ages. Initial medical management usually includes oxygen supplementation, nitrates, aspirin, intravenous unfractionated heparin, and beta-blocker therapy. If symptoms persist, coronary angiography is the preferred test and should be performed without delay. The type of intervention should be individualized based on the etiology of acute coronary syndrome, patient characteristics, and facilities available at the presenting medical center. The goal is to restore coronary blood flow promptly to accomplish tissue reperfusion, which is best accomplished by percutaneous coronary intervention if the cause is atherosclerotic coronary disease. The results of percutaneous coronary intervention in women with coronary dissection are, however, suboptimal and associated with high risk of propagation of the existing dissection. For this reason, a conservative approach is recommended in stable patients with coronary artery dissection (123).

When a patient with acute myocardial infarction presents to a medical center that does not have interventional cardiac catheterization facilities, options include emergent transfer to a center that has these capabilities or emergent thrombolysis in patients with ST-elevation myocardial infarction, or both, with subsequent planned transfer. Complications of maternal acute coronary syndrome include heart failure, cardiogenic shock, ventricular arrhythmias, recurrent myocardial infarction, and death. Data regarding timing and mode of delivery are limited.

Maternal Cardiac Arrest

Although maternal cardiac arrest occurs infrequently, the health care provider should be prepared to manage this situation in any health care facility (124). Maternal cardiac arrest etiologies include pregnancy-related and nonpregnancy-related conditions. The American Heart Association recommends the use of an alphabetical categorization for the differential diagnosis of maternal cardiac arrest that underscores the importance of a broad-based approach (125) (see Box 2).

Among the various etiologies for maternal cardiac arrest in patients admitted for delivery, hemorrhage is the most common (38.1%), followed by amniotic fluid embolism (13.3%) (126). Approximately 10% of pregnant or postpartum women with acute coronary syndrome and 4% with venous thromboembolism experience a maternal cardiac arrest (126).

An obstetric care provider is among the members of a multidisciplinary team that should be assembled immediately with the announcement of a facility alert "maternal code" (125). A health care facility that deals with obstetric patients should have 24-hour access to an experienced maternal code team. Management of cardiac arrest in the pregnant or postpartum patient requires familiarity with the physiologic adaptations of pregnancy that affect the execution of interventions dictated by basic and advanced cardiac life support. There are six key concepts to emphasize for the pregnant cardiac arrest patient:

1. Increased oxygen demand coupled with alteration in pharyngeal/laryngeal landmarks and a greater tendency toward aspiration upon loss of consciousness necessitate prioritization of bag mask ventilation with 100 percent oxygen and early intubation with a small endotracheal tube by an experienced health care provider (6–7 mm) (125).

2. Aortocaval compression by a uterus larger than 20 weeks of gestation should be reduced with a one-handed or two-handed manual left uterine displacement maneuver very early in the resuscitation process while the patient remains in the full supine position on a backboard to maximize cardiac compression efforts (127, 128).
3. Simultaneous concurrent interventions are recommended in contrast to a sequential approach used in nonpregnant populations (128) (See Fig. 2).
4. Preparations for fetal delivery should be initiated in parallel with maternal resuscitative efforts.
5. Perform high-quality chest compressions on a backboard at a rate of 100–120 per minute using the same landmarks over the mid-lower sternum as left lateral uterine displacement is accomplished.
6. Oxygenation remains a primary goal using a ratio of 30:2 chest compressions/ventilation efforts initially supplied by bag mask ventilation with 100% oxygen.

Otherwise intervention is similar to management of cardiac arrest in the nonpregnant state. Defibrillation pads are placed to enable rhythm analysis. Use of an automated external defibrillator may facilitate rhythm analysis when rescuers are less acquainted with this task. Use of an automated external defibrillator, however, does not obviate the requirement for resuscitation skill training (128). Although there is only a theoretical risk of electrocution from defibrillation, fetal monitors should be removed to allow maternal status to guide resuscitation interventions. Prompt biphasic defibrillation should be performed for appropriate shockable rhythms with reassessment of rhythm/pulse every 2 minutes, taking care to minimize interruptions in chest compressions. Although there can be a reluctance to use medications during pregnancy, the gravity of maternal cardiac arrest is such that medications should be used in resuscitation. Epinephrine is the vasopressor of choice and should be administered by intravenous or intraosseous access above the diaphragm. A timekeeper should keep the resuscitation team aware of the time that has transpired since cardiac arrest (125).

Perimortem Cesarean Delivery/ Resuscitative Hysterotomy

When initial interventions are unsuccessful, the American Heart Association recommends timely consideration of perimortem cesarean delivery or resuscitative hysterotomy (129) when the uterus is sized 20 weeks of gestation or more. Because achieving the shortest time from cardiac arrest to delivery clearly enhances maternal and neonatal outcomes, efforts should be made to facilitate delivery as rapidly as possible from cardiac arrest, with the target to deliver within a 4–5-minute window. When return of spontaneous circulation is very unlikely, or arrest is unwitnessed, postponing delivery 4–5 minutes is not necessary (128, 130). Preparations to undertake resuscitative hysterotomy should begin immediately during the first minute of maternal cardiac arrest or apparent rapidly declining maternal cardiac function. Health care providers should be aware that there is no obvious threshold for either death or damage at 4 minutes. Instead there is a progressive decrease in the likelihood of injury-free survival for the woman and fetus with lengthening time since cardiac arrest (131). Survival curves for women and newborns have shown 50% injury-free survival rates with perimortem cesarean as late as 25 minutes after maternal cardiac arrest (131); therefore, delivery may be of benefit even if it does not occur within 4 minutes.

Box 2. Alphabetical Categorization for the Differential Diagnosis of Maternal Cardiac Arrest

- A (anesthetic complications, accidents)
- B (bleeding)
- C (cardiovascular disorders)
- D (drugs such as magnesium sulfate)
- E (embolism including venous thromboembolism and amniotic fluid embolism)
- F (fever including sepsis)
- G (general including metabolic and electrolyte)
- H (hypertensive disorders including stroke)

Ideally, perimortem cesarean delivery should occur at the site of the arrest because transport compromises cardiopulmonary resuscitation and also leads to further time delay (124). Initiation of perimortem cesarean delivery requires a scalpel, which usually is contained in the code cart's perimortem cesarean delivery kit (125). A vertical skin incision may be fastest to accomplish and provides more options for further exploratory surgery. If return of cardiac function has not occurred with perimortem cesarean delivery, alternatively open-chest direct cardiac massage can be attempted (128). Cardiopulmonary bypass and extracorporeal membrane oxygenation have been successfully employed for etiologies requiring time-limited cardiopulmonary support, such as local anesthetic drug toxicity, acute cardiac decompensation related peripartum cardiomyopathy, and acute respiratory distress syndrome (128).

The infrequency of maternal cardiac arrest underscores the need for regular team training and practice of

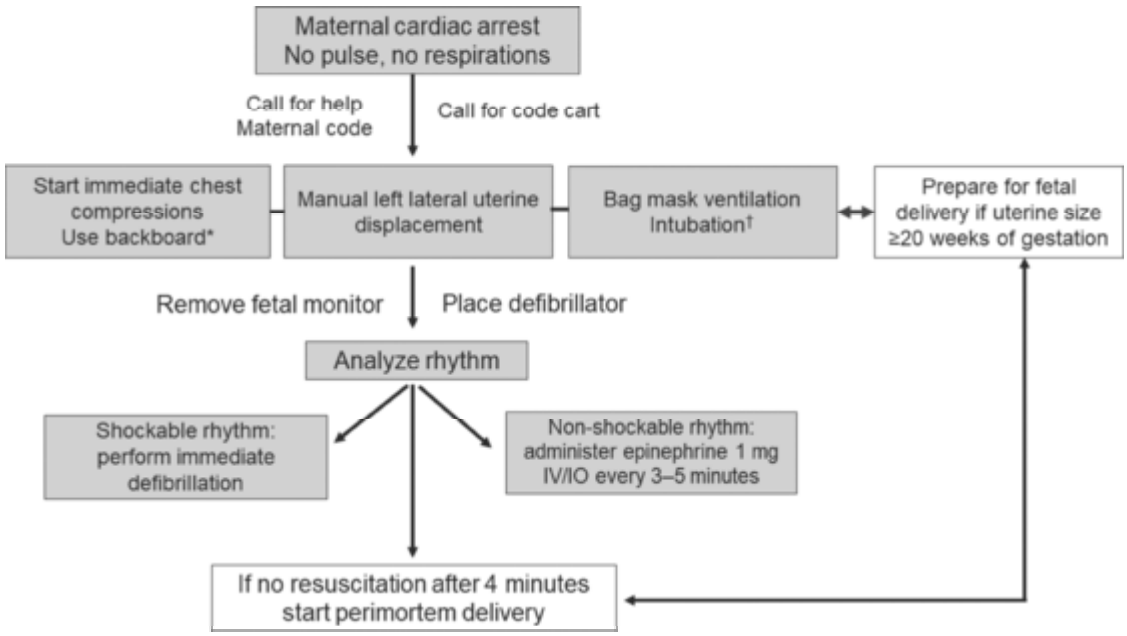

Figure 2. Maternal Resuscitation Algorithm. Abbreviations: IO, Intraosseous; IV, intravenous. *High-quality chest compressions on a backboard are performed at a rate of 100–120 per minute. †Prioritization of bag mask ventilation with 100 percent oxygen. Oxygenation remains a primary goal using a ratio of 30:2 (chest compressions/ventilation efforts). (Modified from Zelop CM, Einav S, Mhyre JM, Martin S. Cardiac arrest during pregnancy: ongoing clinical conundrum. Am J Obstet Gynecol 2018;219:52–61.)

resuscitation skills and scenarios through simulation training (128).

▶ ***What are the general approaches to pregnancy management antepartum, intrapartum, and postpartum for the patient with cardiovascular disease?***

Antepartum Management Principles

Pregnant women with cardiac disease should give birth at a hospital with the appropriate maternal level of care (60). The resources needed to minimize maternal and fetal complications should be anticipated, outlined, and documented before delivery. A comprehensive plan of care for the pregnancy, delivery, and postpartum periods should be available readily in the medical record and easily accessible to all health care providers involved with the woman's care. Women with complex congenital or noncongenital heart disease should be treated by a Pregnancy Heart Team (Table 4) (52, 80, 132) and should undergo comprehensive cardiac diagnostic evaluation as directed by the team and the diagnosis. In women with congenital heart disease, screening fetal echocardiogram is indicated at 18–22 weeks of gestation because the risk of congenital heart defect in the fetus is estimated at 4–10% (133, 134). Fetal growth assessment by either serial clinical examination or ultrasonography should be considered because fetal growth restriction occurs in many types of maternal congenital and acquired cardiac lesions (133, 135).

Women with chronic medical conditions, such as pregestational diabetes or chronic hypertension, can develop cardiac and other vascular complications of their disease (46, 47). Daily low-dose aspirin prophylaxis is recommended in women at high risk of preeclampsia and should be initiated between 12–28 weeks of gestation and continued until delivery. Similar prophylaxis should be considered for women with more than one of several moderate risk factors for preeclampsia (136). The precise blood pressure level at which antihypertensive therapy is indicated during pregnancy in women with cardiovascular disease continues to be debated. The use of blood pressure-lowering medications is recommended for secondary prevention of recurrent cardiovascular disease events in nonpregnant patients with clinical cardiovascular disease (defined as coronary heart disease, congestive heart failure, and stroke) and an average systolic blood pressure of 130 mm Hg or higher or an average diastolic blood pressure of 80 mm Hg or higher (137). Few clinical trials on this topic have been conducted in pregnancy and the evidence is limited (47). Prompt treatment of severe hypertension (systolic blood pressure more than 160 mm Hg and diastolic blood pressure more than

110 mm Hg) is recommended to prevent complications (47, 138). Left ventricular hypertrophy with impairment of diastolic function may develop in the setting of long-term hypertension. This scenario may place the pregnant woman at risk of cardiogenic pulmonary edema due to the baseline volume increase in pregnancy and after intravenous fluid boluses. Pulmonary edema in the patient with preeclampsia may be cardiogenic or noncardiogenic in origin or a combination of both. Echocardiography can help differentiate between the two entities. An echocardiogram should be performed in any pregnant or postpartum patient with pulmonary edema possibly due to peripartum cardiomyopathy or preeclampsia.

In general, regular physical activity during pregnancy and postpartum improves or maintains physical fitness, helps with weight management, reduces the risk of gestational diabetes in obese women, and enhances psychologic well-being. During pregnancy complicated by cardiac disease, the woman should be carefully evaluated by a Pregnancy Heart Team (Table 4) before recommendations are made regarding physical activity participation (139) to ensure that a patient does not have a cardiac reason to avoid exercise.

Intrapartum Management Principles

A detailed delivery plan should be determined between 20–30 weeks of gestation and recorded in the medical record. An individualized plan through shared decision making with the patient and the Pregnancy Heart Team (Table 4) is recommended. This strategy should include management of induction, delivery, and postpartum concerns and a surveillance plan. Women with stable cardiac disease can undergo a vaginal delivery at 39 weeks of gestation, with cesarean delivery reserved for obstetric indications (140). Some patients with very high-risk cardiac conditions may not be able to tolerate the fluctuations in cardiac output or Valsalva efforts that occur during vaginal delivery. For many of these patients, regional anesthesia during labor may provide sufficient pain relief (thereby minimizing catecholamine release and resultant cardiac output fluctuations) to render a vaginal delivery feasible. A Pregnancy Heart Team (Table 4) should determine which patients are not candidates for vaginal delivery or require assisted second stage of labor during pregnancy. In the absence of spontaneous onset of labor or indicated delivery before term, scheduled induction of labor for pregnant women with cardiac disease between 39–40 weeks of gestation may be considered with input from the Pregnancy Heart Team.

Anticoagulation must be carefully reviewed and managed by the Pregnancy Heart Team during pregnancy and adjusted appropriately at the time of neuraxial anesthesia and delivery. For women who are receiving prophylactic low-molecular-weight heparin, discontinuation is recommended at least 12 hours before scheduled induction of labor or cesarean delivery. A 24-hour interval is recommended for patients on an adjusted-dose regimen (44, 141, 142). For unfractionated heparin doses of 7,500 units subcutaneously twice a day or more, a 12-hour interval as well as evaluation of coagulation status with laboratory testing are recommended. Women receiving anticoagulation therapy may be converted from warfarin or low-molecular-weight heparin to the shorter half-life unfractionated heparin in anticipation of delivery, depending upon the institution's protocol. An alternative may be to stop anticoagulation and induce labor within 24 hours, if clinically appropriate. If conversion to unfractionated heparin is planned, timing should be based upon the likelihood of spontaneous labor with the goal of minimizing the time without anticoagulation coverage. This approach is especially important in a patient with a mechanical valve prosthesis (44, 88, 119).

The most common intrapartum cardiac complications include pulmonary edema or arrhythmias (54, 59, 133). These patients require a high level of surveillance and care. For women with a history of arrhythmias and for those who develop an arrhythmia during pregnancy, intrapartum cardiac monitoring is recommended. (52). Pulmonary edema usually can be prevented by maintaining a meticulous fluid balance. Expert consensus is that antibiotic prophylaxis administered at the time of delivery is reasonable for the subset of patients at increased risk of developing infective endocarditis, such as those with a history of previous infective endocarditis, and for patients at high risk of experiencing an adverse outcome from infective endocarditis (88, 91).

Obstetric Anesthesia Principles

Cardiac disease patients may require an elevated level of monitoring and anesthetic care for all obstetric procedures (eg, dilation and curettage or evacuation or cerclage) as well as vaginal or cesarean delivery. Consultation with an anesthesiologist should be performed antepartum for anesthetic, cardiac, and obstetric risk assessment and planning.

Under the direction of an anesthesiologist, cardiac disease patients undergoing vaginal delivery should be offered epidural labor analgesia, and cardiac disease patients undergoing cesarean delivery should have neuraxial anesthesia, if possible. Cardiovascular events (usually arrhythmia) are significantly decreased with epidural use (143). Exceptions for neuraxial anesthesia include the usual anesthetic contraindications and patients receiving pharmacologic anticoagulation as noted above (141, 142, 144). Consideration also should be

given to modifying neuraxial anesthesia management for patients at risk of cardiovascular decompensation related to reduction of systemic vascular resistance. Such patients include those with left ventricular outflow tract obstruction or cyanotic congenital heart disease.

Immediate Postpartum Management Principles

The postpartum period is a time of heightened risk of cardiovascular disease-related maternal morbidity and mortality (80) as evidenced by a threefold increase in the rate of postpartum hospitalizations for chronic heart disease in the past decade (14). Among cardiovascular disease-related mortality, peripartum cardiomyopathy (25–100 per 100,000 live births) is identified as the leading (23%) cause of late postpartum death (10, 144). Aortic dissection and acute coronary syndromes typically are diagnosed in the early postpartum period and are associated with a high risk of maternal mortality (15, 145–147). The incidence of acute coronary syndrome is estimated at 2.7–8.1 per 100,000 deliveries, a rate known to be threefold to fourfold higher during the pregnancy and postpartum periods compared with nonpregnant women matched for age (15, 17, 118, 119, 148). Cardiac disease is particularly linked to late maternal death as long as 1 year postpartum (10).

Women with cardiac disease are at high risk of immediate complications during the early puerperium (first 7 days after delivery) and as long as 6 months postpartum (26). This risk is compounded by the common concurrence of immediate postpartum obstetric complications, such as hypertensive disorders, hemorrhage, and infection. An elevated level of care or a prolonged period of monitoring may be necessary, particularly for patients at risk of cardiogenic pulmonary edema and arrhythmias or in the setting of concurrent obstetric or surgical complications. Consideration should be given to careful and frequent monitoring of the signs and symptoms of cardiovascular disease (Table 2) using pulse oximetry, lung auscultation, the recording of fluid balance, and for the development of shortness of breath or cough. Cardiovascular testing may be appropriate and individualized to presenting features. Early consultation with a cardiologist and possible transfer of the patient to a facility with a higher level of care should be expedited if maternal complications related either to known disease or to new-onset, acquired maternal heart disease develop at any time during the course of care.

Each facility should review the available venous thromboembolism risk assessment protocols and adopt and implement one of them in a systematic way to reduce the incidence of venous thromboembolism in the postpartum period (44). Cesarean delivery, particularly when complicated by postpartum hemorrhage or infection, as well as medical factors or pregnancy complications, increases the risk of venous thromboembolism. Although current evidence is insufficient to recommend universal adoption of pharmacologic prophylaxis for venous thromboembolism after cesarean delivery, for selected high-risk patients in whom significant risk factors persist after delivery, prophylaxis may be considered (44). If thromboprophylaxis is considered, evidence suggests that in women with a BMI of 35 or more, weight-based dosage (0.5 mg/kg enoxaparin every 12 hours) compared to fixed dosage will achieve significantly higher anti-Xa concentrations within the adequate prophylaxis range ($P<.01$) (149, 150). However, the optimal dose, route, and duration of thromboprophylaxis need further evaluation. In the absence of clear, randomized controlled trial evidence, practitioners can rely on consensus-derived clinical practice guidelines or recommendations from national and international societies (44).

Pharmacologic Considerations

Health care providers should be aware of cardiac medications with obstetric implications (Table 5) as well as obstetric medications with cardiac implications (Table 7). Obstetrician–gynecologists and other health care providers should consult lactation pharmacology resources for current information on individual medications because inappropriate advice often can lead women to discontinue breastfeeding unnecessarily (151).

▶ ***How should in-hospital postpartum care be altered for women with or at risk of cardiovascular disease?***

Postpartum Considerations After Delivery Hospitalization

Complications are frequently encountered in the days, weeks, and months after delivery in women with known cardiovascular disease and in those with latent cardiovascular disease. Women with multiple risk factors for cardiovascular disease (See Box 3) may be particularly at risk of manifesting symptoms for the first time during their postpartum course. A postpartum follow-up visit (early postpartum visit) with either the primary care provider or cardiologist is recommended within 7–10 days of delivery for women with hypertensive disorders or 7–14 days of delivery for women with heart disease/cardiovascular disorders. Ideally, future pregnancy intentions and commensurate contraceptive needs should be discussed before delivery or hospital discharge and reassessed at each postpartum visit.

Table 7. Obstetric Medications With Cardiac Influences

Drug	Cardiovascular Side Effects	Cardiac Conditions Contraindicated	Special Considerations
Corticosteroids (Betamethasone or Dexamethasone)	Fluid retention Electrolyte disturbance Hypertension	Use with caution in patients with heart failure or hypertension	Recent history of myocardial infarction; risk of left ventricular free wall rupture
Hydroxyprogesterone	Fluid retention Electrolyte disturbance Hypertension	Use with caution in patients with cardiac dysfunction	
Prostaglandin (PGE_2)	None reported		
Misoprostol	Rare		
Oxytocin	Arrhythmias Hypotension		Titrate carefully and avoid rapid intravenous bolus
Magnesium Sulfate	Hypotension Vasodilation Syncope	Caution in patients with heart block	Titrate carefully in hypertrophic obstructive cardiomyopathy and stenotic valvular lesions especially aortic stenosis
Terbutaline	Tachycardia Hypotension Arrhythmias Myocardial ischemia	Hypertrophic obstructive cardiomyopathy Patients at risk of arrhythmias or ischemia Stenotic valvular lesions especially mitral stenosis	Do not use beyond 48–72 hours
Methylergonovine	Coronary artery vasospasm Hypertension Arrhythmias	Coronary artery disease or risk for ischemia Aortopathies	Do not give intravenously
Carboprost Tromethamine	Hypertension Palpitations Tachycardia Vasodepressor syncope Pulmonary hypertension	Pulmonary hypertension Cyanotic congenital heart disease Pulmonary edema	Can cause bronchospasm Do not give intravenously
Tranexamic Acid			Use with caution in uncorrected cardiovascular disease due to thrombosis

Data from Facts & Comparisons. St. Louis (MO): Wolters Kluwer Health, Inc; 2019. Available at: http://fco.factsandcomparisons.com/lco/action/home. Retrieved January 22, 2019.

Optimal care for women with known cardiovascular disease during this critical period requires a team-based approach, such as with a Pregnancy Heart Team (23, 47, 138), and a cardiovascular disease risk assessment by a maternal care provider (Fig. 1). Mortality reviews indicate that cardiovascular disease signs and symptoms are not recognized readily by the patient, family, or the health care provider and that there are delays in access to health care related to transportation or other financial barriers (10). All postpartum women with cardiovascular disease and those identified as at high risk of cardiovascular disease should be educated on their individual risk. They should be instructed when and how to seek medical care and be provided with phone numbers and a printed or electronic copy of their discharge summary, including an explanation of signs and symptoms that should

prompt timely assessment. These women benefit from an early outpatient visit within 7–14 days after delivery to facilitate overall assessment of well-being and symptoms or functional status, or both. To facilitate patient adherence to appointments, it is important to address barriers to care, such as socioeconomic variability, insurance status, access to health care, and physical distance to the nearest hospital.

Contraceptive options, including immediate postpartum placement of long-acting reversible contraceptive methods, should be discussed in the prenatal period, and plans to execute should be implemented before hospital discharge to minimize the risk of short-interval recurrent pregnancy.

Breastfeeding has important short-term and long-term health benefits for the woman. Cardiac patients should be encouraged to breastfeed during the postpartum hospital stay and in the outpatient setting because most medications are considered safe (Table 5) (152). Breastfeeding has favorable effects not only on hypertension through positive effects on the maternal vasculature but fosters a favorable lipid and hormonal milieu along with improved mother-infant bonding (153). Women whose cumulative lifetime duration of breastfeeding is 6–12 months are 10% less likely to develop cardiovascular disease (154).

It is important to emphasize that the overwhelming majority of cardiovascular disease mortality occurs beyond the conventional postpartum period, including the first 42 days after delivery (10). Thus, a long-term care plan is crucial. Women identified as high risk (Fig. 1) should be evaluated at 3 months in a comprehensive cardiovascular postpartum visit. Payment models that provide health care coverage for the 3-month visit for these high-risk patients should be developed. This 3-month comprehensive cardiovascular postpartum visit with the Pregnancy Heart Team, the obstetrician–gynecologist, or other primary care provider should be individualized to each patient and should include a history of pertinent symptoms, a physical examination, an assessment of height and weight (BMI), waist circumference, heart rate, respiratory rate, blood pressure, and oxygen saturation. Laboratory testing, including fasting blood glucose or hemoglobin A_{1c}, and a complete lipid profile should be considered. Patients should have a yearly follow-up with their primary care physician. Health care providers should establish and maintain an ongoing partnership with a cardiologist or primary care physician, or both, who will be available for future care. Bundled payments for maternity care should be expanded to include this intensive classification (as many as three visits in the first 3 months postpartum) for a more individualized approach to these women. Ongoing collaborative care of the woman with cardiovascular disease or at risk of future cardiovascular disease is essential to reducing morbidity and mortality, optimizing the woman's health in preparation for future pregnancies, and promoting long-term cardiovascular health (26, 139).

▶ ***What are the contraceptive options and considerations for women with heart or cardiovascular disease, or both?***

Contraception Considerations

Decisions regarding the most appropriate contraceptive option for a woman require discussion of her future pregnancy desires and personal preferences, as well as critical assessment of the patient's underlying disease and the relative risks and benefits of the contraceptive option considered. The Centers for Disease Control and Prevention and the World Health Organization have established a four-tier scale related to medical eligibility criteria for contraceptive use that provides clinicians an assessment of the relative risks and benefits of contraceptive methods in various medical settings (155–157). Clinicians can access this detailed clinical guidance at https://www.cdc.gov/reproductivehealth/contraception/pdf/summary-chart-us-medical-eligibility-criteria_508tagged.pdf. See also the American College of Obstetricians and Gynecologists' For More Information web page.

Intrauterine devices are the recommended nonpermanent option for women with high-risk cardiovascular conditions (155, 158). Intrauterine devices are highly effective and reliable long-acting reversible contraception. Multiple intrauterine device options (copper and progestin containing) are available based on patient preference, contraindications, and desire for future fertility. Annual failure rates with intrauterine devices use are less than 1%, and duration of action ranges from 3 to 10 years depending on the device used. Intrauterine device placement can be undertaken in the clinician's office and poses minimal risk for women with underlying cardiac disease (155, 158). Although expulsion rates are increased (10–27%) with placement at the time of delivery, immediate postpartum intrauterine device placement after delivery of the placenta is also a consideration for women with high-risk cardiac disease to ensure there is no gap in contraceptive protection (159). Women should be counseled about the increased expulsion risk as well as signs and symptoms of expulsion (159).

Progestin-only contraceptives (oral, depot medroxyprogesterone acetate injection, or implant) are potentially effective alternatives for women with cardiac disease. The progestin-only pill is limited primarily to use in the immediate postpartum period in lactating women. This option, however, has lower efficacy (more than 9% failure rate) for pregnancy prevention (155, 160, 161). Intramuscular depot medroxyprogesterone acetate is a highly

Box 3. Risk Factors for Maternal Cardiovascular Disease

- Non-Hispanic black race
- Older age (more than 40 years)
- Obesity
- Hypertensive disorders of pregnancy (preeclampsia, eclampsia, or hemolysis, elevated liver enzymes, and low platelet count syndrome)
- Chronic disease (chronic hypertension or pregestational diabetes mellitus)
- Obstructive sleep apnea (moderate to severe)
- History of preterm delivery
- Strong family history of heart disease
- Exposure to cardiotoxic drugs

effective contraceptive modality and appears to be a safe option for women with valvular heart disease, cardiomyopathy, and well-controlled hypertension (155, 162). For women receiving therapeutic anticoagulation, depot medroxyprogesterone acetate injections theoretically can increase risk of hematoma formation. Reversible bone loss, diminution of protective high-density lipoprotein, and increased triglycerides have been noted secondary to the hypoestrogenic effect of depot medroxyprogesterone acetate (163, 164). The progestin implant is highly efficacious and appears to be a safe option for most women with hypertension or known cardiac disease. Use in women with current or previous ischemic heart disease or cerebrovascular accident is limited secondary to increased concern for thrombosis (155). There also may be risk of hematoma formation at the time of insertion or removal, or both, in women who are anticoagulated.

Combined hormonal contraception (eg, oral, ring, or patch), although effective, may pose significant risk for women depending on the patient's underlying cardiac condition because of the estrogen component. The use of combined hormonal contraception in women with poorly controlled hypertension, aged more than 35 years, who are smokers, or who have migraine with aura, is associated with increased risks for exacerbation of high blood pressure, cardiovascular events, such as stroke and acute myocardial infarction, and thromboembolic events (155, 161, 162, 165–169). For women with valvular heart disease, especially those with complicated valvular pathology, combined hormonal contraception may increase the risk of arterial thrombosis and other adverse cardiovascular consequences. Use of combined hormonal contraception in the setting of cardiomyopathy can be associated with fluid retention, which can exacerbate heart failure (170). Because of these concerns, alternative contraceptive options should be considered in women with prothrombogenic states, uncontrolled hypertension, ischemic heart disease, and complicated valvular heart disease (155).

Barrier, fertility awareness-based, and other nonhormonal methods used to lessen the risk of fertilization, although safe, have high risk of contraceptive failure. Therefore, these methods are suboptimal for women who do not desire further childbearing or who have significant cardiovascular disease in which pregnancy is ill-advised or contraindicated. Estimated annual failure rates vary according to the method used. The fertility-awareness method has a failure rate of 24%; withdrawal, 22%; spermicide use, 28%; male condom, 18%; female condom, 21%; sponge, 12–24%; and diaphragm, 12% (155, 160, 171).

Emergency contraception is available for women with contraindications to use of combined hormonal contraception (155, 161). The presence of cardiovascular disease is not a contraindication to the use of emergency contraception (155, 161). Progestin-only emergency contraceptive methods are generally better tolerated and are more efficacious than combined regimens and may be preferred in the setting of cardiovascular disease. Insertion of a copper intrauterine device is an effective method of emergency contraception when inserted within 5 days after unprotected intercourse. The copper intrauterine device provides ongoing contraception and should be made available to patients at high risk of pregnancy morbidity and mortality (158).

Permanent sterilization is one of the most effective contraceptive options for reproductive-aged women who have completed childbearing, especially for women with high-risk cardiac conditions or cardiovascular disease. Paternal vasectomy is a highly effective approach for male sterilization with low complications and failure rates of less than 1% (155, 172, 173). Limitations of vasectomy include the potential for pregnancy in the setting of a nonmonogamous relationship or a sexual relationship with a new partner. Female sterilization may be performed by several approaches (eg, laparoscopy, minilaparotomy, and in combination with cesarean delivery) (172). Although laparoscopy is an effective and safe approach for sterilization, the need for general anesthesia and pneumoperitoneum (with resultant increased intraperitoneal pressure) can alter cardiac and pulmonary function and thereby impose challenges for women with certain critical cardiac abnormalities (174, 175). Low-pressure laparoscopy does not appear to mitigate these operative physiologic effects (176). Minilaparotomy with tubal ligation can be performed under regional anesthesia and may minimize intraoperative risks in women with cardiac disease (172).

▶ ***What are the long-term considerations and implications after pregnancy for women with cardiovascular disease?***

There are immediate and long-term continuity of care considerations for women with congenital or acquired heart and cardiovascular disease. Specific and immediate considerations include the following:

- Ensure proper cardiology follow-up is initiated during pregnancy or postpartum.
- Acknowledge the effect of a chronic diagnosis and possible need for long-term medication use. Consider 3-month prescriptions (or longer) if clinically appropriate (177).
- Refer patients with cardiovascular disease to lactation services when breastfeeding presents challenges, which often arise because of preterm delivery (178).
- Be mindful of the mental health implications of cardiovascular disease during the postpartum period and beyond. Preterm birth also is associated with maternal depression, anxiety, and posttraumatic stress disorder (179). Of note, most medications used to treat these disorders are compatible with breastfeeding, even in conjunction with cardiac medications. Mobilize all available resources to support the patient and her family during this time as indicated.
- Discuss future pregnancy intentions and provide a commensurate form of contraception.
- Screen patients routinely at postpartum follow-up visits for depressive symptoms and evidence of posttraumatic stress disorder and refer to social services or psychologic services, or both, as indicated (179).

These are priorities early in the puerperium because many women lose health insurance beyond the first 42 days postpartum. These steps are especially relevant in the postpartum period when women with cardiovascular disease are focused on newborn care and are less likely to prioritize their own health.

Continuity of Care Considerations for Women With Cardiovascular Disease Risk Factors

Acute (gestational hypertension, preeclampsia) and chronic hypertensive disorders of pregnancy are important identifiers of patients at risk of cardiovascular disease (23). Gestational hypertension and preeclampsia increase the risk of future cardiovascular disease by severalfold, and the risk is even higher in women with recurrent preeclampsia, preterm birth at less than 37 weeks of gestation, or intrauterine growth restriction (29, 180–186). Not only do women with hypertensive disorders of pregnancy have a substantially higher risk of future cardiovascular disease, they also have a threefold to fourfold increase in the risk of chronic hypertension, a 4.2-fold increase in the risk of heart failure, an 81% increase in the risk of stroke, a 5-fold to 12-fold increased risk of developing end-stage renal disease, and double the risk of atrial arrhythmias, coronary heart disease, and mortality when compared with women with normotensive pregnancies (184, 187). Exposure to severe maternal preeclampsia is an independent risk factor for long-term cardiovascular morbidity in offspring born at term (188).

The presence of gestational complications reliably identifies women with underlying, often unrecognized, cardiovascular risk factors (189, 190). Because approximately 20% of women have one or more of these complications (191), risk screening is recommended (192) within the first year postpartum (191). Cardiovascular assessment and follow-up at 3 months postpartum is recommended for women with the following conditions:

- Hypertension, chronic/essential or hypertensive disorder of pregnancy (ie, gestational hypertension, preeclampsia, eclampsia, hemolysis, elevated liver enzymes, and low platelet syndrome, chronic hypertension [with or without superimposed preeclampsia])
- Gestational diabetes mellitus
- Intrauterine fetal growth restriction (particularly less than the 5th percentile for gestational age or less than 2,500 g at term)
- Idiopathic preterm birth
- Placental abruption
- Obesity/excessive pregnancy weight gain/postpartum weight retention
- Sleep disorders/moderate-to-severe obstructive sleep apnea (193–197)
- Maternal age older than 40 years

Cardiovascular risk screening within 3 months postpartum includes a detailed medical history (including history of cardiovascular disease), postpartum medication monitoring (such as antihypertensive medication), a physical examination, and basic biochemical testing (see Box 4).

After cardiovascular screening is complete, women should be counseled with regard to their identified risk factors. The goal of targeted cardiovascular risk assessment and patient education is to promote patient self-awareness and self-initiation of preventive actions. The American Heart Association's Life's Simple 7 describes

Box 4. Postpartum Cardiovascular Risk Screening

Medical history

- Smoking (number of cigarettes per day, number of years smoked)
- Physical activity (times per week, duration)
- Breast feeding (how long)
- History of hypertension, diabetes, or cardiovascular disease
- First degree family history of cardiovascular disease, hypertension, or diabetes

Physical examination

- Resting blood pressure and heart rate
- Body mass index and waist circumference

Biochemical testing

- Cholesterol/lipid profile
- Fasting glucose (or oral glucose tolerance testing if patient had gestational diabetes)
- Urine protein assessment (protein:creatinine ratio)

Nutrition assessment

seven steps to achieve a healthy lifestyle (198). Tests for borderline or elevated blood pressure or lipid abnormalities, or both, should be repeated after 6–12 months of lifestyle modification and, if persistently elevated, initiation of pharmacologic treatment should be considered.

Ongoing Postpartum Care After the 3-Month Cardiovascular Assessment Visit

Continuing follow-up as indicated after the 3-month comprehensive cardiovascular postpartum evaluation provides the opportunity for counseling, planning, and intervention to optimize underlying medical conditions to improve future pregnancy outcomes and cardiovascular health. If not already managed, contraceptive needs can be considered, managed, or modified as needed. In addition to the usual prepregnancy topics such as folic acid usage, restoration to prepregnancy weight should be emphasized because not achieving it increases the risk of future pregnancy complications (199). Weight management strategies include referral to a registered dietitian, peer support, improved access to opportunities for physical activity, and programs that provide child care at no or low cost. Women with pregnancy complications, such as preeclampsia and gestational diabetes, should be counseled regarding the risks of future cardiovascular disease and overt diabetes, respectively. In any future pregnancy, patients with a history of prior preeclampsia should be considered for low-dose aspirin prophylaxis (136). For those who have previous gestational diabetes mellitus, early screening in the next pregnancy is recommended (200). Finally, given the benefits for the infant and the cardiometabolic benefits for the woman (201), breastfeeding should be recommended, and community support identified, to increase breastfeeding success after future pregnancies. During the postpartum period, health care providers may include a primary care provider and various other specialists, and communication across the clinical team should continue. However, because coordinated care can be challenging among many different specialists and subspecialists (202), the patient must be educated about her individualized cardiovascular risk, and a recommended plan of care for future pregnancies should be developed in collaboration with cardiologist colleagues. During postpartum care, opportunities should be developed to expand shared decision making whereby clinicians can understand their patients' goals, values, and preferences for health care and to facilitate a mutually suitable evaluation and management plan for future pregnancies (202).

For More Information

The American College of Obstetricians and Gynecologists has identified additional resources on topics related to this document that may be helpful for ob-gyns, other health care providers, and patients. You may view these resources at www.acog.org/More-Info/PregnancyAndHeartDisease.

These resources are for information only and are not meant to be comprehensive. Referral to these resources does not imply the American College of Obstetricians and Gynecologists' endorsement of the organization, the organization's website, or the content of the resource. The resources may change without notice.

Summary of Recommendations and Conclusions

The following recommendations and conclusions are based on limited or inconsistent scientific evidence (Level B):

- Referral to a hospital setting that represents an appropriate maternal level of care dependent upon the specific cardiac lesion is recommended for all pregnant patients with moderate- to high-risk cardiac conditions (modified WHO risk classes III and IV) because outcomes are significantly better for women in these facilities.

- It may be helpful to obtain a baseline BNP level during pregnancy in women at high risk of or with known heart disease, such as dilated cardiomyopathy and congenital heart disease.
- All pregnant and postpartum patients with chest pain should undergo standard troponin testing and an electrocardiogram to evaluate for acute coronary syndrome.
- Patients should be counseled to avoid pregnancy or consider induced abortion if they have severe heart disease, including an ejection fraction less than 30% or class III/IV heart failure, severe valvular stenosis, Marfan syndrome with aortic diameter more than 45 mm, bicuspid aortic valve with aortic diameter more than 50 mm, or pulmonary arterial hypertension.

The following recommendations and conclusions are based primarily on consensus and expert opinion (Level C):

- Health care providers should become familiar with the signs and symptoms of cardiovascular disease as an important step toward improving maternal outcomes.
- Women with known cardiovascular disease should be evaluated by a cardiologist ideally before pregnancy or as early as possible during the pregnancy for an accurate diagnosis and assessment of the effect pregnancy will have on the underlying cardiovascular disease, to assess the potential risks to the woman and fetus, and to optimize the underlying cardiac condition.
- Patients with moderate and high-risk cardiovascular disease should be managed during pregnancy, delivery, and the postpartum period in medical centers with a multidisciplinary Pregnancy Heart Team that includes obstetric providers, maternal–fetal medicine subspecialists, cardiologists, and an anesthesiologist at a minimum.
- Discussion of cardiovascular disease with the woman should include the possibilities that 1) pregnancy can contribute to a decline in cardiac status that may not return to baseline after the pregnancy; 2) maternal morbidity or mortality is possible; and 3) fetal risk of congenital heart or genetic conditions, fetal growth restriction, preterm birth, intrauterine fetal demise, and perinatal mortality is higher when compared with risk when cardiovascular disease is not present.
- A personalized approach estimating the maternal and fetal hazards related to the patient's specific cardiac disorder and the patient's pregnancy plans can provide anticipatory guidance to help support her decision making. For some patients, the prepregnancy evaluation may suggest a pregnancy risk that is unacceptable. For those women, reproductive alternatives, such as surrogacy or adoption, and effective contraceptive methods should be discussed.
- All women should be assessed for cardiovascular disease in the antepartum and postpartum periods using the California Improving Health Care Response to Cardiovascular Disease in Pregnancy and Postpartum toolkit algorithm.
- All pregnant and postpartum women with known or suspected cardiovascular disease should proceed with further evaluation by a Pregnancy Heart Team consisting of a cardiologist and maternal–fetal medicine subspecialist, or both, and other subspecialists as necessary.
- Testing of maternal cardiac status is warranted during pregnancy or postpartum in women who present with symptoms such as shortness of breath, chest pain, or palpitations and known cardiovascular disease whether symptomatic or asymptomatic, or both.
- An echocardiogram should be performed in pregnant or postpartum women with known or suspected congenital heart disease (including presumed corrected cardiac malformations), valvular and aortic disease, cardiomyopathies, and those with a history of exposure to cardiotoxic chemotherapy (eg, doxorubicin hydrochloride).
- Congenital heart disease in the woman should prompt fetal echocardiography, and conversely, identification of congenital heart disease in a fetus or neonate may prompt screening for parental congenital heart disease.
- Women with asymptomatic valve disease should be monitored by a cardiologist and may require additional testing or care during pregnancy. The frequency of monitoring necessary is indicated in the patient's modified WHO classification.
- Any pregnant woman who presents with an arrhythmia should undergo evaluation to assess the cause and the possibility of underlying structural heart disease.
- Pregnant or postpartum women who present with shortness of breath, chest discomfort, palpitations, arrhythmias, or fluid retention should be evaluated for peripartum cardiomyopathy. An echocardiogram is generally the most important diagnostic test.
- Every pregnant or postpartum patient with chest pain or cardiac symptoms should have consideration of acute coronary syndrome.
- Although maternal cardiac arrest occurs infrequently, the health care provider should be prepared to manage this situation in any health care facility.

- The infrequency of maternal cardiac arrest underscores the need for regular team training and practice of resuscitation skills and scenarios through simulation training.
- Women with complex congenital or noncongenital heart disease should be treated by a Pregnancy Heart Team.
- Women with stable cardiac disease can undergo a vaginal delivery at 39 weeks of gestation, with cesarean delivery reserved for obstetric indications.
- Health care providers should be aware of cardiac medications with obstetric implications as well as obstetric medications with cardiac implications.
- A postpartum follow-up visit (early postpartum visit) with either the primary care provider or cardiologist is recommended within 7–10 days of delivery for women with hypertensive disorders or 7–14 days of delivery for women with heart disease/cardiovascular disorders.
- All postpartum women with cardiovascular disease and those identified as at high risk of cardiovascular disease should be educated on their individual risk.
- Decisions regarding the most appropriate contraceptive option for a woman require discussion of her future pregnancy desires and personal preferences, as well as critical assessment of the patient's underlying disease and the relative risks and benefits of the contraceptive option considered.
- Intrauterine devices are the recommended nonpermanent option for women with high-risk cardiovascular conditions.

References

1. Benjamin EJ, Virani SS, Callaway CW, Chamberlain AM, Chang AR, Cheng S, et al. Heart disease and stroke statistics—2018 update: a report from the American Heart Association. American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee [published erratum appears in Circulation. 2018;137:e493]. Circulation 2018; 137:e67–e492. (Level III)
2. McAloon CJ, Boylan LM, Hamborg T, Stallard N, Osman F, Lim PB, et al. The changing face of cardiovascular disease 2000-2012: an analysis of the World Health Organisation global health estimates data. Int J Cardiol 2016; 224:256–64. (Level II-3)
3. Creanga AA, Berg CJ, Syverson C, Seed K, Bruce FC, Callaghan WM. Pregnancy-related mortality in the United States, 2006-2010. Obstet Gynecol 2015;125:5–12. (Level II-3)
4. Knight M, Bunch K, Tuffnell D, Jayakody H, Shakespeare J, Kotnis R, et al, editors. Saving lives, improving mothers' care—lessons learned to inform maternity care from the UK and Ireland. Confidential Enquiries into Maternal Deaths and Morbidity 2014-16. Oxford (UK): National Perinatal Epidemiology Unit, University of Oxford; 2018. (Level III)
5. Creanga AA, Syverson C, Seed K, Callaghan WM. Pregnancy-related mortality in the United States, 2011-2013. Obstet Gynecol 2017;130:366–73. (Level II-3)
6. Elkayam U, Goland S, Pieper PG, Silverside CK. High-risk cardiac disease in pregnancy: part I. J Am Coll Cardiol 2016;68:396–410. (Level III) (Elkayam 2016A)
7. Thompson JL, Kuklina EV, Bateman BT, Callaghan WM, James AH, Grotegut CA. Medical and obstetric outcomes among pregnant women with congenital heart disease. Obstet Gynecol 2015;126:346–54. (Level II-3)
8. Roos-Hesselink JW, Ruys TP, Stein JI, Thilen U, Webb GD, Niwa K, et al. Outcome of pregnancy in patients with structural or ischaemic heart disease: results of a registry of the European Society of Cardiology. ROPAC Investigators. Eur Heart J 2013;34:657–65. (Level II-3)
9. Briller J, Koch AR, Geller SE. Maternal cardiovascular mortality in Illinois, 2002-2011. Obstet Gynecol 2017; 129:819–26. (Level II-3)
10. Hameed AB, Lawton ES, McCain CL, Morton CH, Mitchell C, Main EK, et al. Pregnancy-related cardiovascular deaths in California: beyond peripartum cardiomyopathy. Am J Obstet Gynecol 2015;213:379.e1–10. (Level III)
11. Curry R, Swan L, Steer PJ. Cardiac disease in pregnancy. Curr Opin Obstet Gynecol 2009;21:508–13. (Level III)
12. Fett JD. Peripartum cardiomyopathy: challenges in diagnosis and management [published erratum appears in Expert Rev Cardiovasc Ther 2016;14:1205]. Expert Rev Cardiovasc Ther 2016;14:1035–41. (Level III)
13. Gunderson EP, Croen LA, Chiang V, Yoshida CK, Walton D, Go AS. Epidemiology of peripartum cardiomyopathy: incidence, predictors, and outcomes. Obstet Gynecol 2011;118:583–91. (Level II-2)
14. Kuklina E, Callaghan W. Chronic heart disease and severe obstetric morbidity among hospitalisations for pregnancy in the USA: 1995-2006. BJOG 2011;118:345–52. (Level II-3)
15. Cantwell R, Clutton-Brock T, Cooper G, Dawson A, Drife J, Garrod D, et al. Saving Mothers' Lives: reviewing maternal deaths to make motherhood safer: 2006-2008. The Eighth Report of the Confidential Enquiries into Maternal Deaths in the United Kingdom [published erratum appears in BJOG 2015 122:e1]. BJOG 2011; 118(suppl 1):1–203. (Level III)
16. Lewis G, editor. The Confidential Enquiry into Maternal and Child Health (CEMACH). Saving Mothers' Lives: reviewing maternal deaths to make motherhood safer—2003-2005. The Seventh Report on Confidential Enquiries into Maternal Deaths in the United Kingdom. London (UK): CEMACH; 2007. (Level III)
17. James AH, Jamison MG, Biswas MS, Brancazio LR, Swamy GK, Myers ER. Acute myocardial infarction in pregnancy: a United States population-based study. Circulation 2006;113:1564–71. (Level II-3)

18. Melchiorre K, Sharma R, Thilaganathan B. Cardiovascular implications in preeclampsia: an overview. Circulation 2014;130:703–14. (Level III)
19. Castleman JS, Ganapathy R, Taki F, Lip GY, Steeds RP, Kotecha D. Echocardiographic structure and function in hypertensive disorders of pregnancy: a systematic review. Circ Cardiovasc Imaging 2016;9(9). (Systematic Review)
20. Kim MJ, Seo J, Cho KI, Yoon SJ, Choi JH, Shin MS. Echocardiographic assessment of structural and hemodynamic changes in hypertension-related pregnancy. J Cardiovasc Ultrasound 2016;24:28–34. (Level II-2)
21. Norman JE, Reynolds RM. The consequences of obesity and excess weight gain in pregnancy [published erratum appears in Proc Nutr Soc 2011;70:514]. Proc Nutr Soc 2011;70:450–6. (Level III)
22. Louis JM, Mogos MF, Salemi JL, Redline S, Salihu HM. Obstructive sleep apnea and severe maternal-infant morbidity/mortality in the United States, 1998-2009. Sleep 2014;37:843–9. (Level II-3)
23. Mosca L, Benjamin EJ, Berra K, Bezanson JL, Dolor RJ, Lloyd-Jones DM, et al. Effectiveness-based guidelines for the prevention of cardiovascular disease in women—2011 update: a guideline from the American Heart Association [published erratum appears in J Am Coll Cardiol 2012;59:1663]. J Am Coll Cardiol 2011;57:1404–23. (Level III)
24. Racial and ethnic disparities in obstetrics and gynecology. Committee Opinion No. 649. American College of Obstetricians and Gynecologists. Obstet Gynecol 2015;126:e130–4. (Level III)
25. Institute of Medicine. Unequal treatment: confronting racial and ethnic disparities in health care. Washington, DC: National Academies Press; 2003. (Level III). Available at https://www.ncbi.nlm.nih.gov/pubmed/25032386.
26. Optimizing postpartum care. ACOG Committee Opinion No. 736. American College of Obstetricians and Gynecologists. Obstet Gynecol 2018;131:e140–50. (Level III)
27. Brown HL, Warner JJ, Gianos E, Gulati M, Hill AJ, Hollier LM, et al. Promoting risk identification and reduction of cardiovascular disease in women through collaboration with obstetricians and gynecologists: a Presidential Advisory from the American Heart Association and the American College of Obstetricians and Gynecologists. Circulation 2018;137:e843–52. (Level III)
28. Gunderson EP. Childbearing and obesity in women: weight before, during, and after pregnancy. Obstet Gynecol Clin North Am 2009;36:317–32, ix. (Level III)
29. Heida KY, Bots ML, de Groot CJ, van Dunne FM, Hammoud NM, Hoek A, et al. Cardiovascular risk management after reproductive and pregnancy-related disorders: a Dutch multidisciplinary evidence-based guideline. Eur J Prev Cardiol 2016;23:1863–79. (Level III)
30. Sanghavi M, Rutherford JD. Cardiovascular physiology of pregnancy. Circulation 2014;130:1003–8. (Level III)
31. Nama V, Antonios TF, Onwude J, Manyonda IT. Midtrimester blood pressure drop in normal pregnancy: myth or reality? J Hypertens 2011;29:763–8. (Level II-2)
32. Shen M, Tan H, Zhou S, Smith GN, Walker MC, Wen SW. Trajectory of blood pressure change during pregnancy and the role of pre-gravid blood pressure: a functional data analysis approach. Sci Rep 2017;7:6227. (Level II-2)
33. Kinsella SM, Lohmann G. Supine hypotensive syndrome. Obstet Gynecol 1994;83:774–88. (Level III)
34. Kuhn JC, Falk RS, Langesaeter E. Haemodynamic changes during labour: continuous minimally invasive monitoring in 20 healthy parturients. Int J Obstet Anesth 2017;31:74–83. (Level II-3)
35. Sohnchen N, Melzer K, Tejada BM, Jastrow-Meyer N, Othenin-Girard V, Irion O, et al. Maternal heart rate changes during labour. Eur J Obstet Gynecol Reprod Biol 2011;158:173–8. (Level II-3)
36. Walters BN, Walters T. Hypertension in the puerperium [letter]. Lancet 1987;2:330. (Level III)
37. Sibai BM. Etiology and management of postpartum hypertension-preeclampsia. Am J Obstet Gynecol 2012;206:470–5. (Level III)
38. Castro LC, Hobel CJ, Gornbein J. Plasma levels of atrial natriuretic peptide in normal and hypertensive pregnancies: a meta-analysis. Am J Obstet Gynecol 1994;171:1642–51. (Meta-Analysis)
39. Savu O, Jurcut R, Giusca S, van Mieghem T, Gussi I, Popescu BA, et al. Morphological and functional adaptation of the maternal heart during pregnancy. Circ Cardiovasc Imaging 2012;5:289–97. (Level II-2)
40. Ducas RA, Elliott JE, Melnyk SF, Premecz S, daSilva M, Cleverley K, et al. Cardiovascular magnetic resonance in pregnancy: insights from the cardiac hemodynamic imaging and remodeling in pregnancy (CHIRP) study. J Cardiovasc Magn Reson 2014;16:1. (Level II-2)
41. Melchiorre K, Sharma R, Khalil A, Thilaganathan B. Maternal cardiovascular function in normal pregnancy: evidence of maladaptation to chronic volume overload. Hypertension 2016;67:754–62. (Level II-3)
42. Robson SC, Hunter S, Boys RJ, Dunlop W. Serial study of factors influencing changes in cardiac output during human pregnancy. Am J Physiol 1989;256:H1060–5. (Level III)
43. Goland S, Perelman S, Asalih N, Shimoni S, Walfish O, Hallak M, et al. Shortness of breath during pregnancy: could a cardiac factor be involved? Clin Cardiol 2015;38:598–603. (Level II-2)
44. Thromboembolism in pregnancy. ACOG Practice Bulletin No. 196. American College of Obstetricians and Gynecologists [published erratum appears in Obstet Gynecol 2018;132:1068]. Obstet Gynecol 2018;132:e1–17. (Level III)
45. Bariatric surgery and pregnancy. ACOG Practice Bulletin No. 105. American College of Obstetricians and Gynecologists. Obstet Gynecol 2009;113:1405–13. (Level III)
46. Pregestational diabetes mellitus. ACOG Practice Bulletin No. 201. American College of Obstetricians and Gynecologists. Obstet Gynecol 2018;132:e228–48. (Level III)
47. Chronic hypertension in pregnancy. ACOG Practice Bulletin No. 203. American College of Obstetricians and Gynecologists. Obstet Gynecol 2019;133:e26–e50. (Level III)

48. Smoking cessation during pregnancy. Committee Opinion No. 721. American College of Obstetricians and Gynecologists. Obstet Gynecol 2017;130:e200–4. (Level III)

49. Kalia SS, Adelman K, Bale SJ, Chung WK, Eng C, Evans JP, et al. Recommendations for reporting of secondary findings in clinical exome and genome sequencing, 2016 update (ACMG SF v2.0): a policy statement of the American College of Medical Genetics and Genomics [published erratum appears in Genet Med 2017;19:484]. Genet Med 2017;19:249–55. (Level III)

50. Wolfe DS, Hameed AB, Taub CC, Zaidi AN, Bortnick AE. Addressing maternal mortality: the pregnant cardiac patient. Am J Obstet Gynecol 2019;220(2):167.e1–167.e8. (Level III)

51. Simpson LL. Maternal cardiac disease: update for the clinician. Obstet Gynecol 2012;119:345–59. (Level III)

52. Canobbio MM, Warnes CA, Aboulhosn J, Connolly HM, Khanna A, Koos BJ, et al. Management of pregnancy in patients with complex congenital heart disease: a scientific statement for healthcare professionals from the American Heart Association. American Heart Association Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, Council on Cardiovascular Disease in the Young, Council on Functional Genomics and Translational Biology, and Council on Quality of Care and Outcomes Research. Circulation 2017;135:e50–87. (Level III)

53. Connolly HM. Managing congenital heart disease in the obstetric patient. Semin Perinatol 2018;42:39–48. (Level III)

54. Siu SC, Sermer M, Colman JM, Alvarez AN, Mercier LA, Morton BC, et al. Prospective multicenter study of pregnancy outcomes in women with heart disease. Cardiac Disease in Pregnancy (CARPREG) Investigators. Circulation 2001;104:515–21. (Level II-2)

55. Drenthen W, Boersma E, Balci A, Moons P, Roos-Hesselink JW, Mulder BJ, et al. Predictors of pregnancy complications in women with congenital heart disease. ZAHARA Investigators. Eur Heart J 2010;31:2124–32. (Level II-3)

56. Balci A, Sollie-Szarynska KM, van der Bijl AG, Ruys TP, Mulder BJ, Roos-Hesselink JW, et al. Prospective validation and assessment of cardiovascular and offspring risk models for pregnant women with congenital heart disease. ZAHARA-II investigators. Heart 2014;100:1373–81. (Level II-2)

57. Ruys TP, Maggioni A, Johnson MR, Sliwa K, Tavazzi L, Schwerzmann M, et al. Cardiac medication during pregnancy, data from the ROPAC. Int J Cardiol 2014;177:124–8. (Level II-2)

58. Simpson LL. Preconception considerations. Semin Perinatol 2014;38:236–9. (Level III)

59. Silversides CK, Grewal J, Mason J, Sermer M, Kiess M, Rychel V, et al. Pregnancy outcomes in women with heart disease: the CARPREG II study. J Am Coll Cardiol 2018;71:2419–30. (Level II-2)

60. Levels of maternal care. Obstetric Care Consensus No. 2. American College of Obstetricians and Gynecologists. Obstet Gynecol 2015;125:502–15. (Level III)

61. Januzzi JL Jr, Chen-Tournoux AA, Christenson RH, Doros G, Hollander JE, Levy PD, et al. N-terminal pro-B-type natriuretic peptide in the emergency department: the ICON-RELOADED Study. ICON-RELOADED Investigators. J Am Coll Cardiol 2018;71:1191–200. (Level II-1)

62. Hameed AB, Chan K, Ghamsary M, Elkayam U. Longitudinal changes in the B-type natriuretic peptide levels in normal pregnancy and postpartum. Clin Cardiol 2009;32:60. (Level II-2)

63. Mayama M, Yoshihara M, Uno K, Tano S, Takeda T, Ukai M, et al. Factors influencing brain natriuretic peptide levels in healthy pregnant women. Int J Cardiol 2017;228:749–53. (Level II-2)

64. McCullough PA, Nowak RM, McCord J, Hollander JE, Herrmann HC, Steg PG, et al. B-type natriuretic peptide and clinical judgment in emergency diagnosis of heart failure: analysis from Breathing Not Properly (BNP) Multinational Study. Circulation 2002;106:416–22. (Level II-2)

65. Kansal M, Hibbard JU, Briller J. Diastolic function in pregnant patients with cardiac symptoms. Hypertens Pregnancy 2012;31:367–74. (Level II-3)

66. Resnik JL, Hong C, Resnik R, Kazanegra R, Beede J, Bhalla V, et al. Evaluation of B-type natriuretic peptide (BNP) levels in normal and preeclamptic women. Am J Obstet Gynecol 2005;193:450–4. (Level II-2)

67. Kampman MA, Balci A, van Veldhuisen DJ, van Dijk AP, Roos-Hesselink JW, Sollie-Szarynska KM, et al. N-terminal pro-B-type natriuretic peptide predicts cardiovascular complications in pregnant women with congenital heart disease. ZAHARA II investigators. Eur Heart J 2014;35:708–15. (Level II-2)

68. Ker JA, Soma-Pillay P. NT-proBNP: When is it useful in obstetric medicine? Obstet Med 2018;11:3–5. (Level III)

69. Tanous D, Siu SC, Mason J, Greutmann M, Wald RM, Parker JD, et al. B-type natriuretic peptide in pregnant women with heart disease. J Am Coll Cardiol 2010;56:1247–53. (Level II-2)

70. Blatt A, Svirski R, Morawsky G, Uriel N, Neeman O, Sherman D, et al. Short and long-term outcome of pregnant women with preexisting dilated cardiomypathy: an NTproBNP and echocardiography-guided study. Isr Med Assoc J 2010;12:613–6. (Level II-2)

71. Januzzi JL Jr, Bamberg F, Lee H, Truong QA, Nichols JH, Karakas M, et al. High-sensitivity troponin T concentrations in acute chest pain patients evaluated with cardiac computed tomography. Circulation 2010;121:1227–34. (Level II-3)

72. Shade GH Jr, Ross G, Bever FN, Uddin Z, Devireddy L, Gardin JM. Troponin I in the diagnosis of acute myocardial infarction in pregnancy, labor, and post partum. Am J Obstet Gynecol 2002;187:1719–20. (Level III)

73. Smith R, Silversides C, Downey K, Newton G, Macarthur A. Assessing the incidence of peripartum subclinical myocardial ischemia using the troponin T assay: an observational pilot study. Int J Obstet Anesth 2015;24:30–4. (Level II-2)

74. Pergialiotis V, Prodromidou A, Frountzas M, Perrea DN, Papantoniou N. Maternal cardiac troponin levels in preeclampsia: a systematic review. J Matern Fetal Neonatal Med 2016;29:3386–90. (Systematic Review)

75. M S, S C, Brid SV. Electrocardiographic Qrs axis, Q wave and T-wave changes in 2nd and 3rd trimester of normal pregnancy. J Clin Diagn Res 2014;8:21. (Level II-2)

76. Worrell JA, Cullinan JA, Youree CC, Carroll FE, Lorenz CH. The plain chest radiograph and clinical management of pulmonary edema in pregnancy. J Reprod Med 1996; 41:629–32. (Level II-3)

77. Campos O, Andrade JL, Bocanegra J, Ambrose JA, Carvalho AC, Harada K, et al. Physiologic multivalvular regurgitation during pregnancy: a longitudinal Doppler echocardiographic study. Int J Cardiol 1993;40:265–72. (Level II-3)

78. Desai DK, Moodley J, Naidoo DP. Echocardiographic assessment of cardiovascular hemodynamics in normal pregnancy. Obstet Gynecol 2004;104:20–9. (Level II-2)

79. Chung E, Leinwand LA. Pregnancy as a cardiac stress model. Cardiovasc Res 2014;101:561–70. (Level III)

80. Regitz-Zagrosek V, Roos-Hesselink JW, Bauersachs J, Blomstrom-Lundqvist C, Cifkova R, De Bonis M, et al. 2018 ESC guidelines for the management of cardiovascular diseases during pregnancy. ESC Scientific Document Group. Eur Heart J 2018;39:3165–241. (Level III)

81. Guidelines for diagnostic imaging during pregnancy and lactation. Committee Opinion No. 723. American College of Obstetricians and Gynecologists. Obstet Gynecol 2017; 130:e210–6. (Level III)

82. Strizek B, Jani JC, Mucyo E, De Keyzer F, Pauwels I, Ziane S, et al. Safety of MR imaging at 1.5 T in fetuses: a retrospective case–control study of birth weights and the effects of acoustic noise. Radiology 2015;275:530–7. (Level II-2)

83. Cruz MO, Hibbard JU, Alexander T, Briller J. Ambulatory arrhythmia monitoring in pregnant patients with palpitations. Am J Perinatol 2013;30:53–8. (Level II-2)

84. Pieper PG, Lameijer H, Hoendermis ES. Pregnancy and pulmonary hypertension. Best Pract Res Clin Obstet Gynaecol 2014;28:579–91. (Systematic Review)

85. Weiss BM, Zemp L, Seifert B, Hess OM. Outcome of pulmonary vascular disease in pregnancy: a systematic overview from 1978 through 1996. J Am Coll Cardiol 1998;31:1650–7. (Level III)

86. Bedard E, Dimopoulos K, Gatzoulis MA. Has there been any progress made on pregnancy outcomes among women with pulmonary arterial hypertension? Eur Heart J 2009;30:256–65. (Systematic Review)

87. Galie N, Humbert M, Vachiery JL, Gibbs S, Lang I, Torbicki A, et al. 2015 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension: The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS): Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT). ESC Scientific Document Group. Eur Heart J 2016;37:67–119. (Level III)

88. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP 3rd, Fleisher LA, et al. 2017 AHA/ACC focused update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation 2017;135:e1159–95. (Level III)

89. Steinberg ZL, Dominguez-Islas CP, Otto CM, Stout KK, Krieger EV. Maternal and fetal outcomes of anticoagulation in pregnant women with mechanical heart valves. J Am Coll Cardiol 2017;69:2681–91. (Meta-Analysis)

90. Carnicelli A. Anticoagulation for valvular heart disease. Washington, DC: American College of Cardiology; 2015. Available at https://www.acc.org/latest-in-cardiology/articles/2015/05/18/09/58/anticoagulation-for-valvular-heart-disease. (Level III)

91. Use of prophylactic antibiotics in labor and delivery. ACOG Practice Bulletin No. 199. American College of Obstetricians and Gynecologists. Obstet Gynecol 2018; 132:e103–19. (Level III)

92. Lima FV, Parikh PB, Zhu J, Yang J, Stergiopoulos K. Association of cardiomyopathy with adverse cardiac events in pregnant women at the time of delivery. JACC Heart Fail 2015;3:257–66. (Level II-2)

93. Avila WS, Rossi EG, Ramires JA, Grinberg M, Bortolotto MR, Zugaib M, et al. Pregnancy in patients with heart disease: experience with 1,000 cases. Clin Cardiol 2003; 26:135–42. (Level II-2)

94. Grewal J, Siu SC, Ross HJ, Mason J, Balint OH, Sermer M, et al. Pregnancy outcomes in women with dilated cardiomyopathy. J Am Coll Cardiol 2009;55:45–52. (Level II-2)

95. Goland S, van Hagen IM, Elbaz-Greener G, Elkayam U, Shotan A, Merz WM, et al. Pregnancy in women with hypertrophic cardiomyopathy: data from the European Society of Cardiology initiated Registry of Pregnancy and Cardiac disease (ROPAC). Eur Heart J 2017;38: 2683–90. (Level II-2)

96. Elkayam U, Goland S, Pieper PG, Silversides CK. High-risk cardiac disease in pregnancy: part II. J Am Coll Cardiol 2016;68:502–16. (Level III) (Elkayam 2016B)

97. Vaidya VR, Arora S, Patel N, Badheka AO, Patel N, Agnihotri K, et al. Burden of arrhythmia in pregnancy. Circulation 2017;135:619–21. (Level II-3)

98. Arany Z, Elkayam U. Peripartum cardiomyopathy. Circulation 2016;133:1397–409. (Level III)

99. Pearson GD, Veille JC, Rahimtoola S, Hsia J, Oakley CM, Hosenpud JD, et al. Peripartum cardiomyopathy: National Heart, Lung, and Blood Institute and Office of Rare Diseases (National Institutes of Health) workshop recommendations and review. JAMA 2000;283:1183–8. (Level III)

100. Elkayam U, Akhter MW, Singh H, Khan S, Bitar F, Hameed A, et al. Pregnancy-associated cardiomyopathy: clinical characteristics and a comparison between early

and late presentation. Circulation 2005;111:2050–5. (Level II-2)

101. Sundstrom JB, Fett JD, Carraway RD, Ansari AA. Is peripartum cardiomyopathy an organ-specific autoimmune disease? Autoimmun Rev 2002;1:73–7. (Level III)
102. Patten IS, Rana S, Shahul S, Rowe GC, Jang C, Liu L, et al. Cardiac angiogenic imbalance leads to peripartum cardiomyopathy. Nature 2012;485:333–8. (Level III)
103. Ware JS, Li J, Mazaika E, Yasso CM, DeSouza T, Cappola TP, et al. Shared genetic predisposition in peripartum and dilated cardiomyopathies. IMAC-2 and IPAC Investigators. N Engl J Med 2016;374:233–41. (Level II-3)
104. McNamara DM, Elkayam U, Alharethi R, Damp J, Hsich E, Ewald G, et al. Clinical outcomes for peripartum cardiomyopathy in North America: results of the IPAC study (Investigations of Pregnancy-Associated Cardiomyopathy). IPAC Investigators. J Am Coll Cardiol 2015;66: 905–14. (Level II-2)
105. Haghikia A, Podewski E, Libhaber E, Labidi S, Fischer D, Roentgen P, et al. Phenotyping and outcome on contemporary management in a German cohort of patients with peripartum cardiomyopathy. Basic Res Cardiol 2013;108: 366. (Level II-2)
106. Blauwet LA, Cooper LT. Diagnosis and management of peripartum cardiomyopathy. Heart 2011;97:1970–81. (Level III)
107. Brar SS, Khan SS, Sandhu GK, Jorgensen MB, Parikh N, Hsu JW, et al. Incidence, mortality, and racial differences in peripartum cardiomyopathy. Am J Cardiol 2007;100: 302–4. (Level II-2)
108. Gentry MB, Dias JK, Luis A, Patel R, Thornton J, Reed GL. African-American women have a higher risk for developing peripartum cardiomyopathy. J Am Coll Cardiol 2010;55:654–9. (Level II-2)
109. Goland S, Modi K, Hatamizadeh P, Elkayam U. Differences in clinical profile of African-American women with peripartum cardiomyopathy in the United States. J Card Fail 2013;19:214–8. (Level II-2)
110. Irizarry OC, Levine LD, Lewey J, Boyer T, Riis V, Elovitz MA, et al. Comparison of clinical characteristics and outcomes of peripartum cardiomyopathy between African American and non-African American women. JAMA Cardiol 2017;2:1256–60. (Level II-2)
111. Elkayam U, Tummala PP, Rao K, Akhter MW, Karaalp IS, Wani OR, et al. Maternal and fetal outcomes of subsequent pregnancies in women with peripartum cardiomyopathy [published erratum appears in N Engl J Med 2001; 345:552]. N Engl J Med 2001;344:1567–71. (Level II-2)
112. Fett JD, Fristoe KL, Welsh SN. Risk of heart failure relapse in subsequent pregnancy among peripartum cardiomyopathy mothers. Int J Gynaecol Obstet 2010;109: 34–6. (Level II-2)
113. Codsi E, Rose CH, Blauwet LA. Subsequent pregnancy outcomes in patients with peripartum cardiomyopathy. Obstet Gynecol 2018;131:322–7. (Level II-2)
114. Sliwa K, Hilfiker-Kleiner D, Petrie MC, Mebazaa A, Pieske B, Buchmann E, et al. Current state of knowledge on aetiology, diagnosis, management, and therapy of peripartum cardiomyopathy: a position statement from the Heart Failure Association of the European Society of Cardiology Working Group on peripartum cardiomyopathy. Eur J Heart Fail 2010;12:767–78. (Level III)
115. Hilfiker-Kleiner D, Haghikia A, Berliner D, Vogel-Claussen J, Schwab J, Franke A, et al. Bromocriptine for the treatment of peripartum cardiomyopathy: a multicentre randomized study. Eur Heart J 2017;38:2671–9. (Level I)
116. Safe prevention of the primary cesarean delivery. Obstetric Care Consensus No. 1. American College of Obstetricians and Gynecologists. Obstet Gynecol 2014;123:693–711. (Level III)
117. Habli M, O'Brien T, Nowack E, Khoury S, Barton JR, Sibai B. Peripartum cardiomyopathy: prognostic factors for long-term maternal outcome. Am J Obstet Gynecol 2008;199:415.e1–5. (Level II-2)
118. Smilowitz NR, Gupta N, Guo Y, Zhong J, Weinberg CR, Reynolds HR, et al. Acute myocardial infarction during pregnancy and the puerperium in the United States. Mayo Clin Proc 2018;93:1404–14. (Level II-2)
119. Elkayam U, Jalnapurkar S, Barakkat MN, Khatri N, Kealey AJ, Mehra A, et al. Pregnancy-associated acute myocardial infarction: a review of contemporary experience in 150 cases between 2006 and 2011. Circulation 2014;129: 1695–702. (Level III)
120. Firoz T, Magee LA. Acute myocardial infarction in the obstetric patient. Obstet Med 2012;5:50–7. (Level III)
121. Lee C, Saw J. Very early antepartum pregnancy-associated spontaneous coronary artery dissection case report. Cardiovasc Diagn Ther 2018;8:512–5. (Level III)
122. Tweet MS, Kok SN, Hayes SN. Spontaneous coronary artery dissection in women: what is known and what is yet to be understood. Clin Cardiol 2018;41:203–10. (Level III)
123. Havakuk O, Goland S, Mehra A, Elkayam U. Pregnancy and the risk of spontaneous coronary artery dissection: an analysis of 120 contemporary cases. Circ Cardiovasc Interv 2017;10:e004941. (Level III)
124. Lipman SS, Wong JY, Arafeh J, Cohen SE, Carvalho B. Transport decreases the quality of cardiopulmonary resuscitation during simulated maternal cardiac arrest. Anesth Analg 2013;116:162–7. (Level I)
125. Jeejeebhoy FM, Zelop CM, Lipman S, Carvalho B, Joglar J, Mhyre JM, et al. Cardiac arrest in pregnancy: a scientific statement from the American Heart Association. American Heart Association Emergency Cardiovascular Care Committee, Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation, Council on Cardiovascular Diseases in the Young, and Council on Clinical Cardiology. Circulation 2015;132:1747–73. (Level III)
126. Mhyre JM, Tsen LC, Einav S, Kuklina EV, Leffert LR, Bateman BT. Cardiac arrest during hospitalization for delivery in the United States, 1998-2011. Anesthesiology 2014;120:810–8. (Level II-3)
127. Kundra P, Khanna S, Habeebullah S, Ravishankar M. Manual displacement of the uterus during Caesarean section. Anaesthesia 2007;62:460–5. (Level I)

128. Zelop CM, Einav S, Mhyre JM, Martin S. Cardiac arrest during pregnancy: ongoing clinical conundrum. Am J Obstet Gynecol 2018;219:52–61. (Level III)

129. Rose CH, Faksh A, Traynor KD, Cabrera D, Arendt KW, Brost BC. Challenging the 4- to 5-minute rule: from perimortem cesarean to resuscitative hysterotomy. Am J Obstet Gynecol 2015;213:653–6, 653.e1. (Level III)

130. Beckett VA, Knight M, Sharpe P. The CAPS Study: incidence, management and outcomes of cardiac arrest in pregnancy in the UK: a prospective, descriptive study. BJOG 2017;124:1374–81. (Level II-2)

131. Benson MD, Padovano A, Bourjeily G, Zhou Y. Maternal collapse: challenging the four-minute rule. EBioMedicine 2016;6:253–7. (Level III)

132. Stout KK, Daniels CJ, Aboulhosn JA, Bozkurt B, Broberg CS, Colman JM, et al. 2018 AHA/ACC guideline for the management of adults with congenital heart disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines [preprint]. J Am Coll Cardiol 2018; DOI: 10.1016/j.jacc.2018.08.1028. (Level III)

133. Drenthen W, Pieper PG, Roos-Hesselink JW, van Lottum WA, Voors AA, Mulder BJ, et al. Outcome of pregnancy in women with congenital heart disease: a literature review. ZAHARA Investigators. J Am Coll Cardiol 2007;49:2303–11. (Systematic Review)

134. Peyvandi S, Ingall E, Woyciechowski S, Garbarini J, Mitchell LE, Goldmuntz E. Risk of congenital heart disease in relatives of probands with conotruncal cardiac defects: an evaluation of 1,620 families. Am J Med Genet A 2014;164A:1490–5. (Level II-2)

135. Cauldwell M, Steer P, Sterrenburg M, Wallace S, Malin G, Ulivi G, et al. Birth weight in pregnancies complicated by maternal heart disease [preprint]. Heart 2018; DOI: 10.1136/heartjnl-2018–313551. (Level II-2)

136. Low-dose aspirin use during pregnancy. ACOG Committee Opinion No. 743. American College of Obstetricians and Gynecologists. Obstet Gynecol 2018;132:e44–52. (Level III)

137. Whelton PK, Carey RM, Aronow WS, Casey DE Jr, Collins KJ, Dennison Himmelfarb C, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines [published erratum appears in J Am Coll Cardiol 2018; 71:2275–9]. J Am Coll Cardiol 2018;71:e127–248. (Level III)

138. Gestational hypertension and preeclampsia. ACOG Practice Bulletin No. 202. American College of Obstetricians and Gynecologists. Obstet Gynecol 2019;133:e1–25. (Level III)

139. Physical activity and exercise during pregnancy and the postpartum period. Committee Opinion No. 650. American College of Obstetricians and Gynecologists. Obstet Gynecol 2015;126:e135–42. (Level III)

140. Ruys TP, Roos-Hesselink JW, Pijuan-Domenech A, Vasario E, Gaisin IR, Iung B, et al. Is a planned caesarean section in women with cardiac disease beneficial? ROPAC investigators. Heart 2015;101:530–6. (Level II-2)

141. Horlocker TT, Vandermeuelen E, Kopp SL, Gogarten W, Leffert LR, Benzon HT. Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (Fourth Edition) [published erratum appears in Reg Anesth Pain Med 2018;43:566]. Reg Anesth Pain Med 2018;43:263–309. (Level III)

142. Leffert L, Butwick A, Carvalho B, Arendt K, Bates SM, Friedman A, et al. The Society for Obstetric Anesthesia and Perinatology Consensus Statement on the anesthetic management of pregnant and postpartum women receiving thromboprophylaxis or higher dose anticoagulants. Members of the SOAP VTE Taskforce. Anesth Analg 2018;126:928–44. (Level III)

143. Tanaka H, Kamiya C, Katsuragi S, Tanaka K, Yoshimatsu J, Ikeda T. Effect of epidural anesthesia in labor; pregnancy with cardiovascular disease. Taiwan J Obstet Gynecol 2018;57:190–3. (Level II-2)

144. Main EK, McCain CL, Morton CH, Holtby S, Lawton ES. Pregnancy-related mortality in California: causes, characteristics, and improvement opportunities. Obstet Gynecol 2015;125:938–47. (Level III)

145. Ruys TP, Cornette J, Roos-Hesselink JW. Pregnancy and delivery in cardiac disease. J Cardiol 2013;61:107–12. (Level III)

146. Khairy P, Ionescu-Ittu R, Mackie AS, Abrahamowicz M, Pilote L, Marelli AJ. Changing mortality in congenital heart disease. J Am Coll Cardiol 2010;56:1149–57. (Level II-2)

147. Kuklina EV, Callaghan WM. Cardiomyopathy and other myocardial disorders among hospitalizations for pregnancy in the United States: 2004-2006. Obstet Gynecol 2010;115:93–100. (Level II-3)

148. Roth A, Elkayam U. Acute myocardial infarction associated with pregnancy. J Am Coll Cardiol 2008;52:171–80. (Level III)

149. Overcash RT, Somers AT, LaCoursiere DY. Enoxaparin dosing after cesarean delivery in morbidly obese women. Obstet Gynecol 2015;125:1371–6. (Level II-1)

150. Stephenson ML, Serra AE, Neeper JM, Caballero DC, McNulty J. A randomized controlled trial of differing doses of postcesarean enoxaparin thromboprophylaxis in obese women. J Perinatol 2016;36:95–9. (Level I)

151. Optimizing support for breastfeeding as part of obstetric practice. ACOG Committee Opinion No. 756. American College of Obstetricians and Gynecologists. Obstet Gynecol 2018;132:e187–96. (Level III)

152. Kearney L, Wright P, Fhadil S, Thomas M. Postpartum cardiomyopathy and considerations for breastfeeding. Card Fail Rev 2018;4:112–8. (Level III)

153. Lupton SJ, Chiu CL, Lujic S, Hennessy A, Lind JM. Association between parity and breastfeeding with maternal high blood pressure. Am J Obstet Gynecol 2013;208:454.e1–7. (Level II-2)

154. Schwarz EB, Ray RM, Stuebe AM, Allison MA, Ness RB, Freiberg MS, et al. Duration of lactation and risk factors for maternal cardiovascular disease. Obstet Gynecol 2009;113:974–82. (Level II-2)

155. Curtis KM, Tepper NK, Jatlaoui TC, Berry-Bibee E, Horton LG, Zapata LB, et al. U.S. medical eligibility criteria for contraceptive use, 2016. MMWR Recomm Rep 2016; 65(RR-3):1–104. (Level III)

156. World Health Organization. Medical eligibility criteria for contraceptive use. 5th ed. Geneva: WHO; 2015. (Level III)

157. Thorne S, Nelson-Piercy C, MacGregor A, Gibbs S, Crowhurst J, Panay N, et al. Pregnancy and contraception in heart disease and pulmonary arterial hypertension. J Fam Plann Reprod Health Care 2006;32:75–81. (Level III)

158. Long-acting reversible contraception: implants and intrauterine devices. Practice Bulletin No. 186. American College of Obstetricians and Gynecologists. Obstet Gynecol 2017;130:e251–69. (Level III)

159. Immediate postpartum long-acting reversible contraception. Committee Opinion No. 670. American College of Obstetricians and Gynecologists. Obstet Gynecol 2016; 128:e32–7. (Level III)

160. Trussell J. Contraceptive failure in the United States. Contraception 2011;83:397–404. (Level III)

161. American College of Obstetricians and Gynecologists. Guidelines for women's health care: a resource manual. 4th ed. Washington, DC: American College of Obstetricians and Gynecologists; 2014. (Level III)

162. Cardiovascular disease and use of oral and injectable progestogen-only contraceptives and combined injectable contraceptives. Results of an international, multicenter, case–control study. World Health Organization Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception. Contraception 1998;57:315–24. (Level II-2)

163. Depot medroxyprogesterone acetate and bone effects. Committee Opinion No. 602. American College of Obstetricians and Gynecologists. Obstet Gynecol 2014;123: 1398–402. (Level III)

164. Sonmezer M, Atabekoglu C, Cengiz B, Dokmeci F, Cengiz SD. Depot-medroxyprogesterone acetate in anticoagulated patients with previous hemorrhagic corpus luteum. Eur J Contracept Reprod Health Care 2005;10:9–14. (Level III)

165. Gillum LA, Mamidipudi SK, Johnston SC. Ischemic stroke risk with oral contraceptives: a meta-analysis. Jama 2000;284:72–8. (Meta-Analysis)

166. Khader YS, Rice J, John L, Abueita O. Oral contraceptives use and the risk of myocardial infarction: a meta-analysis. Contraception 2003;68:11–7. (Systematic Review and Meta-Analysis)

167. Tanis BC, van den Bosch MA, Kemmeren JM, Cats VM, Helmerhorst FM, Algra A, et al. Oral contraceptives and the risk of myocardial infarction. N Engl J Med 2001;345: 1787–93. (Level II-2)

168. Lidegaard O, Edstrom B, Kreiner S. Oral contraceptives and venous thromboembolism: a five-year national case–control study. Contraception 2002;65:187–96. (Level II-2)

169. Lubianca JN, Moreira LB, Gus M, Fuchs FD. Stopping oral contraceptives: an effective blood pressure-lowering intervention in women with hypertension. J Hum Hypertens 2005;19:451–5. (Level II-2)

170. Tepper NK, Paulen ME, Marchbanks PA, Curtis KM. Safety of contraceptive use among women with peripartum cardiomyopathy: a systematic review. Contraception 2010;82:95–101. (Systematic Review)

171. World Health Organization Department of Reproductive Health and Research, (WHO/RHR), Johns Hopkins Bloomberg School of Public Health/Center for Communication Programs (CCP), Knowledge for Health Project. Family planning: a global handbook for providers (2018 update). 3rd ed. Baltimore (MD): CCP; Geneva: WHO; 2018. (Level III)

172. Benefits and risks of sterilization. Practice Bulletin No. 133. American College of Obstetricians and Gynecologists. Obstet Gynecol 2013;121:392–404. (Level III)

173. Amory JK. Male contraception. Fertil Steril 2016;106: 1303–9. (Level III)

174. Fried M, Krska Z, Danzig V. Does the laparoscopic approach significantly affect cardiac functions in laparoscopic surgery? Pilot study in non-obese and morbidly obese patients. Obes Surg 2001;11:293–6. (Level II-1)

175. Safran DB, Orlando R 3rd. Physiologic effects of pneumoperitoneum. Am J Surg 1994;167:281–6. (Level III)

176. Ozdemir-van Brunschot DM, van Laarhoven KC, Scheffer GJ, Pouwels S, Wever KE, Warle MC. What is the evidence for the use of low-pressure pneumoperitoneum? A systematic review. Surg Endosc 2016;30:2049–65. (Systematic Review & Meta-Analysis)

177. Martin A, Payne R, Wilson EC. Long-term costs and health consequences of issuing shorter duration prescriptions for patients with chronic health conditions in the English NHS. Appl Health Econ Health Policy 2018;16: 317–30. (Level III)

178. Callen J, Pinelli J. A review of the literature examining the benefits and challenges, incidence and duration, and barriers to breastfeeding in preterm infants. Adv Neonatal Care 2005;5:92. (Level III)

179. Lotterman JH, Lorenz JM, Bonanno GA. You can't take your baby home yet: a longitudinal study of psychological symptoms in mothers of infants hospitalized in the NICU. J Clin Psychol Med Settings 2019;26:116. (Level II-3)

180. Mongraw-Chaffin ML, Cirillo PM, Cohn BA. Preeclampsia and cardiovascular disease death: prospective evidence from the child health and development studies cohort. Hypertension 2010;56:166–71. (Level II-2)

181. Ray JG, Vermeulen MJ, Schull MJ, Redelmeier DA. Cardiovascular health after maternal placental syndromes (CHAMPS): population-based retrospective cohort study. Lancet 2005;366:1797–803. (Level II-2)

182. Riise HK, Sulo G, Tell GS, Igland J, Nygard O, Iversen AC, et al. Association between gestational hypertension and risk of cardiovascular disease among 617 589 Norwegian women. J Am Heart Assoc 2018;7:e008337. (Level II-2)

183. Wu P, Gulati M, Kwok CS, Wong CW, Narain A, O'Brien S, et al. Preterm delivery and future risk of maternal cardiovascular disease: a systematic review and meta-analysis. J Am

Heart Assoc 2018;7:e007809. (Systematic Review and Meta-Analysis)

184. Coutinho T, Lamai O, Nerenberg K. Hypertensive disorders of pregnancy and cardiovascular diseases: current knowledge and future directions. Curr Treat Options Cardiovasc Med 2018;20:56. (Level III)

185. Bellamy L, Casas JP, Hingorani AD, Williams DJ. Pre-eclampsia and risk of cardiovascular disease and cancer in later life: systematic review and meta-analysis. BMJ 2007;335:974. (Systematic Review and Meta-Analysis)

186. Brouwers L, van der Meiden-van Roest AJ, Savelkoul C, Vogelvang TE, Lely AT, Franx A, et al. Recurrence of pre-eclampsia and the risk of future hypertension and cardiovascular disease: a systematic review and meta-analysis. BJOG 2018;125:1642–54. (Systematic Review and Meta-Analysis)

187. Cunningham MW Jr, LaMarca B. Risk of cardiovascular disease, end-stage renal disease, and stroke in postpartum women and their fetuses after a hypertensive pregnancy. Am J Physiol Regul Integr Comp Physiol 2018;315: R521–8. (Level III)

188. Nahum Sacks K, Friger M, Shoham-Vardi I, Spiegel E, Sergienko R, Landau D, et al. Prenatal exposure to pre-eclampsia as an independent risk factor for long-term cardiovascular morbidity of the offspring. Pregnancy Hypertens 2018;13:181–6. (Level II-2)

189. Smith GN, Walker MC, Liu A, Wen SW, Swansburg M, Ramshaw H, et al. A history of preeclampsia identifies women who have underlying cardiovascular risk factors. Pre-Eclampsia New Emerging Team, (PE-NET). Am J Obstet Gynecol 2009;200:58.e1–8. (Level II-2)

190. Cusimano MC, Pudwell J, Roddy M, Cho CK, Smith GN. The maternal health clinic: an initiative for cardiovascular risk identification in women with pregnancy-related complications. Am J Obstet Gynecol 2014;210:438.e1–9. (Level II-2)

191. Smith GN, Pudwell J, Roddy M. The maternal health clinic: a new window of opportunity for early heart disease risk screening and intervention for women with pregnancy complications. J Obstet Gynaecol Can 2013;35: 831–9. (Level III)

192. Spaan J, Peeters L, Spaanderman M, Brown M. Cardiovascular risk management after a hypertensive disorder of pregnancy. Hypertension 2012;60:1368–73. (Level III)

193. Wang X, Ouyang Y, Wang Z, Zhao G, Liu L, Bi Y. Obstructive sleep apnea and risk of cardiovascular disease and all-cause mortality: a meta-analysis of prospective cohort studies. Int J Cardiol 2013;169:207–14. (Meta-Analysis)

194. Bourjeily G, Danilack VA, Bublitz MH, Lipkind H, Muri J, Caldwell D, et al. Obstructive sleep apnea in pregnancy is associated with adverse maternal outcomes: a national cohort. Sleep Med 2017;38:50–7. (Level II-2)

195. Bertisch SM, Pollock BD, Mittleman MA, Buysse DJ, Bazzano LA, Gottlieb DJ, et al. Insomnia with objective short sleep duration and risk of incident cardiovascular disease and all-cause mortality: Sleep Heart Health Study. Sleep 2018;41(6): zsy047. (Level II-2)

196. Liu L, Su G, Wang S, Zhu B. The prevalence of obstructive sleep apnea and its association with pregnancy-related health outcomes: a systematic review and meta-analysis [preprint]. Sleep Breath 2018; DOI: 10. 1007/s11325-018-1714-7. (Systematic Review and Meta-Analysis)

197. Khattak HK, Hayat F, Pamboukian SV, Hahn HS, Schwartz BP, Stein PK. Obstructive sleep apnea in heart failure: review of prevalence, treatment with continuous positive airway pressure, and prognosis. Tex Heart Inst J 2018;45:151–61. (Level III)

198. Lloyd-Jones DM, Hong Y, Labarthe D, Mozaffarian D, Appel LJ, Van Horn L, et al. Defining and setting national goals for cardiovascular health promotion and disease reduction: the American Heart Association's strategic Impact Goal through 2020 and beyond. American Heart Association Strategic Planning Task Force and Statistics Committee. Circulation 2010;121:586–613. (Level III)

199. Villamor E, Cnattingius S. Interpregnancy weight change and risk of adverse pregnancy outcomes: a population-based study. Lancet 2006;368:1164–70. (Level II-2)

200. Gestational diabetes mellitus. ACOG Practice Bulletin No. 190. American College of Obstetricians and Gynecologists. Obstet Gynecol 2018;131:e49–64. (Level III)

201. Stuebe AM, Schwarz EB. The risks and benefits of infant feeding practices for women and their children. J Perinatol 2010;30:155–62. (Level III)

202. Dawson AJ, Krastev Y, Parsonage WA, Peek M, Lust K, Sullivan EA. Experiences of women with cardiac disease in pregnancy: a systematic review and metasynthesis. BMJ Open 2018;8:022755. (Systematic Review and Meta-Analysis)

The MEDLINE database, the Cochrane Library, and the American College of Obstetricians and Gynecologists' own internal resources and documents were used to conduct a literature search to locate relevant articles published between January 2010–February 2019. The search was restricted to articles published in the English language. Priority was given to articles reporting results of original research, although review articles and commentaries also were consulted. Abstracts of research presented at symposia and scientific conferences were not considered adequate for inclusion in this document. Guidelines published by organizations or institutions such as the National Institutes of Health and the American College of Obstetricians and Gynecologists were reviewed, and additional studies were located by reviewing bibliographies of identified articles. When reliable research was not available, expert opinions from obstetrician–gynecologists were used.

Studies were reviewed and evaluated for quality according to the method outlined by the U.S. Preventive Services Task Force:

- I Evidence obtained from at least one properly designed randomized controlled trial.
- II-1 Evidence obtained from well-designed controlled trials without randomization.
- II-2 Evidence obtained from well-designed cohort or case–control analytic studies, preferably from more than one center or research group.
- II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.
- III Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Based on the highest level of evidence found in the data, recommendations are provided and graded according to the following categories:

Level A—Recommendations are based on good and consistent scientific evidence.

Level B—Recommendations are based on limited or inconsistent scientific evidence.

Level C—Recommendations are based primarily on consensus and expert opinion.

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Prelabor Rupture of Membranes

Preterm birth occurs in approximately 10% of all births in the United States and is a major contributor to perinatal morbidity and mortality (1–3). Prelabor rupture of membranes (PROM) that occurs preterm complicates approximately 2–3% of all pregnancies in the United States, representing a significant proportion of preterm births, whereas term PROM occurs in approximately 8% of pregnancies (4–6). The optimal approach to assessment and treatment of women with term and preterm PROM remains challenging. Management decisions depend on gestational age and evaluation of the relative risks of delivery versus the risks (eg, infection, abruptio placentae, and umbilical cord accident) of expectant management when pregnancy is allowed to progress to a later gestational age. The purpose of this document is to review the current understanding of this condition and to provide management guidelines that have been validated by appropriately conducted outcome-based research when available. Additional guidelines on the basis of consensus and expert opinion also are presented. This Practice Bulletin is updated to include information about diagnosis of PROM, expectant management of PROM at term, and timing of delivery for patients with preterm PROM between 34 0/7 weeks of gestation and 36 6/7 weeks of gestation.

Background

The definition of *prelabor rupture of membranes* is rupture of membranes before the onset of labor. Membrane rupture before labor that occurs before 37 weeks of gestation is referred to as "preterm prelabor rupture of membranes." Management of preterm and term PROM is influenced by gestational age and the presence of complicating factors such as clinical infection, abruptio placentae, labor, or abnormal fetal testing. An accurate assessment of gestational age and knowledge of the maternal, fetal, and neonatal risks are essential to appropriate evaluation, counseling, and care of patients with PROM.

Etiology of Prelabor Rupture of Membranes

Membrane rupture may occur for a variety of reasons. Although membrane rupture at term can result from a normal physiologic weakening of the membranes combined with shearing forces created by uterine contractions, preterm PROM can result from a wide array of pathologic mechanisms that act individually or in concert (7, 8). Intraamniotic infection has been shown to be commonly associated with preterm PROM, especially at earlier gestational ages (9, 10).

A history of preterm PROM is a major risk factor for preterm PROM or preterm labor in a subsequent pregnancy (11–13). Additional risk factors associated with preterm PROM are similar to those associated with spontaneous preterm birth and include short cervical length, second-trimester and third-trimester bleeding, low body mass index, low socioeconomic status, cigarette smoking, and illicit drug use (14–17). Although each of these risk factors is associated with preterm PROM, the condition often occurs in the absence of recognized risk factors or an obvious cause.

Term Prelabor Rupture of Membranes

At term, PROM complicates approximately 8% of pregnancies and generally is followed by the prompt

onset of spontaneous labor and delivery (6). In a large randomized trial, one half of women with term PROM who were managed expectantly had an interval of membrane rupture to delivery of 33 hours, and 95% gave birth within 94–107 hours of membrane rupture with the use of oxytocin or prostaglandin when, during expectant management, induction was indicated or an endpoint of 4 days of expectant management was reached (18). The most significant maternal consequence of term PROM is intrauterine infection, the risk of which increases with the duration of membrane rupture.

Preterm Prelabor Rupture of Membranes

Regardless of obstetric management or clinical presentation, birth within 1 week of membrane rupture occurs in at least one half of patients with preterm PROM (8). Latency after membrane rupture is inversely correlated with the gestational age at membrane rupture (19). Cessation of amniotic fluid leakage with restoration of normal amniotic fluid volume may infrequently occur in the setting of spontaneous preterm PROM but can be associated with favorable outcomes (20–22).

Among women with preterm PROM, clinically evident intraamniotic infection occurs in 15–35% of cases and postpartum infection occurs in approximately 15–25% of cases. The incidence of infection is higher at earlier gestational ages (9, 23–25). Abruptio placentae complicates 2–5% of pregnancies with preterm PROM (26, 27).

The most significant risks to the fetus after preterm PROM are complications of prematurity. Respiratory distress has been reported to be the most common complication of preterm birth (28, 29). Sepsis, intraventricular hemorrhage, and necrotizing enterocolitis also are associated with prematurity but are less common near term. Preterm PROM has been associated with an increased risk of neurodevelopmental impairment (30–32), and early gestational age at membrane rupture also has been associated with an increased risk of neonatal white matter damage (33). However, there are no data that suggest that immediate delivery after presentation with PROM will avert these risks. A large cohort study suggests that prolonged latency duration, when adjusted for gestational age, does not worsen neonatal prognosis with respect to survival, survival without morbidity, and early-onset sepsis (34).

Periviable Prelabor Rupture of Membranes

Rupture of the membranes before viability occurs in less than 1% of pregnancies. The probability of neonatal death and morbidity associated with PROM decreases with longer latency and advancing gestational age (35, 36). In a review of periviable PROM occurring between 14 weeks of gestation and 24 weeks of gestation, perinatal deaths were more or less equally divided between stillbirths and neonatal deaths. Neonatal survival rates in patients expectantly managed for periviable PROM were much higher following membrane rupture after 22 weeks of gestation compared with membrane rupture before 22 weeks of gestation (57.7% versus 14.4%, respectively) (37). A second retrospective study of patients between 20 weeks of gestation and 24 weeks of gestation with periviable PROM who elected expectant management showed similar results, with neonatal survival of 22% of the newborns of patients with membrane rupture before 22 weeks of gestation and 58% for those with membrane rupture at 22 and 23 weeks of gestation (36). Most studies of second-trimester and periviable PROM are retrospective and include only expectantly managed cases. Thus, they likely overestimate survival rates because of selection bias. Survival data may vary by institution.

Significant maternal complications that occur after periviable PROM include intraamniotic infection, endometritis, abruptio placentae, and retained placenta (37). One center found that 14% of women with periviable PROM experienced significant maternal morbidity, including sepsis, transfusion, hemorrhage, infection, acute renal injury, and readmission (38). Although it occurs infrequently, life-threatening maternal infection may complicate expectant management of periviable PROM. Maternal sepsis is reported in approximately 1–5% of cases (36–38), and isolated maternal deaths due to infection have been reported in this setting.

Latency periods appear to be prolonged with second-trimester preterm PROM compared with PROM during later gestational ages. However, 40–50% of patients with periviable PROM will give birth within the first week and approximately 70–80% will give birth within 2–5 weeks after membrane rupture (36, 37, 39, 40).

The rate of pulmonary hypoplasia after preterm PROM before 24 weeks of gestation varies widely among reports and may be subject to variable reporting but is in the range of 2–20%. (35, 41–43). Pulmonary hypoplasia is associated with a high risk of mortality (37) but is rarely lethal when rupture of membranes occurs at or after 23–24 weeks of gestation (44), presumably because alveolar growth adequate to support postnatal development already has occurred. Early gestational age at membrane rupture and low residual amniotic fluid volume are the primary determinants of the incidence of pulmonary hypoplasia (46, 47). One retrospective cohort study demonstrated that persistent oligohydramnios in

cases of periviable PROM may correlate with lower survival rates and adverse neurodevelopmental outcomes (48). Prolonged oligohydramnios also can result in fetal deformations, including Potter-like facies (eg, low-set ears and epicanthal folds) and limb contractures or other positioning abnormalities. The reported frequency of skeletal deformations varies widely (1.5–38%) but many of these resolve with postnatal growth and physical therapy (37, 49).

Clinical Considerations and Recommendations

▶ *How is prelabor rupture of membranes diagnosed?*

Most cases of PROM can be diagnosed on the basis of the patient's history and physical examination. Examination should be performed in a manner that minimizes the risk of introducing infection. Because digital cervical examinations increase the risk of infection and add little information to results available with speculum examination, they generally should be avoided unless the patient appears to be in active labor or delivery seems imminent (50, 51). Sterile speculum examination provides an opportunity to inspect for cervicitis and prolapse of the umbilical cord or fetal parts, assess cervical dilatation and effacement, and obtain cultures as appropriate.

The diagnosis of membrane rupture typically is confirmed by conventional clinical assessment, which includes the visualization of amniotic fluid passing from the cervical canal and pooling in the vagina, a simple pH test of vaginal fluid, or arborization (ferning) of dried vaginal fluid, which is identified under microscopic evaluation. The normal pH of vaginal secretions is generally 3.8–4.5 whereas amniotic fluid usually has a pH of 7.1–7.3. False-positive test results may occur in the presence of blood or semen, alkaline antiseptics, certain lubricants, trichomonas, or bacterial vaginosis. Alternatively, false-negative test results may occur with prolonged membrane rupture and minimal residual fluid.

In equivocal cases, additional tests may aid in the diagnosis. Ultrasonographic examination of amniotic fluid volume may be a useful adjunct but is not diagnostic. Fetal fibronectin is a sensitive but nonspecific test for ruptured membranes; a negative test result suggests intact membranes, but a positive test result is not diagnostic of PROM (52). Several commercially available tests for amniotic proteins are currently on the market, with reported high sensitivity for PROM (53, 54). However, false-positive test result rates of 19–30% have been reported in patients with clinically intact membranes and symptoms of labor (55, 56). These tests are appealing in light of the requirements of regulatory bodies related to Clinical Laboratory Improvement Amendments of 1988 quality standards on the point-of-care methods of clinical assessment such as Nitrazine and fern testing. The studies evaluating these protein tests are problematic because most of them use conventional clinical assessment (pooling, ferning, pH) as controls or gold standards for the diagnosis of rupture of membranes, calling into question their utility in equivocal cases (53, 54, 57, 58). Additionally, the U.S. Food and Drug Administration released a letter to health care providers in response to adverse events related to their use, including 13 fetal deaths and multiple reports of health complications in pregnant women. The U.S. Food and Drug Administration letter reminded health care providers that these tests should not be used without other clinical assessments because of concerns about "misuse, overreliance, and inaccurate interpretation of lab test results from rupture of membranes tests used to detect rupture of membranes in pregnant women. These can lead to serious adverse events, including fetal death, infection, and other health complications in pregnant women." (59) At most these test kits should be considered selectively relative to standard methods of diagnosis.

If the diagnosis remains unclear after a full evaluation, and if the benefits of the procedure outweigh the risks, membrane rupture can be diagnosed with ultrasonographically guided transabdominal instillation of indigo carmine dye, followed by the passage of blue-dyed fluid into the vagina, which is documented by a stained tampon or pad that is removed 20–30 minutes later. It is important to note that maternal urine also will turn blue or blue-green and should not be confused with amniotic fluid. Recent shortages of indigo carmine dye have complicated the availability of this procedure, and alternatives, such as fluorescein, have been suggested (60).

▶ *What does initial management involve once prelabor rupture of membranes has been confirmed?*

In all patients with PROM, gestational age, fetal presentation, and fetal well-being (61) should be determined. The examination should evaluate for evidence of intrauterine infection and abruptio placentae. If results are not already available and if an indication for treatment is not already present, culture for group B streptococci (GBS) should be obtained when expectant management is being considered.

In patients with preterm PROM, an initial period of electronic fetal heart rate monitoring and uterine activity

monitoring offers the opportunity to identify abnormal fetal heart rate tracings and to evaluate for contractions (62). Management after confirmation of the diagnosis of PROM is dependent primarily on gestational age and is discussed in more detail in the following paragraphs. Abnormal fetal testing or evidence of intraamniotic infection are indications for delivery. Vaginal bleeding should raise concern for abruptio placentae, which should prompt consideration of delivery, with the decision based on fetal status, the amount of bleeding, and gestational age. In general, digital examination should be used sparingly and judiciously.

▶ *What is the optimal method of initial management for a patient with prelabor rupture of membranes at term?*

Gestational age and fetal position should be confirmed, and fetal heart rate monitoring should be used, to assess fetal status. Group B streptococcal prophylaxis should be given based on prior culture results or intrapartum risk factors if cultures have not been performed previously (63).

A meta-analysis of 23 randomized controlled trials (8,615 women) found that induction of labor reduced the time from rupture of membrane to birth and the rates of chorioamnionitis or endometritis, or both, and also reduced admission to the neonatal intensive care unit without increasing the rates of cesarean birth or operative vaginal delivery (6). The largest of these trials also found that women viewed induction of labor more positively than expectant management (18). Induction of labor with vaginal prostaglandins has been shown to be equally effective for labor induction compared with oxytocin but was associated with higher rates of chorioamnionitis (18). Infection also is a concern with mechanical methods of cervical ripening, such as the Foley catheter balloon, but there are insufficient data on which to base a firm recommendation for mechanical methods of cervical ripening in the setting of PROM. One trial comparing Foley catheter balloon with oxytocin to oxytocin alone in women with PROM demonstrated an increased risk with Foley balloon (8% compared with 0%, $P<.01$), though this was not seen in another similar trial (64, 65). A meta-analysis of four trials suggests that use of prophylactic antibiotics may reduce infection morbidity, but prompt induction of labor was not standard care in either study. Thus, there is insufficient evidence to justify the routine use of prophylactic antibiotics with PROM at term in the absence of an indication for GBS prophylaxis (66, 67).

Meta-analysis data indicate that patients with term PROM benefit from induction of labor compared with expectant management. Induction may help reduce infection in the woman and neonate without increasing the risk for cesarean birth (6). For women with PROM at 37 0/7 weeks of gestation or more, if spontaneous labor does not occur near the time of presentation in those who do not have contraindication to labor, labor induction should be recommended, although the choice of expectant management for a short period of time may be appropriately offered. In the cases in which expectant management is chosen, given that nearly 80% and 95% of patients start labor spontaneously within 12 hours and 24 hours respectively, a period of 12–24 hours of expectant management is reasonable as long as the clinical and fetal conditions are reassuring, and the patient is adequately counseled regarding the risks of prolonged PROM and the limitations of available data. For women who are GBS positive, administration of antibiotics for GBS prophylaxis should not be delayed while awaiting labor, and immediate induction rather than expectant management is recommended (63). During induction of labor with oxytocin, a sufficient period of adequate contractions (at least 12–18 hours) should be allowed for the latent phase of labor to progress before diagnosing failed induction and moving to cesarean birth (68–72).

▶ *When is delivery recommended for the preterm fetus in the presence of prelabor rupture of membranes?*

Abnormal results from fetal testing, clinical intraamniotic infection, and significant abruptio placentae are clear indications for delivery. Otherwise, gestational age is a primary factor when considering delivery versus expectant management (Box 1).

However, the optimal gestational age for delivery is unclear and controversial. A meta-analysis of 12 randomized controlled trials, including 3,617 women, concluded there was evidence to guide clinical practice toward expectant management regarding the risks and benefits of expectant management versus delivery in the setting of preterm PROM (73). Although there was no difference in neonatal sepsis between women who gave birth immediately compared with those managed expectantly, immediate birth had higher risks for neonatal respiratory distress, need for ventilation, neonatal mortality, neonatal intensive care unit admission, and likelihood of cesarean birth. In patients with no contraindications to continuing the pregnancy, such as abnormal results from fetal testing or intrauterine infection, expectant management likely provides benefit for the woman and newborn. Patients with preterm PROM before 34 0/7 weeks of gestation should be managed expectantly if no maternal or fetal contraindications exist (73, 74).

Box 1. Management of Prelabor Rupture of Membranes by Gestational Age Categories in Patients With Normal Antenatal Testing

Term (37 0/7 weeks of gestation or more)

- GBS prophylaxis as indicated
- Treat intraamniotic infection if present
- Proceed toward delivery (induction or cesarean as appropriate/indicated)

Late Preterm (34 0/7–36 6/7 weeks of gestation)

- Expectant management or proceed toward delivery (see text) (induction or cesarean as appropriate/indicated)
- Single-course of corticosteroids, if steroids not previously given, if proceeding with induction or delivery in no less than 24 hours and no more than 7 days, and no evidence of chorioamnionitis*
- GBS screening and prophylaxis as indicated
- Treat intraamniotic infection if present (and proceed toward delivery)

Preterm (24 0/7–33 6/7 weeks of gestation)

- Expectant management
- Antibiotics recommended to prolong latency if there are no contraindications
- Single-course of corticosteroids; insufficient evidence for or against rescue course
- Treat intraamniotic infection if present (and proceed to delivery)
- A vaginal–rectal swab for GBS culture should be obtained at the time of initial presentation and GBS prophylaxis administered as indicated.
- Magnesium sulfate for neuroprotection before anticipated delivery for pregnancies <32 0/7 weeks of gestation, if there are no contraindications†

Periviable (Less than 23–24 weeks of gestation)‡,§

- Patient counseling; consider neonatology and maternal–fetal medicine consultation
- Expectant management or induction of labor
- Antibiotics may be considered as early as 20 0/7 weeks of gestation
- GBS prophylaxis is not recommended before viability‖
- Corticosteroids are not recommended before viability‖
- Tocolysis is not recommended before viability‖
- Magnesium sulfate for neuroprotection is not recommended before viability†,‖

Abbreviation: GBS, group B streptococci.
*Do not delay delivery for steroids; steroids should not be administered for an imminent cesarean birth.
†Magnesium sulfate for neuroprotection in accordance with one of the larger studies.
‡The combination of birth weight, gestational age, and sex provide the best estimate of chances of survival and should be considered in individual cases.
§Periviable birth. Obstetric Care Consensus No. 6. American College of Obstetricians and Gynecologists. 2017;130:187–99.
‖May be considered for pregnant women as early as 23 0/7 weeks of gestation.

At 34 0/7 weeks of gestation and before 37 0/7 weeks of gestation, delivery has traditionally been recommended for all women with ruptured membranes. However, a recent large randomized trial of 1,839 women that evaluated immediate delivery (shortly after diagnosis and preferably within 24 hours) versus expectant management in patients with PROM between 34 0/7 weeks of gestation and 36 6/7 weeks of gestation suggests benefits to expectant management (75). Expectant management was according to local practice at participating centers, with 73% of patients managed in a hospital setting. There was no significant difference in the primary outcome—neonatal sepsis—or in the secondary outcome of composite neonatal morbidity. Infants in the immediate delivery group had higher rates of respiratory distress (relative risk [RR], 1.6; 95% CI, 1.1–2.3) and mechanical ventilation (RR, 1.4; 95% CI, 1.0–1.8) and spent more days in intensive care (4 days versus 2 days). However, maternal adverse outcomes, such as hemorrhage and infection, were approximately twofold higher with expectant management, although the rate of cesarean birth was lower (RR, 1.4; 95% CI, 1.2–1.7). According to the authors, the findings suggest that if expectant management is chosen, it should include careful monitoring of symptoms and signs of

maternal infection, chorioamnionitis, and antepartum hemorrhage. This monitoring may be done best in a hospital setting. An individual participant data meta-analysis of three trials showed similar results, with no difference in composite adverse neonatal outcome or neonatal sepsis when comparing expectant management with immediate delivery. In addition, immediate delivery resulted in higher rates of respiratory distress syndrome, intensive care admission, and cesarean birth (76). Either expectant management or immediate delivery in patients with PROM between 34 0/7 weeks of gestation and 36 6/7 weeks of gestation is a reasonable option, although the balance between benefit and risk, from both maternal and neonatal perspectives, should be carefully considered, and patients should be counseled clearly. Care should be individualized through shared decision making, and expectant management should not extend beyond 37 0/7 weeks of gestation. Latency antibiotics are not appropriate in this setting.

▶ *What general approaches are used in cases of preterm prelabor rupture of membranes managed expectantly?*

Expectant management of preterm PROM generally consists of hospital admission with periodic assessment for infection, abruptio placentae, umbilical cord compression, fetal well-being, and labor. There is no consensus on the optimal frequency of assessment, but an acceptable strategy would include periodic ultrasonographic monitoring of fetal growth and periodic fetal heart rate monitoring. A temperature elevation may indicate intrauterine infection. Prompt diagnosis of intraamniotic infection in preterm pregnancy requires a high index of suspicion because early signs and symptoms may be subtle. In the absence of fever, other clinical criteria, such as abdominal or fundal tenderness and maternal or fetal tachycardia, have variable sensitivity and specificity for diagnosing infection. Serial monitoring of leukocyte counts and other markers of inflammation have not been proved to be useful and are nonspecific when there is no clinical evidence of infection, especially if antenatal corticosteroids have been administered (77). Specific treatment considerations regarding tocolytics, corticosteroids, antibiotics, magnesium sulfate, and timing of delivery are discussed in detail below.

For cases of expectant management of periviable PROM, it is reasonable to evaluate and monitor such patients for a short period looking for signs of abnormalities as above. After a period of assessment in the hospital, outpatient management may be possible, as there is less concern for timely intervention for a periviable fetus. Expectant management of periviable PROM has significant maternal risks that are important to monitor carefully when choosing outpatient management. Such outpatient expectant management should involve frequent temperature evaluations, clear counseling on how to monitor for the signs and symptoms of abnormalities (eg, abdominal pain, vaginal bleeding, abnormal discharge), and frequent evaluations by a health care provider. Hospitalization often occurs around the time of viability when intervention for fetal indications is desired.

The use of 17-hydroxyprogesterone caproate to extend latency in cases of preterm PROM has been evaluated in two randomized trials. One trial involving 1,523 patients was stopped when a planned interim analysis suggested futility in continuing (78). There was no significant difference in interval to delivery or in composite adverse perinatal outcome, indicating that 17-hydroxyprogesterone caproate should not be used in patients with preterm PROM specifically for the purpose of extending latency. The second trial was stopped prematurely because of poor enrollment after 21 patients. This trial also did not find any benefit from 17-hydroxyprogesterone caproate (79). There are no data regarding the utility or safety of using vaginal progesterone in cases of preterm PROM. Given this lack of data and the theoretical risk of introducing infection with the administration of a daily vaginal drug in the presence of ruptured membranes, the use of vaginal progesterone is cases of preterm PROM is not recommended.

▶ *Should tocolytic agents be considered for patients with preterm prelabor rupture of membranes?*

The use of tocolytic agents in the setting of preterm PROM is controversial, and practice patterns among specialists vary widely (80). There are insufficient data to support or refute the use of tocolytic therapy in the setting of preterm PROM. A meta-analysis of eight trials evaluating the efficacy of tocolytic agents in preterm PROM is of limited use because women were only treated in two of the trials (81, 82) with latency antibiotics and corticosteroids, both of which have become part of standard management (83). The use of tocolytic therapy was associated with a longer latency period and a lower risk of delivery within 48 hours but also was associated with a higher risk of chorioamnionitis in pregnancies before 34 0/7 weeks of gestation. In summary, tocolytic agents may be associated with

a prolongation of pregnancy and an increased risk of chorioamnionitis without proven maternal or neonatal benefit, although their use has not been evaluated adequately with latency antibiotics and corticosteroids. In the setting of ruptured membranes with active labor, although tocolytic therapy has not been shown to prolong latency or improve neonatal outcomes, data are limited. Tocolytic agents can be considered in preterm PROM for steroid benefit to the neonate, especially at earlier gestational ages, or for maternal transport but should be used cautiously and avoided if there is evidence of infection or abruption. Tocolytic therapy is not recommended in the setting of preterm PROM between 34 0/7 weeks of gestation and 36 6/7 weeks of gestation.

▶ *Should antenatal corticosteroids be administered to patients with preterm prelabor rupture of membranes?*

The use of antenatal corticosteroids after preterm PROM has been evaluated in a number of clinical trials and has been shown to reduce neonatal mortality, respiratory distress syndrome, intraventricular hemorrhage, and necrotizing enterocolitis (84–86). Current data suggest that antenatal corticosteroids are not associated with increased risks of maternal or neonatal infection regardless of gestational age. A single course of corticosteroids is recommended for pregnant women between 24 0/7 weeks of gestation and 33 6/7 weeks of gestation and may be considered for pregnant women who are at risk of preterm birth within 7 days, including for those with ruptured membranes, as early as 23 0/7 weeks of gestation (87–89). A Cochrane meta-analysis reinforces the beneficial effect of this therapy regardless of membrane status and concludes that a single course of antenatal corticosteroids should be considered routine for all preterm deliveries (84).

Recent data indicate that administration of betamethasone in the late preterm period between 34 0/7 weeks of gestation and 36 6/7 weeks of gestation reduces respiratory morbidity in newborns (90). Although a subgroup analysis was not done, approximately 22% of study patients had preterm PROM. A single course of corticosteroids is recommended for pregnant women between 34 0/7 weeks of gestation and 36 6/7 weeks of gestation at risk of preterm birth within 7 days and who have not received a previous course of antenatal corticosteroids if proceeding with induction or delivery in no less than 24 hours and no more than 7 days (89). Late preterm administration of antenatal corticosteroids is not indicated in women diagnosed with clinical chorioamnionitis. Furthermore, delivery should not be delayed, and antenatal corticosteroids should not be used in the late preterm period (89).

There are no data that support the use of corticosteroids before viability, and administration of corticosteroids in this setting is not currently recommended. Weekly administration of corticosteroids has been associated with a reduction in birth weight and head circumference and is not recommended (91–93). Whether to administer a rescue course of corticosteroids with PROM at any gestational age is controversial, and there is insufficient evidence to make a recommendation for or against. A retrospective cohort study and a secondary analysis of a prospective cohort study suggest that corticosteroids do not increase the risk of chorioamnionitis (94, 95). If used as a rescue course, corticosteroids could be provided as early as 7 days from the prior dose, if indicated by the clinical scenario. A single repeat course of antenatal corticosteroids can be considered in women with preterm PROM who are less than 34 0/7 weeks of gestation, are at risk of preterm delivery within 7 days, and whose prior course of antenatal corticosteroids was administered more than 14 days previously. However, delivery should not be delayed to achieve a rescue course.

▶ *Should magnesium sulfate for fetal neuroprotection be administered to patients with preterm prelabor rupture of membranes?*

Randomized controlled trials have demonstrated that maternal administration of magnesium sulfate used for fetal neuroprotection when birth is anticipated before 32 0/7 weeks of gestation reduces the risk of cerebral palsy in surviving infants (RR, 0.71; 95% CI, 0.55–0.91) (96). In the largest of these trials, 85% of the women enrolled had preterm PROM between 24 weeks of gestation and 32 weeks of gestation (97). Magnesium sulfate administration for this indication does not appear to affect latency interval (98). The optimal treatment regimen for fetal neuroprotection remains unclear, and different regimens were used in different trials. With respect to the use of magnesium sulfate for fetal neuroprotection, hospitals should develop uniform and specific guidelines for their departments regarding inclusion criteria, treatment regimens, concurrent tocolytic therapy, and monitoring in accordance with one of the larger trials (97, 99, 100). Regardless of the treatment regimen used, women with preterm PROM before 32 0/7 weeks of gestation who are thought to be at risk of imminent delivery should be considered candidates for fetal neuroprotective treatment with magnesium sulfate (101).

▶ *Should antibiotics be administered to patients with preterm prelabor rupture of membranes?*

Administration of broad-spectrum antibiotics prolongs pregnancy, reduces maternal and neonatal infections, and reduces gestational age-dependent morbidity (23, 102, 103). The optimal antibiotic regimen is unclear because multiple regimens have demonstrated benefit. Based on available information, to reduce maternal and neonatal infections and gestational-age-dependent morbidity, a 7-day course of therapy of latency antibiotics with a combination of intravenous ampicillin and erythromycin followed by oral amoxicillin and erythromycin is recommended during expectant management of women with preterm PROM who are at less than 34 0/7 weeks of gestation (23, 102). The regimen used in the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network trial was intravenous ampicillin (2 g every 6 hours) and erythromycin (250 mg every 6 hours) for 48 hours followed by oral amoxicillin (250 mg every 8 hours) and erythromycin base (333 mg every 8 hours) (103). Some centers have replaced the use of erythromycin with azithromycin (such as a single oral dose of azithromycin 1 g) in situations in which erythromycin is not available or not tolerated, and this substitution is a suitable alternative (104, 105). One retrospective cohort study did not find a difference in latency or secondary outcomes such as neonatal survival, sepsis, or respiratory distress between the two medications (106). Another retrospective cohort study that also compared erythromycin and azithromycin likewise found no difference in latency (107). Further, there may be cost benefits to the use of azithromycin. (108) The use of amoxicillin–clavulanic acid has been associated with increased rates of necrotizing enterocolitis and it is not recommended (23, 102). Although there are no well-studied alternative regimens for women allergic to β-lactam antibiotics, it may be reasonable to consider another agent effective against GBS to replace the β-lactam agent. The choice of agent will be influenced by the severity of the reported allergic reaction and antibiotic susceptibility results of the GBS culture, if available (63). Patients with preterm PROM should be screened for GBS. Women with preterm PROM and a viable fetus who are candidates for intrapartum GBS prophylaxis should receive intrapartum GBS prophylaxis to prevent vertical transmission regardless of earlier antibiotic treatments (63, 109). Approaches for GBS prophylaxis should emphasize appropriate principles of antibiotic stewardship.

▶ *Should preterm prelabor rupture of membranes be managed with home care?*

Two small randomized controlled trials that compared hospitalization to home care of women with preterm PROM had insufficient power to demonstrate a meaningful difference in outcome because only 11–18% of the women were eligible for antepartum home care (110, 111). Because latency is frequently brief, infection may present suddenly, and the fetus is at increased risk of umbilical cord compression, hospitalization with surveillance of the woman and her fetus is recommended once viability has been reached. The outpatient management of preterm PROM with a viable fetus has not been studied sufficiently to establish safety and, therefore, is not recommended. Periviable PROM may be considered for home care after a period of assessment in the hospital, as discussed previously.

▶ *How should a patient with preterm prelabor rupture of membranes and a cervical cerclage be treated?*

There are no complete prospective studies with which to guide the care of women with preterm PROM who have a cervical cerclage. One randomized trial that was terminated early because of concern regarding lack of power during the interim analysis failed to determine differences in outcomes between removal and retention of cervical cerclage in preterm PROM (112). Results from retrospective studies have not been consistent, but generally have found that cerclage retention for more than 24 hours after preterm PROM is associated with pregnancy prolongation (113). Because of the nonrandomized nature of the reports, it is unclear how factors, such as labor or infection, contributed to decisions for cerclage removal, which may have yielded biased results. In some, but not all studies, cerclage retention with preterm PROM has been associated with increased rates of neonatal mortality from sepsis, neonatal sepsis, respiratory distress syndrome, and maternal chorioamnionitis (113, 114). A firm recommendation regarding whether a cerclage should be removed after preterm PROM cannot be made, and either removal or retention is reasonable. Regardless, if a cerclage remains in place with preterm PROM, prolonged antibiotic prophylaxis beyond 7 days is not recommended.

▶ *What is the optimal management of a patient with preterm prelabor rupture of membranes and herpes simplex virus infection or human immunodeficiency virus?*

Neonatal herpes simplex virus (HSV) infection usually results from maternal–fetal transmission during delivery.

The risk of vertical transmission with delivery in patients with subclinical shedding at the time of labor as a result of having acquired genital HSV in the third trimester is reported to be between 30% and 50%, compared with only 3% in cases of maternal symptomatic reactivation of HSV at the time of labor (115). The literature regarding expectant management of preterm PROM with active maternal HSV infection is limited to small case series and case reports (116, 117). All patients were treated with acyclovir, and cesarean birth was performed if lesions were present at the time of delivery. No cases of vertical transmission were reported.

There is no consensus on the gestational age at which the risk of prematurity in women with preterm PROM outweighs the potential risk of neonatal HSV infection. In the setting of PROM with recurrent active infection, expectant management is recommended before 34 0/7 weeks of gestation. Antiviral therapy should be initiated when expectant management is elected, and corticosteroids, antibiotics, and magnesium sulfate for neuroprotection should be provided as clinically indicated. The decision to use corticosteroids should be based on the balance between the risk of pulmonary immaturity and the risk of neonatal herpes. If active disease or prodromal symptoms are present at the onset of labor or when delivery is indicated, cesarean birth is recommended.

Optimal management of preterm PROM in the setting of primary HSV infection is less clear because of the increased risk of vertical transmission. Antiviral therapy is advocated, and if lesions are present at the time of delivery, cesarean birth is recommended. In general, cesarean birth is not recommended for women with a history of HSV infection but no active genital lesions or prodromal symptoms during labor (118). However, for women with a primary or nonprimary first-episode genital HSV infection during the third trimester of pregnancy, cesarean birth may be offered due to the possibility of prolonged viral shedding (119, 120).

The optimal management of the patient with human immunodeficiency virus (HIV) and preterm PROM also is uncertain because there are no adequate data from patients with prolonged rupture of membranes. Early observations showed that the duration of the interval between membrane rupture and labor correlated with risk of transmission to the newborn (121), but current data suggest that the duration the interval between membrane rupture and labor is not correlated with risk of vertical transmission in patients who receive highly active antiretroviral therapy, have a low viral load, and receive antepartum and intrapartum zidovudine (122, 123). Also, a series of 10 patients with preterm PROM who were managed expectantly while receiving antiretroviral therapy had no cases of HIV transmission to the newborn despite viral loads as high as 23,000 copies per mL. The latent periods ranged from 4 hours to 4 days in this series, and all had a cesarean birth (124).

The management of patients with HIV infection who have preterm PROM should be individualized with consideration of factors including gestational age, current antiretroviral regimen, and viral load. In cases involving a very early gestational age in which the patient is being treated with antiretroviral medications and the viral load is low, a period of expectant management is likely to be appropriate. In all cases, the patient should be managed in consultation with a physician with expertise in management of HIV in pregnancy. Furthermore, standard antepartum and intrapartum treatment guidelines should be followed, and management choices should be fully discussed with the patient (125).

▶ *How does care differ for patients with prelabor rupture of membranes that occurs before neonatal viability?*

Women presenting with PROM before neonatal viability should be counseled regarding the risks and benefits of expectant management versus immediate delivery. Counseling should include a realistic appraisal of neonatal outcomes (87). Immediate delivery (termination of pregnancy by induction of labor or dilation and evacuation) and expectant management should be offered. Physicians should provide patients with the most current and accurate information possible (87).

If the patient opts for expectant management and is clinically stable with no evidence of infection after evaluation, outpatient management and surveillance can be considered. Precautions should be reviewed with the patient, and the patient should come to the hospital if she develops symptoms of infection, labor, or abruptio placentae. Patients should monitor body temperatures. Typically, women with periviable PROM who have been cared for as outpatients are admitted to the hospital once the pregnancy has reached viability and the patient would accept interventions for delivery on behalf of the fetus.

Administration of antenatal corticosteroids and latency antibiotics for fetal maturation upon reaching viability is appropriate given that early delivery remains likely. Multiple ultrasonographic methods (such as thoracic measurements and ratios, flow velocities in pulmonary vessels, and three-dimensional estimations of lung volume) have been studied to evaluate pulmonary development in the antepartum period, but all are

of limited accuracy and cannot be considered sufficiently reliable for clinical management (47). Because most studies of antibiotic prophylaxis with preterm PROM enrolled patients only after 24 0/7 weeks of gestation, there are no adequate data to assess the risks and benefits of such treatment at earlier (periviable) gestational ages. However, it is reasonable to consider a course of broad-spectrum antibiotics for pregnancy prolongation in patients with periviable PROM who choose expectant management (87). There is no evidence to support the use of tocolytic agents in the setting of periviable PROM, and in this setting, it is not recommended.

▶ ***What is the expected outcome of prelabor rupture of membranes after second-trimester amniocentesis?***

In studies of women undergoing second-trimester amniocentesis for prenatal diagnosis of genetic disorders, the risk of PROM is less than 1% (126–128). In contrast to patients with spontaneous PROM in the second trimester, reaccumulation of normal amniotic fluid volume and favorable outcomes are expected. In one series of 11 patients with periviable PROM after genetic amniocentesis, there was one periviable pregnancy loss, reaccumulation of normal amniotic fluid occurred within 1 month in 72% of patients, and the perinatal survival rate was 91% (126).

After appropriate counseling, patients with periviable PROM after genetic amniocentesis typically are managed expectantly as outpatients. Precautions regarding symptoms of chorioamnionitis and miscarriage should be given. Regular follow-up visits with ultrasonographic examinations to assess amniotic fluid volume are recommended.

▶ ***How should a patient with a history of preterm prelabor of membranes be managed in future pregnancies?***

Patients with prior preterm PROM have an increased risk of recurrent PROM and preterm birth, and a detailed medical and obstetric history should be taken when patients have a history suggestive of these complications. However, there are few studies that examine interventions to prevent recurrent PROM. Women with prior preterm births should be counseled that short interpregnancy intervals, particularly those shorter than 6 months, may differentially and negatively affect subsequent pregnancy outcomes (129).

Patients with a history of preterm PROM were included in studies of progesterone supplementation for preterm birth recurrence reduction, but most studies did not report the specific proportion of women with PROM in the study group or separately analyze results in those patients (130, 131). However, given the potential benefit of progesterone therapy, women with a single gestation and a prior spontaneous preterm birth (due to either labor with intact membranes or preterm PROM) should be offered progesterone supplementation as clinically indicated to reduce the risk of recurrent spontaneous preterm birth.

Although vaginal ultrasonographic measurement of the cervix is a safe and reliable means of evaluating the risk of preterm birth related to cervical length, there have been no well-designed trials of cervical surveillance in women with a history of preterm PROM. Similar to the progesterone studies, trials that evaluated cervical assessment, vaginal progesterone, and cerclage included women with prior preterm PROM, but their specific data were not reported (132, 133). Thus, as with women with spontaneous preterm births, consideration can be given to transvaginal cervical length screening. Cerclage placement is associated with significant decreases in preterm birth outcomes, offers perinatal benefits, and may be considered in women with the following combination of history and ultrasonographic findings: a current singleton pregnancy, prior spontaneous preterm birth at less than 34 weeks of gestation, and short cervical length (less than 25 mm) before 24 weeks of gestation (134). There are no data on which to base a recommendation regarding the optimal gestational age for initiating surveillance or frequency of monitoring.

Summary of Recommendations and Conclusions

The following recommendations are based on good and consistent scientific evidence (Level A):

- ▶ Patients with preterm PROM before 34 0/7 weeks of gestation should be managed expectantly if no maternal or fetal contraindications exist.
- ▶ A single course of corticosteroids is recommended for pregnant women between 24 0/7 weeks of gestation and 33 6/7 weeks of gestation and may be considered for pregnant women who are at risk of preterm birth within 7 days, including for those with ruptured membranes, as early as 23 0/7 weeks of gestation.
- ▶ A single course of corticosteroids is recommended for pregnant women between 34 0/7 weeks of gestation and 36 6/7 weeks of gestation at risk of preterm birth within 7 days and who have not received a previous course of antenatal corticosteroids if proceeding with induction or delivery in no less than 24 hours and no more than 7 days.
- ▶ Women with preterm PROM before 32 0/7 weeks of gestation who are thought to be at risk of imminent

delivery should be considered candidates for fetal neuroprotective treatment with magnesium sulfate.

- To reduce maternal and neonatal infections and gestational-age-dependent morbidity, a 7-day course of therapy of latency antibiotics with a combination of intravenous ampicillin and erythromycin followed by oral amoxicillin and erythromycin is recommended during expectant management of women with preterm PROM who are at less than 34 0/7 weeks of gestation. Some centers have replaced the use of erythromycin with azithromycin in situations in which erythromycin is not available or not tolerated, and this substitution is a suitable alternative.
- Women with preterm PROM and a viable fetus who are candidates for intrapartum GBS prophylaxis should receive intrapartum GBS prophylaxis to prevent vertical transmission regardless of earlier antibiotic treatments.

The following recommendations and conclusions are based on limited and inconsistent scientific evidence (Level B):

- For women with PROM at 37 0/7 weeks of gestation or more, if spontaneous labor does not occur near the time of presentation in those who do not have contraindication to labor, labor induction should be recommended, although the choice of expectant management for a short period of time may be appropriately offered.
- Either expectant management or immediate delivery in patients with PROM between 34 0/7 weeks of gestation and 36 6/7 weeks of gestation is a reasonable option, although the balance between benefit and risk, from both maternal and neonatal perspectives, should be carefully considered, and patients should be counseled clearly. Care should be individualized through shared decision making, and expectant management should not extend beyond 37 0/7 weeks of gestation. Latency antibiotics are not appropriate in this setting.
- In the setting of ruptured membranes with active labor, although tocolytic therapy has not been shown to prolong latency or improve neonatal outcomes, data are limited. Tocolytic agents can be considered in preterm PROM for steroid benefit to the neonate, especially at earlier gestational ages, or for maternal transport but should be used cautiously and avoided if there is evidence of infection or abruption. Tocolytic therapy is not recommended in the setting of preterm PROM between 34 0/7 weeks of gestation and 36 6/7 weeks of gestation.
- Given the potential benefit of progesterone therapy, women with a single gestation and a prior spontaneous preterm birth (due to either labor with intact membranes or preterm PROM) should be offered progesterone supplementation as clinically indicated to reduce the risk of recurrent spontaneous preterm birth.

The following conclusions are based primarily on consensus and expert opinion (Level C):

- The diagnosis of membrane rupture typically is confirmed by conventional clinical assessment, which includes the visualization of amniotic fluid passing from the cervical canal and pooling in the vagina, a simple pH test of vaginal fluid, or arborization (fern) of dried vaginal fluid, which is identified under microscopic evaluation.
- The outpatient management of preterm PROM with a viable fetus has not been studied sufficiently to establish safety and, therefore, is not recommended. Periviable PROM may be considered for home care after a period of assessment in the hospital.

References

1. Martin JA, Hamilton BE, Osterman MJ. Births in the United States, 2017. NCHS Data Brief No. 318. Hyattsville (MD): National Center for Health Statistics; 2018A. Available at: https://www.cdc.gov/nchs/data/databriefs/db318.pdf. Retrieved April 16, 2019. (Level III)
2. Martin JA, Hamilton BE, Osterman MJ, Driscoll AK, Drake P. Births: final data for 2017. Natl Vital Stat Rep 2018B;67(8):1–49. (Level II-3)
3. Matthews TJ, MacDorman MF, Thoma ME. Infant mortality statistics from the 2013 period linked birth/infant death data set. Natl Vital Stat Rep 2015;64:1–30. (Level II-3)
4. Mercer BM. Preterm premature rupture of the membranes: current approaches to evaluation and management. Obstet Gynecol Clin North Am 2005;32:411–28. (Level III)
5. Martin JA, Hamilton BE, Sutton PD, Ventura SJ, Menacker F, Munson ML. Births: final data for 2003. Natl Vital Stat Rep 2005;54(2):1–116. (Level II-3)
6. Middleton P, Shepherd E, Flenady V, McBain RD, Crowther CA. Planned early birth versus expectant management (waiting) for prelabour rupture of membranes at term (37 weeks or more). Cochrane Database of Systematic Review 2017, Issue 1. Art. No.: CD005302. (Systematic Review and Meta-Analysis)
7. Moore RM, Mansour JM, Redline RW, Mercer BM, Moore JJ. The physiology of fetal membrane rupture: insight gained from the determination of physical properties. Placenta 2006;27:1037–51. (Level III)
8. Mercer BM. Preterm premature rupture of the membranes. Obstet Gynecol 2003;101:178–93. (Level III)

9. Garite TJ, Freeman RK. Chorioamnionitis in the preterm gestation. Obstet Gynecol 1982;59:539–45. (Level II-3)
10. Seo K, McGregor JA, French JI. Preterm birth is associated with increased risk of maternal and neonatal infection. Obstet Gynecol 1992;79:75–80. (Level II-2)
11. Mercer BM, Goldenberg RL, Moawad AH, Meis PJ, Iams JD, Das AF, et al. The preterm prediction study: effect of gestational age and cause of preterm birth on subsequent obstetric outcome. National Institute of Child Health and Human Development Maternal–Fetal Medicine Units Network. Am J Obstet Gynecol 1999;181:1216–21. (Level II-2)
12. Asrat T, Lewis DF, Garite TJ, Major CA, Nageotte MP, Towers CV, et al. Rate of recurrence of preterm premature rupture of membranes in consecutive pregnancies. Am J Obstet Gynecol 1991;165:1111–5. (Level II-2)
13. Lee T, Carpenter MW, Heber WW, Silver HM. Preterm premature rupture of membranes: risks of recurrent complications in the next pregnancy among a population-based sample of gravid women. Am J Obstet Gynecol 2003;188:209–13. (Level II-2)
14. Mercer BM, Goldenberg RL, Meis PJ, Moawad AH, Shellhaas C, Das A, et al. The Preterm Prediction Study: prediction of preterm premature rupture of membranes through clinical findings and ancillary testing. The National Institute of Child Health and Human Development Maternal–Fetal Medicine Units Network. Am J Obstet Gynecol 2000;183:738–45. (Level II-2)
15. Harger JH, Hsing AW, Tuomala RE, Gibbs RS, Mead PB, Eschenbach DA, et al. Risk factors for preterm premature rupture of fetal membranes: a multicenter case-control study. Am J Obstet Gynecol 1990;163:130–7. (Level II-2)
16. Berkowitz GS, Blackmore-Prince C, Lapinski RH, Savitz DA. Risk factors for preterm birth subtypes. Epidemiology 1998;9:279–85. (Level II-3)
17. Ferguson SE, Smith GN, Salenieks ME, Windrim R, Walker MC. Preterm premature rupture of membranes. Nutritional and socioeconomic factors. Obstet Gynecol 2002;100:1250–6. (Level II-2)
18. Hannah ME, Ohlsson A, Farine D, Hewson SA, Hodnett ED, Myhr TL, et al. Induction of labor compared with expectant management for prelabor rupture of the membranes at term. TERMPROM Study Group. N Engl J Med 1996;334:1005–10. (Level I)
19. Melamed N, Hadar E, Ben-Haroush A, Kaplan B, Yogev Y. Factors affecting the duration of the latency period in preterm premature rupture of membranes. J Matern Fetal Neonatal Med 2009;22:1051–6. (Level II-3)
20. Johnson JW, Egerman RS, Moorhead J. Cases with ruptured membranes that "reseal". Am J Obstet Gynecol 1990;163:2. (Level II-2)
21. Vermillion ST, Kooba AM, Soper DE. Amniotic fluid index values after preterm premature rupture of the membranes and subsequent perinatal infection. Am J Obstet Gynecol 2000;183:271–6. (Level II-2)
22. Hadi HA, Hodson CA, Strickland D. Premature rupture of the membranes between 20 and 25 weeks' gestation: role of amniotic fluid volume in perinatal outcome. Am J Obstet Gynecol 1994;170:1139–44. (Level II-2)
23. Kenyon S, Boulvain M, Neilson JP. Antibiotics for preterm rupture of membranes. Cochrane Database of Systematic Reviews 2013, Issue 12. Art. No.: CD001058. (Systematic Review and Meta-Analysis)
24. Beydoun SN, Yasin SY. Premature rupture of the membranes before 28 weeks: conservative management. Am J Obstet Gynecol 1986;155:471–9. (Level III)
25. Ramsey PS, Lieman JM, Brumfield CG, Carlo W. Chorioamnionitis increases neonatal morbidity in pregnancies complicated by preterm premature rupture of membranes. Am J Obstet Gynecol 2005;192:1162–6. (Level II-3)
26. Major CA, de Veciana M, Lewis DF, Morgan MA. Preterm premature rupture of membranes and abruptio placentae: is there an association between these pregnancy complications? Am J Obstet Gynecol 1995;172:672–6. (Level II-3)
27. Ananth CV, Oyelese Y, Srinivas N, Yeo L, Vintzileos AM. Preterm premature rupture of membranes, intrauterine infection, and oligohydramnios: risk factors for placental abruption. Obstet Gynecol 2004;104:71–7. (Level II-3)
28. Lemons JA, Bauer CR, Oh W, Korones SB, Papile LA, Stoll BJ, et al. Very low birth weight outcomes of the National Institute of Child Health and Human Development Neonatal Research Network, January 1995 through December 1996. NICHD Neonatal Research Network. Pediatrics 2001;107:E1. (Level II-3)
29. Stoll BJ, Hansen NI, Bell EF, Shankaran S, Laptook AR, Walsh MC, et al. Neonatal outcomes of extremely preterm infants from the NICHD Neonatal Research Network. Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network. Pediatrics 2010;126:443–56. (Level II-3)
30. Spinillo A, Capuzzo E, Stronati M, Ometto A, Orcesi S, Fazzi E. Effect of preterm premature rupture of membranes on neurodevelopmental outcome: follow up at two years of age. Br J Obstet Gynaecol 1995;102:882–7. (Level II-2)
31. Yoon BH, Romero R, Park JS, Kim CJ, Kim SH, Choi JH, et al. Fetal exposure to an intra-amniotic inflammation and the development of cerebral palsy at the age of three years. Am J Obstet Gynecol 2000;182:675–81. (Level II-2)
32. Drassinower D, Friedman AM, Obican SG, Levin H, Gyamfi-Bannerman C. Prolonged latency of preterm prelabour rupture of membranes and neurodevelopmental outcomes: a secondary analysis. BJOG 2016;123:1629–35. (Level II-2)
33. Locatelli A, Ghidini A, Paterlini G, Patane L, Doria V, Zorloni C, et al. Gestational age at preterm premature rupture of membranes: a risk factor for neonatal white matter damage. Am J Obstet Gynecol 2005;193:947–51. (Level II-3)
34. Lorthe E, Ancel PY, Torchin H, Kaminski M, Langer B, Subtil D, et al. Impact of latency duration on the prognosis of preterm infants after preterm premature rupture of membranes at 24 to 32 weeks' gestation: a national population-based cohort study. J Pediatr 2017;182:47–52.e2. (Level II-2)

35. Manuck TA, Eller AG, Esplin MS, Stoddard GJ, Varner MW, Silver RM. Outcomes of expectantly managed preterm premature rupture of membranes occurring before 24 weeks of gestation. Obstet Gynecol 2009;114:29–37. (Level II-3)
36. Kibel M, Asztalos E, Barrett J, Dunn MS, Tward C, Pittini A, et al. Outcomes of pregnancies complicated by preterm premature rupture of membranes between 20 and 24 weeks of gestation. Obstet Gynecol 2016;128:313–20. (Level II-2)
37. Waters TP, Mercer BM. The management of preterm premature rupture of the membranes near the limit of fetal viability. Am J Obstet Gynecol 2009;201:230–40. (Level III)
38. Dotters-Katz SK, Panzer A, Grace MR, Smid MC, Keku JA, Vladutiu CJ, et al. Maternal morbidity after previable prelabor rupture of membranes. Obstet Gynecol 2017; 129:101–6. (Level II-2)
39. Schucker JL, Mercer BM. Midtrimester premature rupture of the membranes. Semin Perinatol 1996;20:389–400. (Level III)
40. Muris C, Girard B, Creveuil C, Durin L, Herlicoviez M, Dreyfus M. Management of premature rupture of membranes before 25 weeks. Eur J Obstet Gynecol Reprod Biol 2007;131:163–8. (Level III)
41. Kieffer A, Pinto Cardoso G, Thill C, Verspyck E, Marret S. Outcome at two years of very preterm infants born after rupture of membranes before viability. Perinatal Network of Haute-Normandie. PLoS One 2016;11:e0166130. (Level II-2)
42. Sim WH, Araujo Junior E, Da Silva Costa F, Sheehan PM. Maternal and neonatal outcomes following expectant management of preterm prelabour rupture of membranes before viability. J Perinat Med 2017;45:29–44. (Systematic Review)
43. Kiver V, Boos V, Thomas A, Henrich W, Weichert A. Perinatal outcomes after previable preterm premature rupture of membranes before 24 weeks of gestation. J Perinat Med 2018;46:555–65. (Level II-3)
44. Farooqi A, Holmgren PA, Engberg S, Serenius F. Survival and 2-year outcome with expectant management of second-trimester rupture of membranes. Obstet Gynecol 1998;92:895–901. (Level II-3)
45. Winn HN, Chen M, Amon E, Leet TL, Shumway JB, Mostello D. Neonatal pulmonary hypoplasia and perinatal mortality in patients with midtrimester rupture of amniotic membranes—a critical analysis. Am J Obstet Gynecol 2000;182:1638–44. (Level II-2)
46. van Teeffelen AS, van der Ham DP, Oei SG, Porath MM, Willekes C, Mol BW. The accuracy of clinical parameters in the prediction of perinatal pulmonary hypoplasia secondary to midtrimester prelabour rupture of fetal membranes: a meta-analysis. Eur J Obstet Gynecol Reprod Biol 2010;148:3–12. (Systematic Review and Meta-Analysis)
47. van Teeffelen AS, Van Der Heijden J, Oei SG, Porath MM, Willekes C, Opmeer B, et al. Accuracy of imaging parameters in the prediction of lethal pulmonary hypoplasia secondary to mid-trimester prelabor rupture of fetal membranes: a systematic review and meta-analysis. Ultrasound Obstet Gynecol 2012;39:495–9. (Systematic Review and Meta-Analysis)
48. Lee JY, Ahn TG, Jun JK. Short-term and long-term postnatal outcomes of expectant management after previable preterm premature rupture of membranes with and without persistent oligohydramnios. Obstet Gynecol 2015; 126:947–53. (Level II-2)
49. Blott M, Greenough A. Neonatal outcome after prolonged rupture of the membranes starting in the second trimester. Arch Dis Child 1988;63:1146–50. PMID: 3196069. (Level III)
50. Alexander JM, Mercer BM, Miodovnik M, Thurnau GR, Goldenberg RL, Das AF, et al. The impact of digital cervical examination on expectantly managed preterm rupture of membranes. Am J Obstet Gynecol 2000;183: 1003–7. (Level II-2)
51. Munson LA, Graham A, Koos BJ, Valenzuela GJ. Is there a need for digital examination in patients with spontaneous rupture of the membranes? Am J Obstet Gynecol 1985;153:562–3. (Level III)
52. Eriksen NL, Parisi VM, Daoust S, Flamm B, Garite TJ, Cox SM. Fetal fibronectin: a method for detecting the presence of amniotic fluid. Obstet Gynecol 1992;80: 451–4. (Level II-2)
53. Lee SE, Park JS, Norwitz ER, Kim KW, Park HS, Jun JK. Measurement of placental alpha-microglobulin-1 in cervicovaginal discharge to diagnose rupture of membranes. Obstet Gynecol 2007;109:634–40. (Level II-3)
54. Cousins LM, Smok DP, Lovett SM, Poeltler DM. AmniSure placental alpha microglobulin-1 rapid immunoassay versus standard diagnostic methods for detection of rupture of membranes. Am J Perinatol 2005;22:317–20. Level II-3)
55. Lee SM, Lee J, Seong HS, Lee SE, Park JS, Romero R, et al. The clinical significance of a positive Amnisure test in women with term labor with intact membranes. J Matern Fetal Neonatal Med 2009;22:305–10. (Level II-3)
56. Lee SM, Romero R, Park JW, Kim SM, Park CW, Korzeniewski SJ, et al. The clinical significance of a positive Amnisure test in women with preterm labor and intact membranes. J Matern Fetal Neonatal Med 2012;25: 1690–8. (Level II-2)
57. Igbinosa I, Moore FA 3rd, Johnson C, Block JE. Comparison of rapid immunoassays for rupture of fetal membranes. BMC Pregnancy Childbirth 2017;17:128. (Level II-2)
58. Thomasino T, Levi C, Draper M, Neubert AG. Diagnosing rupture of membranes using combination monoclonal/polyclonal immunologic protein detection. J Reprod Med 2013;58:187–94. (Level II-2)
59. U.S. Food and Drug Administration. Risks associated with use of rupture of membranes tests—letter to health care providers. Silver Spring, MD: FDA; 2018. Available at: https://www.fda.gov/medical-devices/letters-health-care-providers/risks-associated-use-rupture-membranes-tests-letter-health-care-providers. Retrieved October 18, 2019. (Level III)

60. Ireland KE, Rodriguez EI, Acosta OM, Ramsey PS. Intra-amniotic dye alternatives for the diagnosis of preterm prelabor rupture of membranes. Obstet Gynecol 2017; 129:1040–5. (Level III)

61. Antepartum fetal surveillance. Practice Bulletin No. 145. American College of Obstetricians and Gynecologists. Obstet Gynecol 2014;124:182–92. (Level III)

62. Smith CV, Greenspoon J, Phelan JP, Platt LD. Clinical utility of the nonstress test in the conservative management of women with preterm spontaneous premature rupture of the membranes. J Reprod Med 1987;32:1–4. (Level II-3)

63. Prevention of group B streptococcal early-onset disease in newborns. ACOG Committee Opinion No. 797. American College of Obstetricians and Gynecologists. Obstet Gynecol 2020;135:eXX–XX. (Level III)

64. Mackeen AD, Durie DE, Lin M, Huls CK, Qureshey E, Paglia MJ, et al. Foley plus oxytocin compared with oxytocin for induction after membrane rupture: a randomized controlled trial. Obstet Gynecol 2018;131:4–11. (Level I)

65. Amorosa JM, Stone J, Factor SH, Booker W, Newland M, Bianco A. A randomized trial of Foley Bulb for Labor Induction in Premature Rupture of Membranes in Nulliparas (FLIP). Am J Obstet Gynecol 2017;217:360.e1–7. (Level I)

66. Wojcieszek AM, Stock OM, Flenady V. Antibiotics for prelabour rupture of membranes at or near term. Cochrane Database of Systematic Reviews 2014, Issue 10. Art. No.: CD001807. (Systematic Review and Meta-Analysis)

67. Ovalle A, Martinez MA, Kakarieka E, Gomez R, Rubio R, Valderrama O, et al. Antibiotic administration in patients with preterm premature rupture of membranes reduces the rate of histological chorioamnionitis: a prospective, randomized, controlled study. J Matern Fetal Neonatal Med 2002;12:35–41. (Level I)

68. Safe prevention of the primary cesarean delivery. Obstetric Care Consensus No. 1. American College of Obstetricians and Gynecologists. Obstet Gynecol 2014;123:693–711. (Level III)

69. Rouse DJ, Weiner SJ, Bloom SL, Varner MW, Spong CY, Ramin SM, et al. Failed labor induction: toward an objective diagnosis. Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Maternal–Fetal Medicine Units Network (MFMU). Obstet Gynecol 2011;117:267–72. (Level III)

70. Rouse DJ, Owen J, Hauth JC. Criteria for failed labor induction: prospective evaluation of a standardized protocol. Obstet Gynecol 2000;96:671–7. (Level II-3)

71. Simon CE, Grobman WA. When has an induction failed? Obstet Gynecol 2005;105:705–9. (Level II-2)

72. Grobman WA, Bailit J, Lai Y, Reddy UM, Wapner RJ, Varner MW, et al. Defining failed induction of labor. Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. Am J Obstet Gynecol 2018;218:122.e1–8. (Level II-3)

73. Bond DM, Middleton P, Levett KM, van der Ham DP, Crowther CA, Buchanan SL, et al. Planned early birth versus expectant management for women with preterm prelabour rupture of membranes prior to 37 weeks' gestation for improving pregnancy outcome. Cochrane Database of Systematic Reviews 2017, Issue 3. Art. No.: CD004735. (Systematic Review and Meta-Analysis)

74. Mercer BM, Crocker LG, Boe NM, Sibai BM. Induction versus expectant management in premature rupture of the membranes with mature amniotic fluid at 32 to 36 weeks: a randomized trial. Am J Obstet Gynecol 1993;169:775–82. (Level I)

75. Morris JM, Roberts CL, Bowen JR, Patterson JA, Bond DM, Algert CS, et al. Immediate delivery compared with expectant management after preterm pre-labour rupture of the membranes close to term (PPROMT trial): a randomised controlled trial. PPROMT Collaboration. Lancet 2016;387:444–52. (Level I)

76. Quist-Nelson J, de Ruigh AA, Seidler AL, van der Ham D. P., Willekes C, Berghella V, et al. Immediate delivery compared with expectant management in late preterm prelabor rupture of membranes: an individual participant data meta-analysis. Preterm Premature Rupture of Membranes Meta-analysis (PPROMM) Collaboration. Obstet Gynecol 2018;131:269–79. (Meta-Analysis)

77. Tita AT, Andrews WW. Diagnosis and management of clinical chorioamnionitis. Clin Perinatol 2010;37:339–54. (Level III)

78. Combs CA, Garite TJ, Maurel K, Abril D, Das A, Clewell W, et al. 17-hydroxyprogesterone caproate for preterm rupture of the membranes: a multicenter, randomized, double-blind, placebo-controlled trial. Obstetrix Collaborative Research Network. Am J Obstet Gynecol 2015;213: 364.e1–12. (Level I)

79. Langen ES, Sit A, Sherwin K, Lyell DJ, Blumenfeld YJ, El-Sayed YY. A double-blind, randomized, placebo-controlled trial of 17 alpha-hydroxyprogesterone caproate in the management of preterm premature rupture of membranes [published erratum appears in Am J Perinatol 2018;35:e1]. Am J Perinatol 2018;35:779–84. (Level I)

80. Fox NS, Gelber SE, Kalish RB, Chasen ST. Contemporary practice patterns and beliefs regarding tocolysis among U.S. maternal-fetal medicine specialists. Obstet Gynecol 2008;112:42–7. (Level III)

81. Dunlop PD, Crowley PA, Lamont RF, Hawkins DF. Preterm ruptured membranes, no contractions. J Obstet Gynaecol 1987;7:92–6. (Level II-1)

82. Ehsanipoor RM, Shrivastava VK, Lee RM, Chan K, Galyean AM, Garite TJ, et al. A randomized, double-masked trial of prophylactic indomethacin tocolysis versus placebo in women with premature rupture of membranes. Am J Perinatol 2011A;28:473–8. (Level I)

83. Mackeen AD, Seibel-Seamon J, Muhammad J, Baxter JK, Berghella V. Tocolytics for preterm premature rupture of membranes. Cochrane Database of Systematic Reviews 2014, Issue 2. Art. No.: CD007062. (Systematic Review and Meta-Analysis)

84. Roberts D, Brown J, Medley N, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database of Systematic Reviews 2017, Issue 3. Art. No.: CD004454. (Systematic Review and Meta-Analysis)

85. Vidaeff AC, Ramin SM. Antenatal corticosteroids after preterm premature rupture of membranes. Clin Obstet Gynecol 2011;54:337–43. Level III)

86. Harding JE, Pang J, Knight DB, Liggins GC. Do antenatal corticosteroids help in the setting of preterm rupture of membranes? Am J Obstet Gynecol 2001;184:131–9. (Level II-2)

87. Periviable birth. Obstetric Care Consensus No. 6. American College of Obstetricians and Gynecologists. Obstet Gynecol 2017;130:e187–99. (Level III)

88. Costantine MM, Weiner SJ. Effects of antenatal exposure to magnesium sulfate on neuroprotection and mortality in preterm infants: a meta-analysis. Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal–Fetal Medicine Units Network. Obstet Gynecol 2009;114:354–64. (Meta-Analysis)

89. Antenatal corticosteroid therapy for fetal maturation. Committee Opinion No. 713. American College of Obstetricians and Gynecologists [published erratum appears in Obstet Gynecol 2017;130:1159]. Obstet Gynecol 2017; 130:e102–9. (Level III)

90. Gyamfi-Bannerman C, Thom EA, Blackwell SC, Tita AT, Reddy UM, Saade GR, et al. Antenatal betamethasone for women at risk for late preterm delivery. NICHD Maternal–Fetal Medicine Units Network. N Engl J Med 2016;374:1311–20. (Level I)

91. Wapner RJ, Sorokin Y, Thom EA, Johnson F, Dudley DJ, Spong CY, et al. Single versus weekly courses of antenatal corticosteroids: evaluation of safety and efficacy. National Institute of Child Health and Human Development Maternal Fetal Medicine Units Network. Am J Obstet Gynecol 2006;195:633–42. (Level I)

92. Bloom SL, Sheffield JS, McIntire DD, Leveno KJ. Antenatal dexamethasone and decreased birth weight. Obstet Gynecol 2001;97:485–90. (Level II-3)

93. Thorp JA, Jones PG, Knox E, Clark RH. Does antenatal corticosteroid therapy affect birth weight and head circumference? Obstet Gynecol 2002;99:101–8. (Level II-3)

94. Brookfield KF, El-Sayed YY, Chao L, Berger V, Naqvi M, Butwick AJ. Antenatal corticosteroids for preterm premature rupture of membranes: single or repeat course? Am J Perinatol 2015;32:537–44. (Level II-2)

95. Gyamfi-Bannerman C, Son M. Preterm premature rupture of membranes and the rate of neonatal sepsis after two courses of antenatal corticosteroids. Obstet Gynecol 2014; 124:999–1003. (Level II-2)

96. Doyle LW, Crowther CA, Middleton P, Marret S, Rouse D. Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus. Cochrane Database of Systematic 83. Reviews 2009, Issue 1. Art. No.: CD004661. (Systematic Review and Meta-Analysis)

97. Rouse DJ, Hirtz DG, Thom E, Varner MW, Spong CY, Mercer BM, et al. A randomized, controlled trial of magnesium sulfate for the prevention of cerebral palsy. Eunice Kennedy Shriver NICHD Maternal–Fetal Medicine Units Network. N Engl J Med 2008;359:895–905. (Level I)

98. Horton AL, Lai Y, Rouse DJ, Spong CY, Leveno KJ, Varner MW, et al. Effect of magnesium sulfate administration for neuroprotection on latency in women with preterm premature rupture of membranes. Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal–Fetal Medicine Units Network. Am J Perinatol 2015;32:387–92. (Level I)

99. Marret S, Marpeau L, Zupan-Simunek V, Eurin D, Leveque C, Hellot MF, et al. Magnesium sulphate given before very-preterm birth to protect infant brain: the randomised controlled PREMAG trial*. PREMAG trial group. BJOG 2007;114:310–8. (Level I)

100. Crowther CA, Hiller JE, Doyle LW, Haslam RR. Effect of magnesium sulfate given for neuroprotection before preterm birth: a randomized controlled trial. Australasian Collaborative Trial of Magnesium Sulphate (ACTOMg SO4) Collaborative Group. JAMA 2003;290:2669–76. (Level I)

101. Magnesium sulfate use in obstetrics. Committee Opinion No. 652. American College of Obstetricians and Gynecologists. Obstet Gynecol 2016;127:e52–3. (Level III)

102. Kenyon SL, Taylor DJ, Tarnow-Mordi W. Broad-spectrum antibiotics for preterm, prelabour rupture of fetal membranes: the ORACLE I randomised trial. ORACLE Collaborative Group [published erratum appears in Lancet 2001; 358:156]. Lancet 2001;357:979–88. (Level I)

103. Mercer BM, Miodovnik M, Thurnau GR, Goldenberg RL, Das AF, Ramsey RD, et al. Antibiotic therapy for reduction of infant morbidity after preterm premature rupture of the membranes. A randomized controlled trial. National Institute of Child Health and Human Development Maternal–Fetal Medicine Units Network. JAMA 1997; 278:989–95. (Level I)

104. American Society of Health-System Pharmacists. Erythromycin lactobionate injection. In: Current drug shortages. Bethesda (MD): ASHP; 2019. Available at: https://www.ashp.org/Drug-Shortages/Current-Shortages/Drug-Shortage-Detail.aspx?id=247. Retrieved July 10, 2019. (Level III)

105. Navathe R, Schoen CN, Heidari P, Bachilova S, Ward A, Tepper J, et al. Azithromycin vs erythromycin for the management of preterm premature rupture of membranes. Am J Obstet Gynecol 2019;221:144.e1–8. (Level II-2)

106. Pierson RC, Gordon SS, Haas DM. A retrospective comparison of antibiotic regimens for preterm premature rupture of membranes. Obstet Gynecol 2014;124:515–9. (Level II-2)

107. Finneran MM, Appiagyei A, Templin M, Mertz H. Comparison of azithromycin versus erythromycin for prolongation of latency in pregnancies complicated by preterm premature rupture of membranes. Am J Perinatol 2017;34: 1102–7. (Level II-2)

108. Finneran MM, Smith DD, Buhimschi CS. Cost analysis of azithromycin versus erythromycin in pregnancies complicated by preterm premature rupture of membranes. Am J Perinatol 2019;36:105–10. (Cost-effectiveness Analysis)

109. Use of prophylactic antibiotics in labor and delivery. ACOG Practice Bulletin No. 199. American College of Obstetricians and Gynecologists. Obstet Gynecol 2018; 132:e103–19. (Level III)

110. Abou El Senoun G, Dowswell T, Mousa HA. Planned home versus hospital care for preterm prelabour rupture of the membranes (PPROM) prior to 37 weeks' gestation. Cochrane Database of Systematic Reviews 2014, Issue 4. Art. No.: CD008053. (Systematic Review and Meta-Analysis)

111. Carlan SJ, O'Brien WF, Parsons MT, Lense JJ. Preterm premature rupture of membranes: a randomized study of home versus hospital management. Obstet Gynecol 1993; 81:61–4. (Level I)

112. Galyean A, Garite TJ, Maurel K, Abril D, Adair CD, Browne P, et al. Removal versus retention of cerclage in preterm premature rupture of membranes: a randomized controlled trial. Obstetrix Perinatal Collaborative Research Network. Am J Obstet Gynecol 2014;211:399.e1–7. (Level I)

113. Giraldo-Isaza MA, Berghella V. Cervical cerclage and preterm PROM. Clin Obstet Gynecol 2011;54:313–20. (Level III)

114. Laskin M, Yinon Y, Whittle WL. Preterm premature rupture of membranes in the presence of cerclage: is the risk for intra-uterine infection and adverse neonatal outcome increased? J Matern Fetal Neonatal Med 2012;25:424–8. (Level II-2)

115. Brown ZA, Gardella C, Wald A, Morrow RA, Corey L. Genital herpes complicating pregnancy [published errata appear in Obstet Gynecol 2007;109:207; Obstet Gynecol 2006;107:428]. Obstet Gynecol 2005;106:845–56. (Level III)

116. Ehsanipoor RM, Major CA. Herpes simplex and HIV infections and preterm PROM. Clin Obstet Gynecol 2011B;54:330–6. (Level III)

117. Major CA, Towers CV, Lewis DF, Garite TJ. Expectant management of preterm premature rupture of membranes complicated by active recurrent genital herpes. Am J Obstet Gynecol 2003;188:1551–4; discussion 1554–5. (Level II-3)

118. Roberts SW, Cox SM, Dax J, Wendel GD Jr, Leveno KJ. Genital herpes during pregnancy: no lesions, no cesarean. Obstet Gynecol 1995;85:261–4. (Level II-2)

119. Brown ZA, Vontver LA, Benedetti J, Critchlow CW, Sells CJ, Berry S, et al. Effects on infants of a first episode of genital herpes during pregnancy. N Engl J Med 1987; 317:1246–51. (Level II-2)

120. Brown ZA, Wald A, Morrow RA, Selke S, Zeh J, Corey L. Effect of serologic status and cesarean delivery on transmission rates of herpes simplex virus from mother to infant. JAMA 2003;289:203–9. (Level II-2)

121. Landesman SH, Kalish LA, Burns DN, Minkoff H, Fox HE, Zorrilla C, et al. Obstetrical factors and the transmission of human immunodeficiency virus type 1 from mother to child. The Women and Infants Transmission Study. N Engl J Med 1996;334:1617–23. (Level II-2)

122. Cotter AM, Brookfield KF, Duthely LM, Gonzalez Quintero VH, Potter JE, O'Sullivan MJ. Duration of membrane rupture and risk of perinatal transmission of HIV-1 in the era of combination antiretroviral therapy. Am J Obstet Gynecol 2012;207:482.e1–5. (Level II-2)

123. Labor and delivery management of women with human immunodeficiency virus infection. ACOG Committee Opinion No. 751. American College of Obstetricians and Gynecologists. Obstet Gynecol 2018;132:e131–7. (Level III)

124. Alvarez JR, Bardeguez A, Iffy L, Apuzzio JJ. Preterm premature rupture of membranes in pregnancies complicated by human immunodeficiency virus infection: a single center's five-year experience. J Matern Fetal Neonatal Med 2007;20:853–7. (Level II-3)

125. Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission. Recommendations for the use of antiretroviral drugs in pregnant women with HIV infection and interventions to reduce perinatal HIV transmission in the United States. Rockville (MD): Department of Health and Human Services; 2018. Available at: https://aidsinfo.nih.gov/contentfiles/lvguidelines/perinatalgl.pdf. Retrieved April 16, 2019. (Level III)

126. Borgida AF, Mills AA, Feldman DM, Rodis JF, Egan JF. Outcome of pregnancies complicated by ruptured membranes after genetic amniocentesis. Am J Obstet Gynecol 2000;183:937–9. (Level II-3)

127. Gold RB, Goyert GL, Schwartz DB, Evans MI, Seabolt LA. Conservative management of second-trimester post-amniocentesis fluid leakage. Obstet Gynecol 1989;74: 745–7. (Level III)

128. Prenatal diagnostic testing for genetic disorders. Practice Bulletin No. 162. American College of Obstetricians and Gynecologists. Obstet Gynecol 2016;127:e108–22. (Level III)

129. Interpregnancy care. Obstetric Care Consensus No. 8. American College of Obstetricians and Gynecologists. Obstet Gynecol 2019;133:e51–72. (Level III)

130. Meis PJ, Klebanoff M, Thom E, Dombrowski MP, Sibai B, Moawad AH, et al. Prevention of recurrent preterm delivery by 17 alpha-hydroxyprogesterone caproate. National Institute of Child Health and Human Development Maternal–Fetal Medicine Units Network [published erratum appears in N Engl J Med 2003;349:1299]. N Engl J Med 2003;348:2379–85. (Level I)

131. Tita AT, Rouse DJ. Progesterone for preterm birth prevention: an evolving intervention. Am J Obstet Gynecol 2009;200:219–24. (Level III)

132. Hassan SS, Romero R, Vidyadhari D, Fusey S, Baxter JK, Khandelwal M, et al. Vaginal progesterone reduces the rate of preterm birth in women with a sonographic short cervix: a multicenter, randomized, double-blind, placebo-controlled trial. PREGNANT Trial. Ultrasound Obstet Gynecol 2011;38:18–31. (Level I)

133. Owen J, Hankins G, Iams JD, Berghella V, Sheffield JS, Perez-Delboy A, et al. Multicenter randomized trial of cerclage for preterm birth prevention in high-risk women with shortened midtrimester cervical length. Am J Obstet Gynecol 2009;201:375.e1–8. (Level I)

134. Berghella V, Rafael TJ, Szychowski JM, Rust OA, Owen J. Cerclage for short cervix on ultrasonography in women with singleton gestations and previous preterm birth: a meta-analysis. Obstet Gynecol 2011;117:663–71. (Systematic Review and Meta-Analysis)

The MEDLINE database, the Cochrane Library, and the American College of Obstetricians and Gynecologists' own internal resources and documents were used to conduct a literature search to locate relevant articles published between January 2000 and March 2019. The search was restricted to articles published in the English language. Priority was given to articles reporting results of original research, although review articles and commentaries also were consulted. Abstracts of research presented at symposia and scientific conferences were not considered adequate for inclusion in this document. Guidelines published by organizations or institutions such as the National Institutes of Health and the American College of Obstetricians and Gynecologists were reviewed, and additional studies were located by reviewing bibliographies of identified articles. When reliable research was not available, expert opinions from obstetrician–gynecologists were used.

Studies were reviewed and evaluated for quality according to the method outlined by the U.S. Preventive Services Task Force:

- I Evidence obtained from at least one properly designed randomized controlled trial.
- II-1 Evidence obtained from well-designed controlled trials without randomization.
- II-2 Evidence obtained from well-designed cohort or case–control analytic studies, preferably from more than one center or research group.
- II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.
- III Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Based on the highest level of evidence found in the data, recommendations are provided and graded according to the following categories:

Level A—Recommendations are based on good and consistent scientific evidence.

Level B—Recommendations are based on limited or inconsistent scientific evidence.

Level C—Recommendations are based primarily on consensus and expert opinion.

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American College of Obstetricians and Gynecologists
409 12th Street SW, Washington, DC 20024-2188

Prelabor rupture of membranes. ACOG Practice Bulletin No. 217. American College of Obstetricians and Gynecologists. Obstet Gynecol 2020;135:e80–97.

This information is designed as an educational resource to aid clinicians in providing obstetric and gynecologic care, and use of this information is voluntary. This information should not be considered as inclusive of all proper treatments or methods of care or as a statement of the standard of care. It is not intended to substitute for the independent professional judgment of the treating clinician. Variations in practice may be warranted when, in the reasonable judgment of the treating clinician, such course of action is indicated by the condition of the patient, limitations of available resources, or advances in knowledge or technology. The American College of Obstetricians and Gynecologists reviews its publications regularly; however, its publications may not reflect the most recent evidence. Any updates to this document can be found on acog.org or by calling the ACOG Resource Center.

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Exhibit B

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF IDAHO
SOUTHERN DIVISION

UNITED STATES OF AMERICA, Plaintiff, v. THE STATE OF IDAHO, Defendant.	Case No. 1:22-cv-329 **DECLARATION OF DR. EMILY CORRIGAN**

DECLARATION OF DR. EMILY CORRIGAN IN SUPPORT OF THE UNITED STATES' MOTION FOR A PRELIMINARY INJUNCTION

I, Emily Corrigan, being first duly sworn under oath, state and depose upon personal knowledge as follows:

1. I am a board-certified Obstetrician-Gynecologist ("Ob-Gyn") physician at Saint Alphonsus Regional Medical Center in Boise, Idaho. In that capacity, I specialize in, among other aspects of care, inpatient management of complicated pregnancies and emergency assessment and management of pregnant women. Saint Alphonsus Regional Medical Center is a tertiary care medical center with a trauma designation and a Level 3 Neonatal Intensive Care Unit. Thus, it is a regional referral center for complicated pregnancies and frequently cares for patients with traumatic injuries during pregnancy. I submit this declaration in support of the Motion for Preliminary Injunction filed by the United States in the above-captioned matter. Unless otherwise stated, the facts set forth herein are true of my own personal knowledge, and if called as a witness to testify in this matter, I could and would testify competently thereto.

2. I graduated from the University of California, San Francisco ("UCSF") School of Medicine in 2006 and subsequently completed my residency in Obstetrics and Gynecology at the University of Maryland Medical Center in 2011. I am Board Certified in General Obstetrics and Gynecology by the American Board of Obstetrics and Gynecology.

3. In 2019, I moved to Idaho after accepting my current employment position as an Obstetric Hospitalist at Saint Alphonsus Regional Medical Center in Boise, Idaho. I have subsequently been elected to the position of Vice Chair of the Department of Obstetrics and Gynecology.

4. My family and I were drawn to Idaho for its natural beauty—including vast mountains and beautiful forests and all the recreation opportunities incumbent therein—along with its desirable pace of life and friendly communities. I also came to Idaho, in part, to fill a serious need for physicians generally, and especially Ob-Gyns, in the state.

5. There are zero residency programs in Obstetrics and Gynecology in the State of Idaho, meaning that all Ob-Gyns must be recruited from out of state. Idaho also has one of the fastest growing populations in the country. This dynamic has created a significant shortage of Ob-Gyns in our state.

6. Over the course of my nearly 15-year career as a practicing Ob-Gyn, I have treated thousands of pregnant women and delivered thousands of healthy babies.

7. Although as physicians we work to help our patients to experience normal pregnancies, culminating in the delivery of a healthy baby, not all pregnancies are as simple and complication-free as physicians and patients would like.

8. At Saint Alphonsus Regional Medical Center, we do not perform purely elective abortions, which are abortions performed in pregnancies that do not seriously threaten the health

or life of the mother. However, there are situations where pregnancy termination in the form of an abortion is the only medical intervention that can preserve a patient's health or save their life. I will describe several recent examples of patients my colleagues and I have treated, which illustrate the dire circumstances that can make it medically necessary to terminate a pregnancy. Currently, our institution cares for patients in circumstances like these once every several months. However, I expect that this number will increase once Idaho Code § 18-622 goes into effect.

Jane Doe 1

9. Jane Doe 1 is a woman in her mid-20s who lives in a rural part of the state hundreds of miles away from Boise. I treated her and the facts I describe here were either personal observations I made or facts relayed to me for the purpose of treating Jane Doe 1.

10. Jane Doe 1 has two children of her own. Like many other women in our state, she decided to become a surrogate (also called gestational carrier) to provide additional income for her family and to help others who are unable to produce their own children. The intended parent and biological father of Jane Doe 1's pregnancy lives overseas.

11. When Jane Doe 1 was at 19-weeks' gestation, she was diagnosed with a pregnancy complication called preterm premature rupture of membranes ("PPROM"). PPROM is a premature breaking open of the amniotic sac. It increases the risk of life-threatening intra-amniotic infection (chorioamnionitis) and also increases the risk that the fetus will not develop normally due to a decrease in the amount of amniotic fluid.

12. Jane Doe 1 consulted with her personal obstetrician after the diagnosis of PPROM but was not advised that evacuation of the uterus was appropriate or necessary. Instead, she was incorrectly advised that terminating the pregnancy was illegal in Idaho following the Supreme

Court's decision in *Dobbs* (which had occurred one week prior) due to Idaho's trigger law (even though Idaho Code § 18-622 was not yet in effect).

13. As her condition worsened, Jane Doe 1 spent several days in consultation with her surrogacy agency to determine her options. Eventually, she drove to Boise and presented to the emergency department at another hospital in the area. At this point, Jane Doe 1 had been experiencing cramps and chills for three days—signs of infection. The treating physician gave her oral antibiotics and told her to return to her regular physician in a week.

14. Administration of oral antibiotics and discharge home is not the medically accepted standard of care for suspected chorioamnionitis. At this point, Jane Doe 1 was experiencing an increased risk of sepsis (a life-threatening condition) and a deepening infection of the uterus that, in addition to the deficient amniotic fluid, would have a direct negative impact on the fetus. In such cases, evacuation of the uterus and intravenous ("IV") antibiotics is the only medically acceptable form of treatment.

15. Eventually, Jane Doe 1 presented to the Labor and Delivery Unit at Saint Alphonsus Regional Medical Center, where I first met her. She had been diagnosed with PPROM almost two weeks prior to presentation and had been experiencing worsening uterine cramping and chills for the past three days. I informed Jane Doe 1 that although fetal cardiac activity was still present, termination of pregnancy was the necessary course of action to preserve her life. The overseas intended parent for whom Jane Doe 1 was carrying the baby agreed with Jane Doe 1 that terminating the pregnancy was the best course of action due to the serious risks to both Jane Doe 1's life and the health of his future child. I discussed with her medical and surgical options for uterine evacuation, and she chose a medical termination.

16. Shortly after she was given medication to induce labor, Jane Doe 1 spiked a high fever. She delivered the fetus after several hours; however, the placenta would not detach from the uterus, causing her to start hemorrhaging. I transferred Jane Doe 1 to the operating room for a uterine curettage to remove the retained placenta. She was also given multiple medications to decrease the bleeding from her uterus. Still, she lost almost two liters of blood and required a blood transfusion. She was continued on IV antibiotics for another 24 hours and was discharged home in stable condition on hospital day number three.

17. Had Jane Doe 1 not received medical care to terminate her pregnancy, her intraamniotic infection would likely have led to sepsis thereby significantly increasing her chance of death.

18. If Idaho Code §18-622 was in effect when Jane Doe 1's case presented, I would have felt the need to consult with a lawyer in addition to the ethics and medical professionals I had already consulted in her case. This additional consultation would have further delayed Jane Doe 1's treatment in addition to taking me away from treating other patients in need.

19. Jane Doe's case illustrates an additional reason why Idaho Code § 18-622 is especially dangerous: Idaho's status as a destination for surrogacy. In my experience, Idaho has a very significant number of women who carry babies as surrogates. The prevalence of surrogacy in Idaho means that many pregnancies in the state are initiated through in vitro fertilization ("IVF") and are likely to be high-risk pregnancies that carry an increased risk of serious health complications for both the mother and the fetus.

Jane Doe 2

20. One year and 8 months ago, Jane Doe 2 presented to an outlying hospital emergency department at 19-weeks' gestation experiencing significant bleeding. I eventually treated her and

the facts I describe here were either personal observations I made or facts relayed to me for the purpose of treating Jane Doe 2.

21. Jane Doe 2 was diagnosed with a placental abruption. This condition occurs when the placenta begins separating from the wall of the uterus before birth. Placental abruption decreases the blood and oxygen supply to the fetus and usually results in vaginal bleeding in the mother.

22. During the time she was under observation at the outside hospital, Jane Doe 2's condition worsened, and she developed disseminated intravascular coagulation ("DIC"). This is a dangerous condition that creates a high risk of death for the mother due to the rapid loss of large volumes of blood. Given that the outside hospital has minimal amounts of blood products in their blood bank, they requested to transfer Jane Doe 2 to Saint Alphonsus Regional Medical Center.

23. I first met Jane Doe 2 in the intensive care unit ("ICU") at Saint Alphonsus Regional Medical Center. The risk of her death at that point was imminent and the fetus still had a detectable heart rate by ultrasound. Although Jane Doe 2 was receiving multiple blood products at this point, her coagulation factors and anemia continued to worsen. The only medically acceptable action to preserve her life was immediate termination of the pregnancy.

24. An emergent dilation and evacuation procedure ("D&E") was advised, and Jane Doe 2 was taken to the operating room. The D&E procedure was uncomplicated. She remained intubated in the ICU overnight and continued to receive multiple blood products. By the next morning, the DIC had resolved and her anemia improved. Jane Doe 2 was transferred out of the ICU at that point and discharged from the hospital two days later.

25. Jane Doe 2's case illustrates the fact that some cases are so critical that there is simply no time to consult with a lawyer and debate, under the law, whether the proper medical standard of care should be used.

Jane Doe 3

26. Ten months ago, Jane Doe 3 presented to the Emergency Department at an outside hospital at 17-weeks' gestation. She was suffering from shortness of breath and high blood pressure. Like Jane Doe 1, Jane Doe 3's pregnancy was the result of IVF. I did not personally treat Jane Doe 3, but I have studied her case in the normal course of my work as part of educational conferences in the Department of Obstetrics and Gynecology at Saint Alphonsus Regional Medical Center.

27. After ruling out other conditions including COVID-19, pneumonia, and a blood clot in her lungs, Jane Doe 3 was diagnosed with pleural effusions, sometimes called "water on the lungs," a condition that causes fluid to accumulate between the tissues that line the lungs and chest. Further examination revealed that Jane Doe 3's pleural effusions were being caused by a case of preeclampsia with severe features. Her fetus had detectable cardiac activity.

28. Preeclampsia is a dangerous pregnancy complication that can result in serious and potentially fatal complications to both the mother and the fetus. It rarely occurs before 20-weeks' gestation. When it occurs before 20-week's gestation, as it did for Jane Doe 3, it is typically severe and carries a high risk of maternal and fetal death.

29. The only medically acceptable standard of care for preeclampsia with severe features in Jane Doe 3's case was to terminate the pregnancy through evacuation of the uterus. She underwent an urgent D&E procedure. The pleural effusions and high blood pressure immediately

began to improve after the pregnancy termination, and she was discharged home in stable condition several days later.

30. Had Idaho Code § 18-622 been in effect, my colleague, Jane Doe 3's treating physician, would have been in the position of assessing her own legal liability instead of simply assessing the patient's best interest.

Idaho Code § 18-622 and the Impact on Providers and Patients

31. Idaho Code § 18-622 is already harming women in Idaho. Specifically, in my experience as I describe above, the threat of criminal prosecution has already deterred doctors from providing medically necessary, life-saving care.

32. Idaho Code § 18-622 is also making it even more difficult to recruit Ob-Gyns to the State of Idaho. As I said, we already have a shortage of Ob-Gyns in Idaho. Idaho Code § 18-622 places physicians in a very difficult position because of a conflict between the State law and our ethical obligations to patients and our obligations under Federal law. If an Ob-Gyn can practice in a state without these conflicts and risks, it is only natural that they would be deterred from practicing here. In fact, at least one of my colleagues has already decided to stop her part-time work at our hospital due to the stress of complying with this law.

33. In addition, in emergency situations, many of which present in the middle of the night, physicians often do not have time to consult with lawyers about whether a decision they believe is warranted by the standard of care and therefore in the best interest of their patient will result in a financially ruinous investigation into their practice or in criminal liability. Also, time spent by physicians in court defending their medical decisions will keep them from their clinical duties for significant periods of time. This will add to the shortages in hospital and clinic coverage, increasing the workload of their practice partners as well as increasing wait times for patients.

34. The fact that a doctor can defend herself in a criminal prosecution does not give me any comfort about the way the law will negatively affect patient care. Having to defend against such a case alone would be incredibly burdensome, stressful, costly, and accordingly, means that the availability of a defense really does not solve the problems presented by the law.

35. Idaho Code § 18-622's threatens to criminalize abortion, even in many medically necessary circumstances, in a state where there is both a shortage of qualified physicians and a disproportionate number of high-risk pregnancies. This puts the health of Idaho women at significant risk.

I declare under penalty of perjury under the laws of the State of Idaho that the foregoing is to the best of my knowledge true and correct. Executed this 8th day of August 2022, in Boise, Idaho.

8/8/22
Date

Emily Corrigan, MD.
Emily Corrigan, M.D.

Exhibit C

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF IDAHO
SOUTHERN DIVISION

UNITED STATES OF AMERICA, Plaintiff, v. THE STATE OF IDAHO, Defendant.	Case No. 1:22-cv-329 **DECLARATION OF KYLIE COOPER, M.D.**

DECLARATION OF KYLIE COOPER, M.D. IN SUPPORT OF THE UNITED STATES' MOTION FOR A PRELIMINARY INJUNCTION

I, Kylie Cooper, being first duly sworn under oath, state and depose upon personal knowledge as follows:

1. I am a double board-certified Obstetrician-Gynecologist ("Ob-Gyn") and Maternal-Fetal Medicine ("MFM") physician at St. Luke's Regional Medical Center in Boise, Idaho. In that capacity, I specialize in high-risk obstetrics. I submit this declaration in support of the Motion for Preliminary Injunction filed by the United States in the above-captioned matter. Unless otherwise stated, the facts set forth herein are true of my own personal knowledge, and if called as a witness to testify in this matter, I could and would testify competently thereto.

2. I graduated from the University of Iowa Carver College of Medicine and subsequently completed my residency in Obstetrics and Gynecology at the University of Vermont. Following residency, I completed my Maternal-Fetal Medicine Fellowship at the University of Vermont. I am the current vice chair of the Idaho section of the American College of Obstetricians and Gynecologists (ACOG). I am teaching faculty for the Primary Care Obstetrics Fellowship with

Full Circle Health Family Medicine Residency which is a program to train family medicine physicians in obstetrical care to be used in their rural practice settings. This is particularly important given that there are no residency programs in OB/Gyn in Idaho. I also serve as an advisory board member for the Idaho Perinatal Project. My professional memberships include ACOG, the Society of Maternal-Fetal Medicine, and the Idaho Medical Association.

3. I came to Idaho specifically for my job as a maternal-fetal medicine physician at St. Luke's Regional Medical Center. As I was interviewing for MFM positions around the country it was clear that Idaho had a great need for high-risk obstetricians given the growing population and multitude of health conditions and pregnancy complications, such as obesity which impacts pregnancy in a multitude of ways. Additionally, there were very few female MFM physicians in Idaho, and I wanted to provide high quality and compassionate care to Idahoan families.

Idaho Code § 18-622 and the Impact on Providers and Patients

4. Over the course of my seven-year career as a practicing Ob-Gyn, I have treated thousands of pregnant women and delivered innumerable babies.

5. Pregnancy is not always straight forward and complication free. As an MFM physician my goal is to achieve the healthiest outcomes possible for my patients; however, there are many situations where pregnancy termination is the medically indicated treatment and is in the best interest of the patient's health and life. I will describe several recent examples of patients whom I have treated, which illustrate some circumstances that make it medically necessary to terminate a pregnancy. These cases occurred between September 2021 and June 2022.

Jane Doe 1

6. Jane Doe 1 presented to the emergency department at 15 weeks gestation feeling unwell and was found to have severe range blood pressures. Her fetus had recently been diagnosed

with triploidy, a chromosomal abnormality with an entire extra set of chromosomes leading to multiple severe birth defects and though there was a fetal heartbeat, this condition was not compatible with life. Fetal triploidy carries an increased risk of development of preeclampsia in the mother. She was admitted to the hospital with persistent stroke range blood pressures requiring high dose antihypertensive therapy and magnesium to reduce her risk for seizures. A diagnosis of preeclampsia with severe features was made. The only cure for preeclampsia is to end a pregnancy either by delivery of the neonate if after viability or by termination of pregnancy if pre-viable. The medical treatment for preeclampsia with severe features in patients who are at a previable gestational age is termination of pregnancy. Given her severe illness placing her at risk for stroke, seizure, pulmonary edema, development of HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets), urgent termination of pregnancy was the recommended treatment to stop her disease progression to preserve her health and life.

7. The only medically acceptable action to preserve her health and life was termination of the pregnancy.

Jane Doe 2

8. Jane Doe 2 presented to the emergency room at 20 weeks gestation with acute and progressive right upper abdominal pain requiring intravenous narcotics. Her pregnancy was complicated by a recent diagnosis of severe intrauterine growth restriction and though there was a fetal heartbeat, there was abnormal amniotic fluid level and abnormal umbilical cord blood flow portending a poor prognosis. She was found to have elevated blood pressures and lab abnormalities consistent with a diagnosis of HELLP syndrome. Her labs quickly deteriorated as would be expected with HELLP syndrome. Her platelets were dropping so quickly she required a platelet transfusion; she had evidence of hemolysis and concern for liver injury based on rising liver

enzymes and upper abdominal pain. HELLP syndrome placed her at risk for Disseminated Intravascular Coagulation (DIC) which is a life-threatening emergency related to the body's inappropriate consumption of blood-clotting factors leading to systemic bleeding, liver hemorrhage and failure, kidney failure, stroke, seizure, pulmonary edema. The only cure is to end a pregnancy either by delivery of the neonate if after viability or by termination of pregnancy if pre-viable. In the setting of pre-viable HELLP syndrome, urgent termination of pregnancy is the necessary treatment to stop her disease progression to preserve her health and life.

9. The only medically acceptable action to preserve her health and life was termination of the pregnancy.

Jane Doe 3

10. Jane Doe 3 presented to the emergency room at 15 weeks gestation with acute onset severe abdominal pain. She was noted to be hypertensive and lab abnormalities were consistent with a diagnosis of HELLP syndrome. Additionally, fetal and placental ultrasound was concerning for anomalies most consistent with fetal triploidy, a lethal fetal condition. Her abdominal pain and rapidly rising liver enzymes were indicative of liver injury, and her platelets were declining rapidly. In the setting of pre-viable HELLP syndrome she was at risk for DIC, liver hemorrhage and failure, kidney failure, stroke, seizure, pulmonary edema. The medically necessary treatment to stop her disease progression and protect her health and life was termination of pregnancy.

11. The only medically acceptable action to preserve her health and life was to terminate the pregnancy.

12. Prior to Idaho's trigger law, my medical training and judgment allowed me to promptly identify what the appropriate standard of care treatment was for these patients. I was

able to expeditiously care for them in the appropriate manner to prevent long-term harm. The trigger law threatens to criminalize medically indicated termination of pregnancy. In the future, though I know what the appropriate medical treatment is for my patients, I would be hesitant to provide the necessary care due to the significant risk to my professional license, my livelihood, my personal security, and the well-being of my family.

I declare under penalty of perjury under the laws of the State of Idaho that the foregoing is to the best of my knowledge true and correct. Executed this 8th day of August 2022, in Boise, Idaho.

8/8/2022
Date

Kylie Cooper MD
Kylie Cooper MD

Exhibit D

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF IDAHO
SOUTHERN DIVISION

UNITED STATES OF AMERICA, Plaintiff, v. THE STATE OF IDAHO, Defendant.	Case No. 1:22-cv-329 **DECLARATION OF STACY T. SEYB, M.D.**

DECLARATION OF STACY T. SEYB, M.D., IN SUPPORT OF THE UNITED STATES' MOTION FOR A PRELIMINARY INJUNCTION

I, Stacy T. Seyb, M.D., being first duly sworn under oath, state and depose upon personal knowledge as follows:

1. I am a board-certified Obstetrician-Gynecologist ("Ob-Gyn") physician at St. Luke's Regional Medical Center in Boise, Idaho. In that capacity, I specialize in Maternal-Fetal Medicine. I submit this declaration in support of the Motion for Preliminary Injunction filed by the United States in the above-captioned matter. Unless otherwise stated, the facts set forth herein are true of my own personal knowledge, and if called as a witness to testify in this matter, I could and would testify competently thereto.

2. I graduated from University of Kansas and subsequently completed my residency in Obstetrics and Gynecology at the University of Colorado and fellowship in Maternal Fetal Medicine at Northwestern University Feinberg School of Medicine. I practiced as a general Ob-Gyn and served as teaching faculty before completing my fellowship specializing in high risk and abnormal pregnancy management.

3. I have practiced as a Maternal-Fetal Medicine provider in Idaho for 22 years working not only on the front lines treating complicated pregnancies but also as a consultant to general OB-Gyn providers and Family Medicine providers providing obstetric care primarily in Southwest Idaho as well as across the state. I worked over a decade with the Idaho March of Dimes improving programming support and updating providers on evolving practices to improve the health of women and children in our state. Currently I serve as a state liaison to Idaho for the Society for Maternal Fetal Medicine.

Idaho Code § 18-622 and the Impact on Providers and Patients

4. Over the course of my nearly 35-year career as a practicing Ob-Gyn, I have treated thousands of pregnant women, delivered thousands of healthy babies, and managed a variety of life-threatening conditions in pregnancy.

5. Although as physicians we work to help our patients to experience normal pregnancies, culminating in the delivery of a healthy baby, not all pregnancies are as simple and complication-free as physicians and patients would like.

6. In the practice of Ob-Gyn, there are situations where pregnancy termination is the only medical intervention that can preserve a patient's health or save their life. Abortion is a very important tool that has contributed to the reduction of the maternal mortality rate from nearly 800 to 25 deaths per 100,000 live births across the United States in the last century. Obstetrics & Gynecology: November 2019 - Volume 134 - Issue 5 - p 1105-1108. I will describe examples of patients my colleagues and I have treated, which illustrate the dire circumstances that can make it medically necessary to terminate a pregnancy. My colleagues and I encounter these pregnancy-related emergencies approximately a dozen times per year.

Jane Doe 1

7. A 22-year old woman at 18 weeks of her pregnancy presented to the Emergency Department and a Medical Screening Exam was remarkable for fever, tender uterus, elevated heart rate and evidence of an intrauterine infection without other obvious sources of infection. Her history was also suspicious, she may have ruptured her bag of water 10 days prior, and ultrasound confirmed both a fetal heartbeat as well as no fluid around the baby confirming that she has a condition termed Septic Abortion. While antibiotics are important for treating severe infections, a general tenet of medicine is that without drainage or removal of infected tissue the infection is unlikely to improve.

8. Had Jane Doe 1 not received both antibiotics and termination of the fetus to allow removal of the infected tissue, the chance of her progressing to severe sepsis and dying was very high. If she survived, other risks of not removing the infection include infertility or hysterectomy, as well as other sequala of sepsis including renal failure and clotting disorder, also known as Disseminated Intervascular Coagulation (DIC). The national standard for treating this condition is both antibiotics and emptying the contents of the uterus.

Jane Doe 2

9. A 35-year old woman presented to the Emergency Department with headache, vision changes, and feeling poorly for a few days. A Medical Screening Examination revealed severe range blood pressures, and laboratory values that were consistent with a pregnancy condition known as pre-eclampsia with severe features. Ultrasound revealed a fetal heartbeat but the fetus was small for dates and the placenta was large, consistent with what is termed a partial molar pregnancy.

10. The only medically acceptable action to preserve her life was termination of the pregnancy. Not only was the pregnancy ultimately not viable due to the nature of the molar pregnancy but removal of the placenta, i.e., delivery was the only cure to reverse the severe pre-eclampsia.

Jane Doe 3

11. A 25-year old woman in her 19th week of pregnancy presented to the Emergency Department after she started bleeding very heavily per vagina. The Medical Screening Examination indicated hypovolemic shock due to her blood loss. Initial resuscitation improved her condition but she continued to bleed in an uncontrolled manner. Although there was a fetal heartbeat present, without further treatment the bleeding was likely to continue. A Dilation and Evacuation (D and E) was performed, terminating the pregnancy.

12. The only medically available tool to stop the bleeding was termination of the pregnancy. If left untreated the risks of life-threatening shock, even with blood replacement were very high.

13. Idaho Code § 18-622 threatens to criminalize abortion, without clear definition of medically necessary circumstances. The assertion that "prevent the death of the pregnant woman" is clear to the medical community is not useful to medical providers because this is not a dichotomous variable.

In the three cases above, the medical standard was clear and if the trigger law goes into effect, providers will likely delay care for fear of criminal prosecution and loss of licensure. For example, as a high-risk pregnancy consultant, I recently received a call from an outside institution where the provider encountered a woman at 20-weeks of gestation, with severe bleeding similar to the one described above, and wanted to transfer her. He was qualified but was afraid of the potential

ramifications of his actions if he proceeded with termination. It was clear that the mother was in danger and that treatment could not be delayed. This situation was clear that termination was the only option, and I reassured this provider and recommended that management. This is one example that providers do not have a clear guide as to what situations will place their livelihood in danger. Providers from all over the state are voicing that they cannot rely upon their medical judgment or best practices for handling pregnancy complications.

14. Idaho Code § 18-622 threatens to make it difficult to recruit Ob-Gyns to the State of Idaho, where we have no in-state training for this specialty. In emergency situations, physicians may delay the medically necessary care because they fear a financially ruinous investigation or criminal liability. If an Ob-Gyn can practice in a state without these conflicts and risks, it is only natural that they would be deterred from practicing here.

I declare under penalty of perjury under the laws of the State of Idaho that the foregoing is to the best of my knowledge true and correct. Executed this 8th day of August 2022, in Boise, Idaho.

8/8/2022

Date

Stacy T. Seyb, M.D.

Exhibit E

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF IDAHO
SOUTHERN DIVISION

United States of America, Plaintiff, v. The State of Idaho, Defendant.	Case No. 1:22-cv-329-BLW

DECLARATION OF DAVID R. WRIGHT

I, David R. Wright, of the Centers for Medicare & Medicaid Services ("CMS") declare that the following statements are true and correct to the best of my knowledge and belief, and that they are based on my personal knowledge as well as information provided to me in the course of my official duties.

1. I am the Director of the Quality, Safety & Oversight Group ("QSOG") in the CMS Center for Clinical Standards & Quality ("CCSQ"), United States Department of Health and Human Services ("HHS"). QSOG provides guidance to state survey agencies and accrediting organizations that evaluate Medicare health and safety standards for providers on behalf of CMS. One of these Medicare health and safety standards is the Emergency Medical Treatment and Labor Act (EMTALA), 42 U.S.C. § 1395dd.

2. Hospitals apply to become Medicare-certified by completing a CMS Form 855, Medicare Enrollment Application (https://www.cms.gov/medicare/cms-forms/cms-forms/downloads/cms855a.pdf).

3. Once the 855 form is submitted and approved, there is a certification process, designed to determine whether a hospital complies with the standards required by Federal law and

regulation, including Medicare Conditions of Participation ("CoPs"). 42 C.F.R. pt. 482 and 2 C.F.R. pt. 485.

4. If approved for Medicare certification, the hospital receives a CMS Form 1561-Health Insurance Benefit Agreement, which is signed by both the hospital and CMS (on behalf of the Secretary of HHS). https://www.cms.gov/Medicare/CMS-Forms/CMS-Forms/Downloads/CMS1561.pdf. The CMS Form 1561 states that "…the provider of services, agrees to conform to the provisions of section 1866 of the Social Security Act and applicable provisions in 42 CFR," which includes EMTALA.

5. The hospital additionally submits an assurance of compliance with Title VI of the Civil Rights Act of 1964, section 504 of the Rehabilitation Act of 1973 as amended.

6. Similar to the affirmations above, when a hospital submits its Medicare cost report following the completion of its fiscal years, the Chief Financial Officer or hospital Administrator must certify that he or she is "familiar with the laws and regulations regarding the provision of health care services, and that the services identified in this cost report were provided in compliance with such laws and regulations," which include EMTALA. *See* https://www.cms.gov/Regulations-and-Guidance/Guidance/Transmittals/Downloads/R3P240f.pdf

7. All of the attestations on these forms and reports discussed above—including the CMS Form 1561, the assurance of compliance with nondiscrimination laws, and the certification on the hospital's Medicare cost report—are essential to the functioning of the Medicare program. CMS reimburses providers only upon the understanding that those providers are complying with the statutes and regulations governing the program.

8. There are 52 Medicare-participating hospitals in Idaho. 39 of these hospitals filed claims with CMS for emergency room costs on their Medicare cost reports.

9. There are sixteen government-owned hospitals that participate in Medicare in Idaho. State Hospital South (Blackfoot, Idaho) is a psychiatric hospital owned by the State of Idaho. Additionally, Madison Memorial Hospital (Rexburg, Idaho), Kootenai Health (Coeur d'Alene, Idaho), Bear Lake Memorial Hospital (Montpelier, Idaho), Benewah Community Hospital (St.

Maries, Idaho), Caribou Medical Center (Soda Springs, Idaho), Cascade Medical Center (Cascade, Idaho), Lost Rivers Medical Center (Arco, Idaho), Minidoka Memorial Hospital (Rupert, Idaho), Nell J. Redfield Memorial Hospital (Malad, Idaho), Power County Hospital District (American Falls, Idaho), Shoshone Medical Center (Kellogg, Idaho), Steele Memorial Medical Center (Salmon, Idaho), Syringa General Hospital (Grangeville, Idaho), Valor Health (Emmett, Idaho), and Weiser Memorial Hospital (Weiser, Idaho) are county-owned hospitals. All of the above-listed hospitals, with the exception of State Hospital South, have filed cost reports that include emergency department costs.

10. Medicare participating hospitals must meet the requirements of the EMTALA statute enacted as Section 1867 of the Social Security Act (42 U.S.C. § 1395dd), the accompanying regulations in 42 CFR § 489.24, and the related requirements at 42 CFR § 489.20(l), (m), (q), and (r). EMTALA requires hospitals with emergency departments to provide an appropriate medical screening examination to any individual who comes to the emergency department and requests such an examination. And EMTALA prohibits hospitals with emergency departments from refusing to examine or treat individuals with an emergency medical condition. The term "hospital" includes critical access hospitals, which are typically smaller hospitals in rural communities that provide limited inpatient and outpatient services.

11. Some obligations under EMTALA apply only to Medicare-participating hospitals that have a dedicated emergency department, e.g., requirements related to providing a medical screening examination and any necessary stabilizing treatment. However, some EMTALA recipient hospital obligations, such as the obligation to provide stabilizing treatment, can also apply to Medicare-participating hospitals that do not have a dedicated emergency department, such as a hospital with specialized capabilities or facilities.

12. A hospital's EMTALA obligations apply both when a patient presents to the emergency department directly or by way of a transfer[1] from another medical provider. A Medicare-participating hospital that has specialized capabilities or facilities may not refuse to accept an appropriate transfer of an individual with an unstabilized emergency medical condition that requires such specialized capabilities or facilities. Hospitals with specialized capabilities or facilities may include, but are not limited to, hospitals with burn units, shock trauma units, neonatal intensive care units, or hospitals that are regional referral centers that serve rural areas as defined by the requirements at 42 CFR 412.96. This requirement to accept a transfer applies to any Medicare-participating hospital with specialized capabilities that has appropriate staff and facilities available to treat the condition, regardless of whether the hospital has a dedicated emergency department.

13. The goal of CMS' health and safety oversight is compliance with the Medicare CoPs and EMTALA, which themselves have the object of ensuring adequate care and advancing beneficiary and general patient health and safety. 42 CFR § 489.53(b) provides the basis for termination of a hospital's Medicare provider agreement for failure to comply with the requirements of EMTALA.

14. Through the passage of EMTALA, Congress obligated the Secretary of HHS to enforce the statute to protect any individual coming to the emergency department requesting examination or treatment for an emergency medical condition. As previously noted, CMS conditions the receipt of Medicare money, in part, on compliance with the EMTALA statute.

15. HHS cannot meet its Congressional EMTALA mandate if state law prohibits providers from providing the full range of care contemplated by the statute. Enforcing EMTALA aligns with the missions of HHS and CMS, of which protecting and promoting access to healthcare and emergency care are paramount.

[1] A Medicare-participating hospital's EMTALA obligations apply regardless of how a patient arrives at its emergency department. However, in cases where a patient has arrived at that hospital through an inappropriate transfer from another Medicare-providing hospital, the receiving facility should also report the inappropriate transfer to CMS. 42 U.S.C. §1395(d)(2)(B).

16. EMTALA assists in protecting those objectives while requiring healthcare providers to render care to all individuals presenting to an emergency department that accepts Medicare funding, regardless of their medical condition, ability to pay for medical services, or directly conflicting state laws.

17. Pursuant to 28 U.S.C. § 1746, I declare under penalty of perjury that the foregoing is true and correct.

Executed this 8th day of August, 2022 in Baltimore, Maryland.

David R. Wright -S
Digitally signed by David R. Wright -S
Date: 2022.08.08 16:09:29 -04'00'

David Wright
Director
Quality, Safety, and Oversight Group
Centers for Clinical Standards & Quality
Centers for Medicare & Medicaid Services
United States Department of Health and Human Services

Exhibit F

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF IDAHO
SOUTHERN DIVISION

UNITED STATES OF AMERICA, *Plaintiff*, v. THE STATE OF IDAHO, *Defendant*.	)	Civ. Action No. 1:22-cv-329

DECLARATION OF BARBARA SHADLE

I, Barbara Shadle, declare as follows:

1. I am an Auditor within the Division of Provider Audit Operations ("DPAO") in the Centers for Medicare and Medicaid Services ("CMS") within the United States Department of Health and Human Services ("HHS"). DPAO is an office within the Financial Services Group of CMS Office of Financial Management. DPAO oversees and coordinates the Medicare cost report audit and reimbursement process, in order to ensure that payments made to institutional providers are accurate. I have held this position since 2018. In my role, I regularly communicate with Medicare Administrative Contractors ("MACs"), which are private insurance companies acting on behalf of CMS that process Medicare claims and cost reports and determine payment amounts to providers. I also review Medicare cost report reimbursement issues. The statements made in this declaration are based on my personal knowledge, information I obtained from DPAO support contractors, and information contained in cost reports submitted by Medicare providers.

2. Institutional providers include hospitals, critical care facilities, and skilled nursing centers. Institutional providers participating in the Medicare program are required to submit a Medicare cost report following the completion of their fiscal years. This Medicare cost report contains the provider's costs, charges, and financial information used to establish the provider's Prospective Payment rates and final Medicare reimbursement.

3. The first page of each provider's submitted cost report requires the Chief Financial Officer or hospital Administrator to certify that he or she is "familiar with the laws and regulations regarding the provision of health care services, and that the services identified in this cost report were provided in compliance with such laws and regulations." A copy of the certification form that must be completed and certified by participating providers is included as Exhibit 1.

4. The laws and regulations to which the certification refers include the Emergency Medical Treatment and Labor Act ("EMTALA"), 42 U.S.C. § 1395dd, as well as other portions of the Social Security Act and accompanying regulations.

5. This certification carries legal consequences. In highlighted capital letters, the form warns: "Misrepresentation or falsification of any information contained in this cost report may be punishable by criminal, civil, and administrative action, fine, and/or imprisonment under federal law. Furthermore, if services identified in this report were provided or procured through the payment directly or indirectly of a kickback or were otherwise illegal, criminal, civil, and administrative fines and/or imprisonment may result."

6. I was asked to identify the amount of Medicare funds provided to hospital emergency departments in Idaho. Based on the data available and supplied by a DPAO support services contractor, I have determined that the total rough estimate of emergency department

payments in Idaho during fiscal years 2018-2020 was approximately $74,739,853 out of the providers' total payments of $3,413,768,066. This total rough estimate was calculated for 39 hospitals as to which costs were able to be identified for emergency department services via data in the Healthcare Cost Report Information System ("HCRIS").

7. The DPAO support services contractor identified this data regarding Medicare payments in Idaho based on finalized cost report information that is loaded to HCRIS where it is housed and can be accessed by CMS for Medicare rate-setting purposes.

8. In institutional providers' cost reports, providers identify their total hospital costs and costs attributable to their emergency departments. *See* Ex. 1, Worksheet A. To determine a rough estimate of emergency department payments, the emergency department costs were divided by total hospital costs to determine a percentage related specifically to the emergency department. I then multiplied this percentage by the hospital's total payments to reach the rough estimate of payments related to emergency department services identified above in paragraph 6.

I declare under penalty of perjury that the foregoing is true and correct. Executed this 8th day of August, 2022 in Baltimore, Maryland.

Barbara Shadle Digitally signed by Barbara Shadle Date: 2022.08.08 17:27:15 -04'00'

Barbara Shadle

Exhibit G

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF IDAHO
SOUTHERN DIVISION

UNITED STATES OF AMERICA, Plaintiff, v. THE STATE OF IDAHO, Defendant.	Case No. 1:22-cv-329-BLW

DECLARATION OF LISA NEWMAN

Pursuant to 28 U.S.C. § 1746, I, Lisa Newman, hereby declare:

1. I am an attorney in the U.S. Department of Justice, Civil Division, Federal Programs Branch. I am assigned to represent the United States in the above-captioned case. The statements made herein are based on my personal knowledge, and on information made available to me in the course of my duties and responsibilities as Government counsel in this case.

2. I submit this declaration in support of the United States' Motion for a Preliminary Injunction.

3. Filed herewith as United States' Exhibits 1-3 are true and correct copies of the following documents that I downloaded from the indicated websites:

Exhibit No.	Exhibit Name
1	Centers for Medicare & Medicaid Service (CMS) Form 855, *available at* https://perma.cc/84T6-S2DP (last visited Aug. 8, 2022)
2	Centers for Medicare & Medicaid Service (CMS) Form 1561, *available at* https://perma.cc/5EPE-YLRE (last visited Aug. 8, 2022)

3	Idaho Dep't of Health & Welfare, *2010-2020 Idaho Resident Births*, *VS Natality – Data Results, 2010-2020*, *available at* https://www.gethealthy.dhw.idaho.gov/idaho-births-vital-statistics (last visited Aug. 8, 2022)

I swear under penalty of perjury that the foregoing is true and correct. Executed on August 8, 2022, in Washington, D.C.

/s/ Lisa Newman
Lisa Newman

Counsel for the United States

NEWMAN DECLARATION: EXHIBIT A

MEDICARE ENROLLMENT APPLICATION

INSTITUTIONAL PROVIDERS

CMS-855A

SEE PAGE 1 TO DETERMINE IF YOU ARE COMPLETING THE CORRECT APPLICATION

SEE PAGE 3 FOR INFORMATION ON WHERE TO MAIL THIS APPLICATION.

SEE PAGE 52 TO FIND A LIST OF THE SUPPORTING DOCUMENTATION THAT MUST BE SUBMITTED WITH THIS APPLICATION.

CMS
CENTERS FOR MEDICARE & MEDICAID SERVICES

DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR MEDICARE & MEDICAID SERVICES

Form Approved OMB
No. 0938-0685
Expires: 08/19

WHO SHOULD COMPLETE THIS APPLICATION

Institutional providers can apply for enrollment in the Medicare program or make a change in their enrollment information using either:

- The Internet-based Provider Enrollment, Chain and Ownership System (PECOS), or
- The paper enrollment application process (e.g., CMS 855A).

For additional information regarding the Medicare enrollment process, including Internet-based PECOS, go to *www.cms.gov/MedicareProviderSupEnroll*.

Institutional providers who are enrolled in the Medicare program, but have not submitted the CMS 855A since 2003, are required to submit a Medicare enrollment application (i.e., Internet-based PECOS or the CMS 855A) as an initial application when reporting a change for the first time.

The following health care organizations must complete this application to initiate the enrollment process:

- Community Mental Health Center
- Comprehensive Outpatient Rehabilitation Facility
- Critical Access Hospital
- End-Stage Renal Disease Facility
- Federally Qualified Health Center
- Histocompatibility Laboratory
- Home Health Agency
- Hospice
- Hospital
- Indian Health Services Facility
- Organ Procurement Organization
- Outpatient Physical Therapy/Occupational Therapy /Speech Pathology Services
- Religious Non-Medical Health Care Institution
- Rural Health Clinic
- Skilled Nursing Facility

If your provider type is not listed above, contact your designated fee-for-service contractor before you submit this application.

Complete this application if you are a health care organization and you:

- Plan to bill Medicare for Part A medical services, or
- Would like to report a change to your existing Part A enrollment data. A change must be reported within 90 days of the effective date of the change; per 42 C.F.R. 424.516(e), changes of ownership or control must be reported within 30 days of the effective date of the change.

BILLING NUMBER INFORMATION

The National Provider Identifier (NPI) is the standard unique health identifier for health care providers and is assigned by the National Plan and Provider Enumeration System (NPPES). **Medicare healthcare providers, except organ procurement organizations, must obtain an NPI prior to enrolling in Medicare or before submitting a change to your existing Medicare enrollment information.** Applying for an NPI is a process separate from Medicare enrollment. To obtain an NPI, you may apply online at *https://NPPES.cms.hhs.gov*. As an organizational health care provider, it is your responsibility to determine if you have "subparts." A subpart is a component of an organization that furnishes healthcare and is not itself a legal entity. If you do have subparts, you must determine if they should obtain their own unique NPIs. Before you complete this enrollment application, you need to make those determinations and obtain NPI(s) accordingly.

IMPORTANT: For NPI purposes, sole proprietors and sole proprietorships are considered to be "Type 1" providers. Organizations (e.g., corporations, partnerships) are treated as "Type 2" entities. When reporting the NPI of a sole proprietor on this application, therefore, the individual's Type 1 NPI should be reported; for organizations, the Type 2 NPI should be furnished.

For more information about subparts, visit *www.cms.gov/NationalProvIdentStand* to view the "Medicare Expectations Subparts Paper."

The Medicare Identification Number, often referred to as the CMS Certification Number (CCN) or Medicare "legacy" number, is a generic term for any number other than the NPI that is used to identify a Medicare provider.

INSTRUCTIONS FOR COMPLETING AND SUBMITTING THIS APPLICATION

- Type or print all information so that it is legible. Do not use pencil.
- Report additional information within a section by copying and completing that section for each additional entry.
- Attach all required supporting documentation.
- Keep a copy of your completed Medicare enrollment package for your records.
- Send the completed application with original signatures and all required documentation to your designated Medicare fee-for-service contractor.

AVOID DELAYS IN YOUR ENROLLMENT

To avoid delays in the enrollment process, you should:

- Complete all required sections.
- Ensure that the legal business name shown in Section 2 matches the name on the tax documents.
- Ensure that the correspondence address shown in Section 2 is the provider's address.
- Enter your NPI in the applicable sections.
- Enter all applicable dates.
- Ensure that the correct person signs the application.
- Send your application and all supporting documentation to the designated fee-for-service contractor.

OBTAINING MEDICARE APPROVAL

The usual process for becoming a certified Medicare provider is as follows:

1. The applicant completes and submits a CMS-855A enrollment application and all supporting documentation to its fee-for-service contractor.
2. The fee-for-service contractor reviews the application and makes a recommendation for approval or denial to the State survey agency, with a copy to the CMS Regional Office.
3. The State agency or approved accreditation organization conducts a survey. Based on the survey results, the State agency makes a recommendation for approval or denial (a certification of compliance or noncompliance) to the CMS Regional Office. Certain provider types may elect voluntary accreditation by a CMS-recognized accrediting organization in lieu of a State survey.
4. A CMS contractor conducts a second contractor review, as needed, to verify that a provider continues to meet the enrollment requirements prior to granting Medicare billing privileges.
5. The CMS Regional Office makes the final decision regarding program eligibility. The CMS Regional Office also works with the Office of Civil Rights to obtain necessary Civil Rights clearances. If approved, the provider must typically sign a provider agreement.

ADDITIONAL INFORMATION

For additional information regarding the Medicare enrollment process, visit *www.cms.gov/MedicareProviderSupEnroll*.

The fee-for-service contractor may request, at any time during the enrollment process, documentation to support or validate information reported on the application. You are responsible for providing this documentation in a timely manner.

The information you provide on this application will not be shared. It is protected under 5 U.S.C. Section 552(b)(4) and/or (b)(6), respectively. For more information, see the last page of this application for the Privacy Act Statement.

MAIL YOUR APPLICATION

The Medicare fee-for-service contractor (also referred to as a fiscal intermediary or a Medicare administrative contractor) that services your State is responsible for processing your enrollment application. To locate the mailing address for your fee-for-service contractor, go to *www.cms.gov/MedicareProviderSupEnroll*.

SECTION 1: BASIC INFORMATION

NEW ENROLLEES

If you are:

- Enrolling with a particular fee-for-service contractor for the first time.
- Undergoing a change of ownership where the new owner will not be accepting assignment of the Medicare assets and liabilities of the seller/former owner.

ENROLLED MEDICARE PROVIDERS

The following actions apply to Medicare providers already enrolled in the program:

Reactivation

To reactivate your Medicare billing privileges, submit this enrollment application. In addition, you must be able to submit a valid claim and meet all current requirements for your provider type before reactivation can occur.

Voluntary Termination

A provider should voluntarily terminate its Medicare enrollment when:

- It will no longer be rendering services to Medicare patients,
- It is planning to cease (or has ceased) operations,
- There has been an acquisition/merger and the new owner will not be using the identification number of the entity it has acquired,
- There has been a consolidation and the identification numbers of the consolidating providers will no longer be used, or
- There has been a change of ownership and the new owner will not be accepting assignment of the Medicare assets and liabilities of the seller/former owner, meaning that the number of the seller/former owner will no longer be used.

NOTE: A voluntary identification number termination cannot be used to circumvent any corrective action plan or any pending/ongoing investigation, nor can it be used to avoid a period of reasonable assurance, where a provider must operate for a certain period without recurrence of the deficiencies that were the basis for the termination. The provider will not be reinstated until the completion of the reasonable assurance period.

Change of Ownership (CHOW)

A CHOW typically occurs when a Medicare provider has been purchased (or leased) by another organization. The CHOW results in the transfer of the old owner's Medicare Identification Number and provider agreement (including any outstanding Medicare debt of the old owner) to the new owner. The regulatory citation for CHOWs can be found at 42 C.F.R. 489.18. If the purchaser (or lessee) elects not to accept a transfer of the provider agreement, then the old agreement should be terminated and the purchaser or lessee is considered a new applicant.

SECTION 1: BASIC INFORMATION *(Continued)*

Acquisition/Merger

An acquisition/merger occurs when a currently enrolled Medicare provider is purchasing or has been purchased by another enrolled provider. Only the purchaser's Medicare Identification Number and tax identification number remain.

Acquisitions/mergers are different from CHOWs. In the case of an acquisition/merger, the seller/former owner's Medicare Identification Number dissolves. In a CHOW, the seller/former owner's provider number typically remains intact and is transferred to the new owner.

Consolidation

A consolidation occurs when two or more enrolled Medicare providers consolidate to form a new business entity.

Consolidations are different from acquisitions/mergers. In an acquisition/merger, two entities combine but the Medicare Identification Number and tax identification number (TIN) of the purchasing entity remain intact. In a consolidation, the TINs and Medicare Identification Numbers of the consolidating entities dissolve and a new TIN and Medicare Identification Number are assigned to the new, consolidated entity.

> Because of the various situations in which a CHOW, acquisition/merger, or consolidation can occur, it is recommended that the provider contact its fee-for-service contractor or its CMS Regional Office if it is unsure as to whether such a transaction has occurred. The provider should also review the applicable federal regulation at 42 C.F.R. 489.18 for additional guidance.

Change of Information

A change of information should be submitted if you are changing, adding, or deleting information under your current tax identification number. Changes in your existing enrollment data must be reported to the Medicare fee-for-service contractor in accordance with 42 C.F.R. 424.516(e).

NOTE: Ownership changes that do not qualify as CHOWs, acquisitions/mergers, or consolidations should be reported here. The most common example involves stock transfers. For instance, assume that a business entity's stock is owned by A, B, and C. A sells his stock to D. While this is an ownership change, it is generally not a formal CHOW under 42 C.F.R. 489.18. Thus, the ownership change from A to D should be reported as a change of information, not a CHOW. If you have any questions on whether an ownership change should be reported as a CHOW or a change of information, contact your fee-for-service contractor or CMS Regional Office.

If you are already enrolled in Medicare and are not receiving Medicare payments via EFT, any change to your enrollment information will require you to submit a CMS-588 application. All future payments will then be made via EFT.

Revalidation

CMS may require you to submit or update your enrollment information. The fee-for-service contractor will notify you when it is time for you to revalidate your enrollment information. Do not submit a revalidation application until you have been contacted by the fee-for-service contractor.

SECTION 1: BASIC INFORMATION *(Continued)*

A. Check one box and complete the required sections

REASON FOR APPLICATION	BILLING NUMBER INFORMATION	REQUIRED SECTIONS
☐ You are a **new enrollee** in Medicare	Enter your Medicare Identification Number (if issued) and the NPI you would like to link to this number in Section 4.	**Complete all applicable** sections except **2F, 2G,** and **2H**
☐ You are enrolling with another fee-for-service contractor's jurisdiction ☐ You are **reactivating** your Medicare enrollment	Enter your Medicare Identification Number (if issued) and the NPI you would like to link to this number in Section 4.	**Complete all applicable** sections except **2F, 2G,** and **2H**
☐ You are **voluntarily terminating** your Medicare enrollment	Effective Date of Termination: Medicare Identification Number(s) to Terminate *(if issued):* National Provider Identifier *(if issued):*	**Complete sections: 1, 2B1, 13,** and either **15** or **16**
☐ There has been a **Change of Ownership (CHOW)** of the Medicare-enrolled provider You are the: ☐ Seller/Former Owner ☐ Buyer/New Owner	Tax Identification Number:	**Seller/Former Owner: 1A, 2F, 13,** and either **15** or **16** **Buyer/New Owner: Complete all** sections except **2G** and **2H**
☐ Your organization has taken part in an **Acquisition** or **Merger** You are the: ☐ Seller/Former Owner ☐ Buyer/New Owner	Medicare Identification Number of the Seller/Former Owner *(if issued):* NPI: Tax Identification Number:	**Seller/Former Owner: 1A, 2G, 13,** and either **15** or **16** **Buyer/New Owner: 1A, 2G, 4, 13,** and either **15** (if you are the authorized official) or **16** (if you are the delegated official), and **6** for the signer if that authorized or delegated official has not been established for this provider.

SECTION 1: BASIC INFORMATION *(Continued)*

A. Check one box and complete the required sections

☐ Your organization has **Consolidated** with another organization You are the: ☐ Former organization ☐ New organization	Medicare Identification Number of the Seller/Former Owner *(if issued):* NPI: Tax Identification Number:	**Former Organizations: 1A, 2H, 13,** and either **15** or **16** **New Organization: Complete all** sections except **2F** and **2G**
☐ You are **changing** your Medicare information	Medicare Identification Number *(if issued):* NPI:	**Go to Section 1B**
☐ You are **revalidating** your Medicare enrollment	Enter your Medicare Identification Number (if issued) and the NPI you would like to link to this number in Section 4.	**Complete all applicable sections except 2F, 2G, and 2H**

SECTION 1: BASIC INFORMATION *(Continued)*

B. Check all that apply and complete the required sections:

	REQUIRED SECTIONS
☐ Identifying Information	**1, 2** (complete only those sections that are changing), **3, 13,** and either **15** (if you are the authorized official) **or 16** (if you are the delegated official), and Section 6 for the signer if that authorized or delegated official has not been established for this provider.
☐ Adverse Legal Actions/Convictions	**1, 2B1, 3, 13,** and either **15** (if you are the authorized official) **or 16** (if you are the delegated official), and Section 6 for the signer if that authorized or delegated official has not been established for this provider.
☐ Practice Location Information, Payment Address & Medical Record Storage Information	**1, 2B1, 3, 4** (complete only those sections that are changing), **13,** and either **15** (if you are the authorized official) **or 16** (if you are the delegated official), and Section 6 for the signer if that authorized or delegated official has not been established for this provider.
☐ Ownership Interest and/or Managing Control Information (Organizations)	**1, 2B1, 3, 5, 13,** and either **15** (if you are the authorized official) **or 16** (if you are the delegated official), and Section 6 for the signer if that authorized or delegated official has not been established for this provider.
☐ Ownership Interest and/or Managing Control Information (Individuals)	**1, 2B1, 3, 6, 13,** and either **15** (if you are the authorized official) **or 16** (if you are the delegated official), and Section 6 for the signer if that authorized or delegated official has not been established for this provider.
☐ Chain Home Office Information	**1, 2B1, 3, 7, 13,** and either **15** (if you are the authorized official) **or 16** (if you are the delegated official), and Section 6 for the signer if that authorized or delegated official has not been established for this provider.
☐ Billing Agency Information	**1, 2B1, 3, 8** (complete only those sections that are changing), **13,** and either **15** (if you are the authorized official) **or 16** (if you are the delegated official), and Section 6 for the signer if that authorized or delegated official has not been established for this provider.
☐ Special Requirements for Home Health Agencies	**1, 2B1, 3, 12, 13,** and either **15** (if you are the authorized official) **or 16** (if you are the delegated official), and Section 6 for the signer if that authorized or delegated official has not been established for this provider.
☐ Authorized Official(s)	**1, 2B1, 3, 6, 13,** and **15.**
☐ Delegated Official(s) (Optional)	**1, 2B1, 3, 6, 13, 15,** and **16**.

SECTION 2: IDENTIFYING INFORMATION

NEW ENROLLEES

Submit separate CMS-855A enrollment applications if the types of providers for which this application is being submitted are separately recognized provider types with different rules regarding Medicare participation. For example, if a provider functions as both a hospital and an end-stage renal disease (ESRD) facility, the provider must complete two separate enrollment applications (CMS-855A)—one for the hospital and one for the ESRD facility. If a hospital performs multiple types of services, only one enrollment application (CMS-855A) is required.

For example, a hospital that has a swing-bed unit need only submit one enrollment application (CMS– 855A). This is because the provider is operating as a single provider type—a hospital—that happens to have a distinct part furnishing different/additional services.

SPECIAL ENROLLMENT NOTES

- If you are adding a psychiatric or rehabilitation unit to a hospital, check the appropriate subcategory under the "Hospital" heading. (A separate enrollment for the psychiatric/rehabilitation unit is not required). The unit should be listed as a practice location in Section 4.
- If you are adding a home health agency (HHA) branch, list it as a practice location in Section 4. A separate enrollment application is not necessary.
- If you are changing hospital types (e.g., general hospital to a psychiatric hospital), indicate this in Section 2. A new/separate enrollment is not necessary.
- If you are adding an HHA sub-unit (as opposed to a branch), this requires an initial enrollment application for the sub-unit.
- If the hospital will focus on certain specialized services, the applicant should analyze whether the facility will be a general hospital or will fall under the category of a specialty hospital. A specialty hospital is defined as a facility that is primarily engaged in cardiac, orthopedic, or surgical care. Based upon Diagnosis Related Group/Major Diagnosis Category (DRG/MDC) and type (medical/surgical), the applicant should project all inpatient discharges expected in the first year of the hospital's operation. Those applicants that project that 45% or more of the hospital's inpatient cases will fall in either cardiac (MDC-5), orthopedic (MDC-8), or surgical care should check the Hospital—Specialty Hospital block in Section 2A2.
- Physician-owned hospital means any participating hospital (as defined in 42 CFR § 489.24) in which a physician, or an immediate family member of a physician has an ownership or investment interest in the hospital. The ownership or investment interest may be through equity, debt, or other means, and includes an interest in an entity that holds an ownership or investment interest in the hospital. This definition does not include a hospital with physician ownership or investment interests that satisfy the requirements at 42 CFR § 411.356(a) or (b).

SECTION 2: IDENTIFYING INFORMATION *(Continued)*

A. Type of Provider

The provider must meet all Federal and State requirements for the type of provider checked. Check only one provider type. If the provider functions as two or more provider types, a separate enrollment application (CMS-855A) must be submitted for each type.

1. Type of Provider (other than Hospitals— See 2A2). Check only one:

☐ Community Mental Health Center
☐ Comprehensive Outpatient Rehabilitation Facility
☐ Critical Access Hospital
☐ End-Stage Renal Disease Facility
☐ Federally Qualified Health Center
☐ Histocompatibility Laboratory
☐ Home Health Agency
☐ Home Health Agency (Sub-unit)
☐ Hospice
☐ Indian Health Services Facility
☐ Organ Procurement Organization
☐ Outpatient Physical Therapy/Occupational Therapy/ Speech Pathology Services
☐ Religious Non-Medical Health Care Institution
☐ Rural Health Clinic
☐ Skilled Nursing Facility
☐ Other (Specify):_____

2. If this provider is a hospital, check all applicable subgroups and units listed below and complete Section 2A3.

☐ Hospital—General
☐ Hospital—Acute Care
☐ Hospital—Children's (excluded from PPS)
☐ Hospital—Long-Term (excluded from PPS)
☐ Hospital—Psychiatric (excluded from PPS)
☐ Hospital—Rehabilitation (excluded from PPS)
☐ Hospital—Short-Term (General and Specialty)
☐ Hospital—Swing-Bed approved
☐ Hospital—Psychiatric Unit
☐ Hospital—Rehabilitation Unit
☐ Hospital—Specialty Hospital (cardiac, orthopedic, or surgical)
☐ Other (Specify):_____

3. If hospital was checked in Section 2A1 or 2A2, does this hospital have a compliance plan that states that the hospital checks all managing employees against the exclusion/debarment lists of both the HHS Office of the Inspector General (OIG) and the General Services Administration (GSA)?

☐ YES ☐ NO

4. Is the provider a physician-owned hospital (as defined in the Special Enrollment Notes on page 9)?

☐ YES ☐ NO

SECTION 2: IDENTIFYING INFORMATION *(Continued)*

B. Identification Information

1. BUSINESS INFORMATION

Legal Business Name (not the "Doing Business As" name) as reported to the Internal Revenue Service

Identify the type of organizational structure of this provider/supplier *(Check one)*

☐ Corporation ☐ Limited Liability Company ☐ Partnership

☐ Sole Proprietor ☐ Other *(Specify)*: _____

Tax Identification Number

Incorporation Date *(mm/dd/yyyy) (if applicable)*	State Where Incorporated *(if applicable)*

Other Name

Type of Other Name

☐ Former Legal Business Name ☐ Doing Business As Name ☐ Other *(Specify)*: _____

Identify how your business is registered with the IRS. (**NOTE:** If your business is a Federal and/or State government provider or supplier indicate "Non-Profit" below):

☐ Proprietary ☐ Non-Profit

NOTE: If a checkbox indicating Proprietaryship or non-profit status is not completed, the provider/supplier will be defaulted to "Proprietary."

What is the supplier's year end cost report date? *(mm/dd/yyyy)*

Is this supplier an Indian Health Facility enrolling with the designated Indian Health Service (IHS) Medicare Administrative Contractor (MAC)?

☐ Yes ☐ No

SECTION 2: IDENTIFYING INFORMATION *(Continued)*

2. STATE LICENSE INFORMATION/CERTIFICATION INFORMATION

Provide the following information if the provider has a State license/certification to operate as the provider type for which you are enrolling.

☐ State License Not Applicable

License Number	State Where Issued
Effective Date *(mm/dd/yyyy)*	Expiration/Renewal Date *(mm/dd/yyyy)*

Certification Information

☐ Certification Not Applicable

Certification Number	State Where Issued
Effective Date *(mm/dd/yyyy)*	Expiration/Renewal Date *(mm/dd/yyyy)*

C. Correspondence Address

Provide contact information for the entity listed in Section 2B1 of this section. Once enrolled, the information provided below will be used by the fee-for-service contractor if it needs to contact you directly. This address cannot be a billing agency's address.

Mailing Address Line 1 *(Street Name and Number)*

Mailing Address Line 2 *(Suite, Room, etc.)*

City/Town	State	ZIP Code + 4

Telephone Number	Fax Number *(if applicable)*	E-mail Address *(if applicable)*

D. Accreditation

Is this provider accredited? ☐ YES ☐ NO

If YES, complete the following:

Date of Accreditation *(mm/dd/yyyy)*	Expiration Date of Accreditation *(mm/dd/yyyy)*

Name of Accrediting Body

Type of Accreditation or Accreditation Program (e.g., hospital accreditation program, home health accreditation, etc.)

E. Comments

Use this section to clarify any information furnished in this section.

SECTION 2: IDENTIFYING INFORMATION *(Continued)*

F. Change of Ownership (CHOW) Information

Both the seller/former owner and the new owner should complete this section. (As the new owner may not know all of the seller/former owner's data, it should furnish this information on an "if known" basis.) The seller/former owner must complete Sections 1A, 2F, 13, and either 15 or 16. (Section 6 must also be completed if the signer has never completed Section 6 before.) The new owner must complete the entire application.

Legal Business Name of "Seller/Former Owner" as reported to the Internal Revenue Service		
"Doing Business As" Name of Seller/Former Owner *(if applicable)*		Old Owner's Medicare Identification Number *(if issued)*
Old Owner's NPI	Effective Date of Transfer *(this can be a future date) (mm/dd/yyyy)*	Name of Fee-For-Service Contractor of Seller/Former Owner

Will the new owner be accepting assignment of the current "Provider Agreement?" ☐ YES ☐ NO

If the answer is "No," then this is an initial enrollment and the new owner should follow the instructions for "New Enrollees" in Section 1 of this form.

Submit one copy of the bill of sale with the application. A copy of the final sales agreement must be submitted once the sale is executed.

G. Acquisitions/Mergers

Effective Date of Acquisition *(mm/dd/yyyy)*

The seller/former owner need only complete Sections 1A, 2G, 13, and either 15 or 16; the new owner must complete Sections 1A, 2G, 4, 13, and either 15 or 16. (Section 6 must also be completed if the signer has never completed Section 6 before.)

1. PROVIDER BEING ACQUIRED

This section is to be completed with information about the currently enrolled provider that is being acquired and will no longer retain its current Medicare provider number as a result of this acquisition.

Legal Business Name of the "Provider Being Acquired" as reported to the Internal Revenue Service
Current Fee-for-Service Contractor

Provide the name and Medicare identification number of all units of the above provider that have separate Medicare identification numbers but have not entered into separate provider agreements, such as swing bed units of a hospital and HHA branches. Also furnish the NPI. Units that already have a separate provider agreement should not be reported here.

NAME/DEPARTMENT	MEDICARE IDENTIFICATION NUMBER (IF ISSUED)	NATIONAL PROVIDER IDENTIFIER

SECTION 2: IDENTIFYING INFORMATION *(Continued)*

2. ACQUIRING PROVIDER

This section is to be completed with information about the organization acquiring the provider identified in Section 2G1.

Legal Business Name of the "Acquiring Provider" as Reported to the Internal Revenue Service	Medicare Identification Number (if issued)
Current Fee-for-Service Contractor	National Provider Identifier

Submit one copy of the bill of sale with the application. A copy of the final sales agreement must be submitted once the sale is executed.

H. Consolidations

The newly formed provider completes the entire application. The providers that are being consolidated are reported below.

1. 1ST CONSOLIDATING PROVIDER

This section is to be completed with information about the 1st currently enrolled provider that, as a result of this consolidation, will no longer retain its current Medicare Identification Number.

Legal Business Name of the "Provider Being Acquired" as reported to the Internal Revenue Service

Current Fee-for-Service Contractor

Effective Date of Consolidation

Provide the name and Medicare identification number of all units of the above provider that have separate Medicare identification numbers but have not entered into separate provider agreements, such as swing-bed units of a hospital and HHA branches. Also furnish the NPI. Units that already have a separate provider agreement should not be reported here.

NAME/DEPARTMENT	MEDICARE IDENTIFICATION NUMBER (IF ISSUED)	NATIONAL PROVIDER IDENTIFIER

2. 2ND CONSOLIDATING PROVIDER

This section is to be completed with information about the 2nd currently enrolled provider that, as a result of this consolidation, will also no longer retain its current Medicare Identification Number.

Legal Business Name of the "Provider Being Acquired" as reported to the Internal Revenue Service

Current Fee-for-Service Contractor

SECTION 2: IDENTIFYING INFORMATION *(Continued)*

Provide the name and Medicare identification number of all units of the above provider that have separate Medicare identification numbers but have not entered into separate provider agreements, such as swing-bed units of a hospital and HHA branches. Also furnish the NPI. Units that already have a separate provider agreement should not be reported here.

NAME/DEPARTMENT	MEDICARE IDENTIFICATION NUMBER (IF ISSUED)	NATIONAL PROVIDER IDENTIFIER

3. NEWLY CREATED PROVIDER IDENTIFICATION INFORMATION

Complete this section with identifying information about the newly created provider resulting from this consolidation.

Legal Business Name of the New Provider as Reported to the Internal Revenue Service	Tax Identification Number

Submit one copy of the bill of sale with the application. A copy of the final sales agreement must be submitted once the sale is executed.

SECTION 3: FINAL ADVERSE LEGAL ACTIONS/CONVICTIONS

This section captures information on final adverse legal actions, such as convictions, exclusions, revocations, and suspensions. All applicable final adverse legal actions must be reported, regardless of whether any records were expunged or any appeals are pending.

Convictions

1. The provider, supplier, or any owner of the provider or supplier was, within the last 10 years preceding enrollment or revalidation of enrollment, convicted of a Federal or State felony offense that CMS has determined to be detrimental to the best interests of the program and its beneficiaries. Offenses include: Felony crimes against persons and other similar crimes for which the individual was convicted, including guilty pleas and adjudicated pre-trial diversions; financial crimes, such as extortion, embezzlement, income tax evasion, insurance fraud and other similar crimes for which the individual was convicted, including guilty pleas and adjudicated pre-trial diversions; any felony that placed the Medicare program or its beneficiaries at immediate risk (such as a malpractice suit that results in a conviction of criminal neglect or misconduct); and any felonies that would result in a mandatory exclusion under Section 1128(a) of the Act.
2. Any misdemeanor conviction, under Federal or State law, related to: (a) the delivery of an item or service under Medicare or a State health care program, or (b) the abuse or neglect of a patient in connection with the delivery of a health care item or service.
3. Any misdemeanor conviction, under Federal or State law, related to theft, fraud, embezzlement, breach of fiduciary duty, or other financial misconduct in connection with the delivery of a health care item or service.
4. Any felony or misdemeanor conviction, under Federal or State law, relating to the interference with or obstruction of any investigation into any criminal offense described in 42 C.F.R. Section 1001.101 or 1001.201.
5. Any felony or misdemeanor conviction, under Federal or State law, relating to the unlawful manufacture, distribution, prescription, or dispensing of a controlled substance.

Exclusions, Revocations or Suspensions

1. Any revocation or suspension of a license to provide health care by any State licensing authority. This includes the surrender of such a license while a formal disciplinary proceeding was pending before a State licensing authority.
2. Any revocation or suspension of accreditation.
3. Any suspension or exclusion from participation in, or any sanction imposed by, a Federal or State health care program, or any debarment from participation in any Federal Executive Branch procurement or non-procurement program.
4. Any current Medicare payment suspension under any Medicare billing number.
5. Any Medicare revocation of any Medicare billing number.

SECTION 3: FINAL ADVERSE ACTIONS/CONVICTIONS *(Continued)*

FINAL ADVERSE LEGAL HISTORY

1. Has your organization, under any current or former name or business identity, ever had a final adverse action listed on page 16 of this application imposed against it?

   ☐ YES–Continue Below ☐ NO–Skip to Section 4

2. If yes, report each final adverse action, when it occurred, the Federal or State agency or the court/administrative body that imposed the action, and the resolution, if any.

   Attach a copy of the final adverse action documentation and resolution.

FINAL ADVERSE LEGAL ACTION	DATE	TAKEN BY	RESOLUTION

SECTION 4: PRACTICE LOCATION INFORMATION

INSTRUCTIONS

- Report all practice locations within the jurisdiction of the Medicare fee-for-service contractor to which you will submit this application.
- If the provider is adding a practice location in the same State and the location requires a separate provider agreement, a separate, complete CMS-855A must be submitted for that location. The location is considered a separate provider for purposes of enrollment, and is not considered a practice location of the main provider. If a provider agreement is not required, the location can be added as a practice location.
- If the provider is adding a practice location in another State and the location requires a separate provider agreement, a separate, complete CMS-855A must be submitted for that location. (This often happens when a home health agency wants to perform services in an adjacent State.)
- If the provider is adding a practice location within another fee-for-service contractor's jurisdiction and the provider is not already enrolled with that fee-for-service contractor, the provider must submit a full, complete CMS-855A to that fee-for-service contractor—regardless of whether a separate provider agreement is required. It cannot add the location as a mere practice location.
- Provide the specific street address as recorded by the United States Postal Service. Do not furnish a P.O. Box.

IMPORTANT: The provider should list its primary practice location first in Section 4A. The "primary practice location" must be associated with the NPI that the provider intends to use to bill for Medicare services.

If you have any questions as to whether the practice location requires a separate State survey or provider agreement, contact your fee-for-service contractor.

Community Mental Health Centers (CMHCs) must report all alternative sites where core services are provided (proposed alternative sites for initial enrollment and actual alternative sites for those CMHCs already participating in Medicare). In accordance with provisions of the Public Health Service Act, a CMHC is required to provide mental health services principally to individuals who reside in a defined geographic area (service area). Therefore, CMHCs must service a distinct and definable community. Those CMHCs operating or proposing to operate outside of this specific community must have a separate provider agreement/number, submit a separate enrollment application, and individually meet the requirements to participate. CMS will determine if the alternative site is permissible or whether the site must have a separate agreement/number. CMS will consider the actual demonstrated transportation pattern of CMHC clients within the community to ensure that all core services and partial hospitalization services are available from each location within the community. A CMHC patient must be able to access and receive services he/she needs at the parent CMHC site or the alternative site within the distinct and definable community served by the parent.

SECTION 4: PRACTICE LOCATION INFORMATION *(Continued)*

Hospitals must report all practice locations where the hospital provides services. Do not report separately enrolled provider types such as skilled nursing facilities (SNFs), HHAs, RHCs, etc., even if these entities are provider-based to the hospital. Suppose a hospital owns a SNF and an HHA. The hospital should not list the SNF and HHA on its application, as they are not locations where the hospital furnishes services.

They are providers that are separate and distinct from the hospital, and will be reported on their respective CMS-855A applications.

Base of Operations Address

- If this provider does not have a physical location where equipment and/or vehicles are stored or from where personnel report on a regular basis, complete this section with information about the location of the dispatcher/scheduler. This situation may occur if the provider operates mobile units that travel continuously from one location directly to another.
- HHAs must complete this section.

Mobile Facility and/or Portable Units

To properly pay claims, Medicare must know when services are provided in a mobile facility or with portable units. (This section is mostly applicable to providers that perform outpatient physical therapy, occupational therapy, and speech pathology services.)

- A “mobile facility” is generally a mobile home, trailer, or other large vehicle that has been converted, equipped, and licensed to render health care services. These vehicles usually travel to local shopping centers or community centers to see and treat patients inside the vehicle.
- A “portable unit” is when the provider transports medical equipment to a fixed location (e.g., a physician’s office or nursing home) to render services to the patient.

SECTION 4: PRACTICE LOCATION INFORMATION *(Continued)*

A. Practice Location Information

Report all practice locations where services will be furnished. If there is more than one location, copy and complete this section for each. Please list your primary practice location first.

To ensure that CMS establishes the correct associations between your Medicare legacy number (if issued) and your NPI, you must list a Medicare legacy number—NPI combination for each practice location. If you have multiple NPIs associated with both a single legacy number and a single practice location, please list below all NPIs and associated legacy numbers for that practice location.

If you are changing, adding, or deleting information, check the applicable box, furnish the effective date, and complete the appropriate fields in this section.

CHECK ONE	☐ **CHANGE**	☐ **ADD**	☐ **DELETE**
DATE *(mm/dd/yyyy)*			

Practice Location Name *("Doing Business As" name if different from Legal Business Name)*

Practice Location Street Address Line 1 *(Street Name and Number – NOT a P.O. Box)*

Practice Location Street Address Line 2 *(Suite, Room, etc.)*

City/Town	State	ZIP Code + 4
Telephone Number	Fax Number *(if applicable)*	E-mail Address *(if applicable)*
Medicare Identification Number *(if issued)*		NPI
Medicare Identification Number *(if issued)*		NPI
Medicare Identification Number *(if issued)*		NPI
Medicare Identification Number *(if issued)*		NPI
CLIA Number for this location *(if applicable)*	FDA/Radiology (Mammography) Certification Number for this location *(if issued)*	

Hospitals and HHAs only *(Identify type of practice location)*:

☐ HHA Branch
☐ Hospital Psychiatric Unit
☐ Hospital Rehabilitation Unit
☐ Hospital Swing-Bed Unit
☐ Main/Primary Hospital Location
☐ OPT Extension Site
☐ Other Hospital Practice Location:_____

SECTION 4: PRACTICE LOCATION INFORMATION *(Continued)*

B. Where Do You Want Remittance Notices Or Special Payments Sent?

If you are changing, adding, or deleting information, check the applicable box, furnish the effective date, and complete the appropriate fields in this section.

CHECK ONE	☐ CHANGE	☐ ADD	☐ DELETE
DATE *(mm/dd/yyyy)*			

Medicare will issue payments via electronic funds transfer (EFT). Since payment will be made by EFT, the "Special Payments" address will indicate where all other payment information (e.g., remittance notices, special payments) are sent.

☐ "Special Payments" address is the same as the practice location (only one address is listed in Section 4A). **Skip to Section 4C.**

☐ "Special Payments" address is different than that listed in Section 4A, or multiple locations are listed. **Provide address below.**

"Special Payments" Address Line 1 *(PO Box or Street Name and Number)*

"Special Payments" Address Line 2 *(Suite, Room, etc.)*

City/Town	State	ZIP Code + 4

C. Where Do You Keep Patients' Medical Records?

If you store patients' medical records (current and/or former patients) at a location other than the location in Section 4A or 4D, complete this section with the address of the storage location.

If this section is not complete, you are indicating that all records are stored at the practice locations reported in Section 4A or 4D. The records must be the provider's records, not the records of another provider. Post Office Boxes and drop boxes are not acceptable as physical addresses where patients' records are maintained.

For mobile facilities/portable units, the patients' medical records must be under the provider's control.

If you are changing, adding, or deleting information, check the applicable box, furnish the effective date, and complete the appropriate fields in this section.

First Medical Record Storage Facility for Current and Former Patients

CHECK ONE	☐ CHANGE	☐ ADD	☐ DELETE
DATE *(mm/dd/yyyy)*			

Storage Facility Address Line 1 *(Street Name and Number)*

Storage Facility Address Line 2 *(Suite, Room, etc.)*

City/Town	State	ZIP Code + 4

SECTION 4: PRACTICE LOCATION INFORMATION *(Continued)*

Second Medical Record Storage Facility for Current and Former Patients

CHECK ONE	☐ CHANGE	☐ ADD	☐ DELETE
DATE *(mm/dd/yyyy)*			

Storage Facility Address Line 1 *(Street Name and Number)*

Storage Facility Address Line 2 *(Suite, Room, etc.)*

City/Town	State	ZIP Code + 4

D. Base of Operations Address for Mobile or Portable Providers (Location of Business Office or Dispatcher/Scheduler)

The base of operations is the location from where personnel are dispatched, where mobile/portable equipment is stored, and when applicable, where vehicles are parked when not in use.

If you are changing, adding, or deleting information, check the applicable box, furnish the effective date, and complete the appropriate fields in this section.

CHECK ONE	☐ CHANGE	☐ ADD	☐ DELETE
DATE *(mm/dd/yyyy)*			

Check here ☐ and skip to Section 4E if the "Base of Operations" address is the same as the "Practice Location" listed in Section 4A.

Street Address Line 1 *(Street Name and Number)*

Street Address Line 2 *(Suite, Room, etc.)*

City/Town		State	ZIP Code + 4
Telephone Number	Fax Number *(if applicable)*	E-mail Address *(if applicable)*	

SECTION 4: PRACTICE LOCATION INFORMATION *(Continued)*

E. Vehicle Information

If the mobile health care services are rendered inside a vehicle, such as a mobile home or trailer, furnish the following vehicle information. Do not furnish information about ambulance vehicles, or vehicles that are used only to transport medical equipment (e.g., when the equipment is transported in a van but is used in a fixed setting, such as a doctor's office). If more than three vehicles are used, copy and complete this section as needed.

If you are changing, adding, or deleting information, check the applicable box, furnish the effective date, and complete the appropriate fields in this section.

CHECK ONE FOR EACH VEHICLE	TYPE OF VEHICLE (van, mobile home, trailer, etc.)	VEHICLE IDENTIFICATION NUMBER
☐ CHANGE ☐ ADD ☐ DELETE		
Effective Date:		
☐ CHANGE ☐ ADD ☐ DELETE		
Effective Date:		
☐ CHANGE ☐ ADD ☐ DELETE		
Effective Date:		

For each vehicle, submit a copy of all health care related permits/licenses/registrations.

F. Geographic Location For Mobile or Portable Providers where the Base of Operations and/or Vehicle Renders Services

For home health agencies (HHAs) and mobile/portable providers, furnish information identifying the geographic area(s) where health care services are rendered.

NOTE: If you provide mobile health care services in more than one State and those States are serviced by different Medicare fee-for-service contractors, complete a separate enrollment application (CMS-855A) for each Medicare fee-for-service contractor's jurisdiction.

1. INITIAL REPORTING AND/OR ADDITIONS

If you are reporting or adding an entire State, it is not necessary to report each city/town. Simply check the box below and specify the State.

☐ Entire State of _____

If services are provided in selected cities/towns, provide the locations below. Only list ZIP codes if you are not servicing the entire city/town.

CITY/TOWN	STATE	ZIP CODE

SECTION 4: PRACTICE LOCATION INFORMATION *(Continued)*

2. DELETIONS

If you are deleting an entire State, it is not necessary to report each city/town. Simply check the box below and specify the State.

☐ Entire State of _____

If services are provided in selected cities/towns, provide the locations below. Only list ZIP codes if you are not servicing the entire city/town.

CITY/TOWN	STATE	ZIP CODE

SECTION 5: OWNERSHIP INTEREST AND/OR MANAGING CONTROL INFORMATION (ORGANIZATIONS)

This section is to be completed with information about any organization that has direct or indirect ownership of, a partnership interest in, and/or managing control of the provider identified in Section 2. If there is more than one organization, copy and complete this section for each. (See examples below of organizations that should be reported in this section.)

Only organizations should be reported in this section. Individuals should be reported in Section 6.

If adding, deleting, or changing information on an existing owner, partner, or managing organization, check the appropriate box, indicate the effective date of the change, complete the appropriate fields in this section, and sign and date the certification statement.

A. Ownership

The following ownership interests must be reported in this section.

1. DIRECT OWNERSHIP INTEREST

Examples of direct ownership are as follows:

- The provider is a skilled nursing facility that is wholly (100%) owned by Company A. As such, the provider would have to report Company A in this section.
- A hospice wants to enroll in Medicare. Company X owns 50% of the hospice. Company X would have to be reported in this section.

In the first example, Company A is considered a direct owner of the skilled nursing facility, in that it actually owns the assets of the business. Similarly, Company X is a direct owner of the hospice mentioned in the second example. It has 50% actual ownership of the hospice.

2. INDIRECT OWNERSHIP INTEREST

Many organizations that directly own a provider are themselves wholly or partly owned by other organizations (or even individuals). This is often the result of the use of holding companies and parent/subsidiary relationships. Such organizations and individuals are considered to be "indirect" owners of the provider. Using the first example in #1 above, if Company B owned 100% of Company A, Company B is considered to be an indirect owner of the provider. In other words, a direct owner has an actual ownership interest in the provider (e.g., owns stock in the business, etc.), whereas an indirect owner has an ownership interest in an organization that owns the provider.

Consider the following example of indirect ownership:

EXAMPLE 1: OWNERSHIP

LEVEL 3	**Individual X**	**Individual Y**
	5%	30%
LEVEL 2	**Company C**	**Company B**
	60%	40%
LEVEL 1	**Company A**	
	100%	

SECTION 5: OWNERSHIP INTEREST AND/OR MANAGING CONTROL INFORMATION (ORGANIZATIONS) *(Continued)*

- Company A owns 100% of the Enrolling Provider
- Company B owns 40% of Company A
- Company C owns 60% of Company A
- Individual X owns 5% of Company C
- Individual Y owns 30% of Company B

In this example, Company A (Level 1) is the direct owner of the provider identified in section 2 of this application. Companies B and C, as well as Individuals X and Y, are indirect owners of the provider. To calculate ownership shares using the above-cited example, utilize the following steps:

LEVEL 1

The diagram above indicates that Company A owns 100% of the Enrolling Provider. Company A must be reported.

LEVEL 2

To calculate the percentage of ownership held by Company C of the Enrolling Provider, multiply:

- The percentage of ownership the LEVEL 1 owner has in the Enrolling Provider
  MULTIPLIED BY
  The percentage of ownership the LEVEL 2 owner has in that LEVEL 1 owner
- Company A, the LEVEL 1 (or direct) owner, owns 100% of the provider. The diagram also indicates that Company C, a LEVEL 2 owner, owns 60% of Company A. As such, multiply 100% (or 1.0) by 60% (.60). The result is .60. Therefore, Company C indirectly owns 60% of the provider, and must be reported.
- Repeat the same procedure for Company B, the other LEVEL 2 owner. Because Company B owns 40% of Company A, multiply this figure by 100% (again, the ownership stake Company A has in the Enrolling Provider). Company B thus owns 40% of the Enrolling Provider, and must be reported.

This process is continued until all LEVEL 2 owners have been accounted for.

LEVEL 3

To calculate the percentage of ownership that Individual X has in the Enrolling Provider, multiply:

- The percentage of ownership the LEVEL 2 owner has in the Enrolling Provider
  MULTIPLIED BY
  The percentage of ownership the LEVEL 3 owner has in that LEVEL 2 owner
- Company C owns 60% of the provider. According to the example above, Individual X (Level 3) owns 5% of Company C. Therefore, multiply 60% (.60) by 5% (.05), resulting in .03. This means that Individual X owns 3% of the provider and does not need to be reported in this application.
- Repeat this process for Company B, which owns 40% of the provider. The diagram states that Individual Y (Level 3) owns 30% of Company B. We thus multiply 40% (.40) by 30% (.30). The result is .12, or 12%. Because Individual Y owns 12% of the provider, Individual Y must be reported in this application (in Section 6: Individuals).

This process is continued until all owners in LEVEL 3 have been accounted for. This process must be repeated for Levels 4 and beyond.

SECTION 5: OWNERSHIP INTEREST AND/OR MANAGING CONTROL INFORMATION (ORGANIZATIONS) *(Continued)*

3. MORTGAGE OR SECURITY INTEREST

All entities with at least a 5% mortgage, deed of trust, or other security interest in the provider must be reported in this section. To calculate whether this interest meets the 5% threshold, use the following formula:

- Dollar amount of the mortgage, deed of trust, or other obligation secured by the provider or any of the property or assets of the provider
  DIVIDED BY
  Dollar amount of the total property and assets of the provider

Example: Two years ago, a provider obtained a $20 million loan from Entity X to add a third floor to its facility. Various assets of the provider secure the mortgage. The total value of the provider's property and assets is $100 million.

Using the formula described above, divide $20 million (the dollar amount of the secured mortgage) by $100 million (the total property and assets of the Enrolling Provider). This results in .20, or 20%. Because Entity X's interest represents at least 5% of the total property and assets of the Enrolling Provider, Entity X must be reported in this section.

4. PARTNERSHIPS

All general partnership interests—regardless of the percentage—must be reported. This includes: (1) all interests in a non-limited partnership, and (2) all general partnership interests in a limited partnership.

For limited partnerships, all limited partners must be reported if their interest in the partnership is at least 10%. To illustrate, assume a provider is a limited partnership. The general partner has a 60% interest in the entity, while the 4 limited partners each own 10%. The general partnership must be reported in this application. Likewise, the 4 limited partners must be reported, as they each own at least 10% of the limited partnership.

SECTION 5: OWNERSHIP INTEREST AND/OR MANAGING CONTROL INFORMATION (ORGANIZATIONS) *(Continued)*

5. ADDITIONAL INFORMATION ON OWNERSHIP

All entities that meet any the requirements above must be reported in this section, including, but not limited to:

- Entities with an investment interest in the provider (e.g., investment firms)
- Banks and financial institutions (e.g., mortgage interests)
- Holding companies
- Trusts and trustees
- Governmental/Tribal Organizations: If a Federal, State, county, city or other level of government, or an Indian tribe, will be legally and financially responsible for Medicare payments received (including any potential overpayments), the name of that government or Indian tribe must be reported as an owner. The provider must submit a letter on the letterhead of the responsible government (e.g., government agency) or tribal organization, which attests that the government or tribal organization will be legally and financially responsible in the event that there is any outstanding debt owed to CMS. This letter must be signed by an "authorized official" of the government or tribal organization who has the authority to legally and financially bind the government or tribal organization to the laws, regulations, and program instructions of Medicare. See Section 15 for further information on "authorized officials."
- Charitable and Religious Organizations: Many non-profit organizations are charitable or religious in nature, and are operated and/or managed by a Board of Trustees or other governing body. The actual name of the Board of Trustees or other governing body should be reported in this section.

In addition to furnishing the information in this section, the provider must submit:

- An organizational diagram identifying all of the entities listed in this section and their relationships with the provider and with each other.
- If the provider is a skilled nursing facility, a diagram identifying the organizational structures of all of its owners, including owners that were not required to be listed in this section or in Section 6.

B. Managing Control

Any organization that exercises operational or managerial control over the provider, or conducts the day-to-day operations of the provider, is a managing organization and must be reported. The organization need not have an ownership interest in the provider in order to qualify as a managing organization. For instance, it could be a management services organization under contract with the provider to furnish management services for the business.

C. Managing Control: Adverse Legal History

This section is to be completed with any adverse legal history information about any ownership organization, partnership and/or organization with managing control of the provider identified in Section 2.

SECTION 5: OWNERSHIP INTEREST AND/OR MANAGING CONTROL INFORMATION (ORGANIZATIONS) *(Continued)*

☐ Not Applicable

If you are changing, adding, or deleting information, check the applicable box, furnish the effective date, and complete the appropriate fields in this section.

CHECK ONE	☐ CHANGE	☐ ADD	☐ DELETE
DATE *(mm/dd/yyyy)*			

A. Ownership/Managing Control Organization

1. IDENTIFYING INFORMATION

Legal Business Name as Reported to the Internal Revenue Service

"Doing Business As" Name *(if applicable)*

Address Line 1 *(Street Name and Number)*

Address Line 2 *(Suite, Room, etc.)*

City/Town	State	ZIP Code + 4

Tax Identification Number *(required)*

Medicare Identification Number(s) *(if issued)*	NPI *(if issued)*

2. TYPE OF ORGANIZATION

Check all that apply:

☐ Corporation
☐ Limited liability Company
☐ Medical provider/supplier
☐ Management services company
☐ Medical staffing company
☐ Holding company
☐ Investment firm
☐ Bank or other financial institution
☐ Consulting firm
☐ For-profit
☐ Non-profit
☐ Other *(please specify)*:

_____

SECTION 5: OWNERSHIP INTEREST AND/OR MANAGING CONTROL INFORMATION (ORGANIZATIONS) *(Continued)*

B. Ownership/Managing Control Information

Identify the type of ownership and/or managing control the organization identified in Section 5.A.1. has in the provider identified in Section 2 of this application. Check all that apply. Complete all information for each type of ownership and/or managing control applicable.

☐ **5% or greater direct ownership interest**

Effective date of 5% or greater direct ownership interest *(mm/dd/yyyy)*

Exact percentage of direct ownership this organization has in the provider

Was this organization solely created to acquire/buy the provider and/or the provider's assets?

☐ Yes ☐ No

If this organization also provides contracted services to the provider, describe the types of services furnished *(e.g., managerial, billing, consultative, medical personnel staffing).*

☐ **5% or greater indirect ownership interest**

Effective date of 5% or greater indirect ownership interest *(mm/dd/yyyy)*

Exact percentage of indirect ownership this organization has in the provider

Was this organization solely created to acquire/buy the provider and/or the provider's assets?

☐ Yes ☐ No

If this organization provides contracted services to the provider, describe the types of services furnished *(e.g., managerial, billing, consultative, medical personnel staffing).*

☐ **5% or greater mortgage interest**

Effective date of 5% or greater mortgage interest *(mm/dd/yyyy)*

Exact percentage of mortgage interest this organization has in the provider

Was this mortgage solely created to acquire/buy the provider and/or the provider's assets?

☐ Yes ☐ No

SECTION 5: OWNERSHIP INTEREST AND/OR MANAGING CONTROL INFORMATION (ORGANIZATIONS) *(Continued)*

B. Managing Control: Identifying Information *(Continued)*

☐ **5% or greater security interest**

Effective date of 5% or greater security interest *(mm/dd/yyyy)*

Exact percentage of security interest this organization has in the provider

Was this security solely created to acquire/buy the provider and/or the provider's assets?

☐ Yes ☐ No

☐ **General Partnership interest**

Effective Date of the general partnership interest *(mm/dd/yyyy)*

Exact percentage of general partnership interest this organization has in the provider

Was this general partnership solely created to acquire/buy the provider and/or the provider's assets?

☐ Yes ☐ No

If this general partnership also provides contracted services to the provider, describe the types of services furnished *(e.g., managerial, billing, consultative, medical personnel staffing).*

☐ **Limited Partnership interest**

Effective Date of the limited partnership interest *(mm/dd/yyyy)*

Exact percentage of limited partnership interest this organization has in the provider

Was this limited partnership solely created to acquire/buy the provider and/or the provider's assets?

☐ Yes ☐ No

If this limited partnership also provides contracted services to the provider, describe the types of services furnished *(e.g., managerial, billing, consultative, medical personnel staffing).*

SECTION 5: OWNERSHIP INTEREST AND/OR MANAGING CONTROL INFORMATION (ORGANIZATIONS) *(Continued)*

B. Managing Control: Identifying Information *(Continued)*

☐ **Operational/Managerial Control**

Effective Date of the operational/managerial control *(mm/dd/yyyy)*

Exact percentage of operational/managerial control this organization has in the provider

If this operational/managerial organization also provides contracted services to the provider, describe the types of services furnished *(e.g., managerial, billing, consultative, medical personnel staffing).*

☐ **Other ownership or control/interest (please specify):** _____

Effective Date of other ownership or control/interest *(mm/dd/yyyy)*

Exact percentage of ownership or control/interest this organization has in the provider

Was this organization solely created to acquire/buy the provider and/or the provider's assets?

☐ Yes ☐ No

If this organization also provides contracted services to the provider, describe the types of services furnished *(e.g., managerial, billing, consultative, medical personnel staffing).*

C. Final Adverse Legal Action History

If reporting a change to existing information, check "Change," provide the effective date of the change, and complete the appropriate fields in this section.

☐ Change ☐ Effective Date:_____

1. Has this organization in Section 5A, under any current or former name or business identity, ever had a final adverse legal action listed on page 16 of this application imposed against it?

   ☐ YES–Continue Below ☐ NO–Skip to Section D

2. If YES, report each final adverse legal action, when it occurred, the Federal or State agency or the court/administrative body that imposed the action, and the resolution, if any.

   Attach a copy of the final adverse legal action documentation and resolution.

FINAL ADVERSE LEGAL ACTION	DATE	TAKEN BY	RESOLUTION

SECTION 6: OWNERSHIP INTEREST AND/OR MANAGING CONTROL INFORMATION (INDIVIDUALS)

This section is to be completed with information about any individual who has direct or indirect ownership of, a partnership interest in, and/or managing control of the provider identified in Section 2 of this application. If there is more than one individual, copy and complete this section for each. Note that the provider must have at least one managing employee.

Only individuals should be reported in this section. Organizations should be reported in Section 5.

If adding, deleting, or changing information on an existing owner, partner, or managing individual, check the appropriate box, indicate the effective date of the change, complete the appropriate fields in this section, and sign and date the certification statement.

A. Ownership and Control

The following ownership control interests, as they are described in the instructions to Section 5, must be reported in this section:

- 5% or greater direct ownership interest
- 5% or greater indirect ownership interest
- 5% or greater mortgage or security interest
- All general partnership interests, regardless of the percentage. This includes: (1) all interests in a non-limited partnership, and (2) all general partnership interests in a limited partnership.
- Limited partnership interests if the individual's interest in the partnership is at least 10%.
- Officers and Directors, if the entity is organized as a corporation.

For more information on these interests, please see Section 5. Note that the diagrams referred to in Section 5(A)(5) of the instructions must include all individuals with any of the ownership interests described above.

All managing employees of the provider must be reported in this section. The term "managing employee" means a general manager, business manager, administrator, director, or other individual who exercises operational or managerial control over, or who directly or indirectly conducts, the day-to-day operations of the provider, either under contract or through some other arrangement, regardless of whether the individual is a W-2 employee of the provider.

NOTE: If a governmental or tribal organization will be legally and financially responsible for Medicare payments received (per the instructions for Governmental/Tribal Organizations in Section 5), the provider is only required to report its managing employees in Section 6. Owners, partners, officers and directors do not need to be reported, except those who are listed as authorized or delegated officials on this application.

B. Adverse Legal History

This section is to be completed with any adverse legal history information about any individual owner, partner and/or individual with managing control of the provider identified in Section 2.

SECTION 6: OWNERSHIP INTEREST AND/OR MANAGING CONTROL INFORMATION (INDIVIDUALS) *(Continued)*

If you are changing, adding, or deleting information, check the applicable box, furnish the effective date, and complete the appropriate fields in this section.

CHECK ONE	☐ CHANGE	☐ ADD	☐ DELETE
DATE *(mm/dd/yyyy)*			

A. Identifying Information

First Name	Middle Initial	Last Name	Jr., Sr., etc.

Medicare Identification Number *(if issued)*	NPI *(if issued)*

Social Security Number *(Required)*	Date of Birth *(mm/dd/yyyy)*	Place of Birth *(State)*	Country of Birth

Identify the type of ownership and/or managing control the individual identified above has in the provider identified in Section 2 of this application. Check all that apply. Complete all information for each type of ownership and/or managing control applicable.

☐ 5% or greater direct ownership interest

Effective Date of 5% or greater direct ownership interest *(mm/dd/yyyy)*

Exact percentage of direct ownership this individual has in the provider

If this individual also provides contracted services to the provider, describe the types of services furnished *(e.g., managerial, billing, consultative, medical personnel staffing, etc.).*

☐ 5% or greater indirect ownership interest

Effective Date of 5% or greater indirect ownership interest *(mm/dd/yyyy)*

Exact percentage of indirect ownership this individual has in the provider

If this individual also provides contracted services to the provider, describe the types of services furnished *(e.g., managerial, billing, consultative, medical personnel staffing, etc.).*

SECTION 6: OWNERSHIP INTEREST AND/OR MANAGING CONTROL INFORMATION (INDIVIDUALS) *(Continued)*

☐ 5% or greater mortgage interest

Effective Date of 5% or greater mortgage interest *(mm/dd/yyyy)*

Exact percentage of mortgage interest this individual has in the provider

If this individual also provides contracted services to the provider, describe the types of services furnished *(e.g., managerial, billing, consultative, medical personnel staffing, etc.).*

☐ 5% or greater security interest

Effective Date of 5% or greater greater security interest *(mm/dd/yyyy)*

Exact percentage of security interest this individual has in the provider

If this individual also provides contracted services to the provider, describe the types of services furnished *(e.g., managerial, billing, consultative, medical personnel staffing, etc.).*

☐ General Partnership interest

Effective Date of the general partnership interest *(mm/dd/yyyy)*

Exact percentage of general partnership interest this individual has in the provider

If applicable, furnish this individual's title within the provider organization *(e.g., CEO, Board member, etc.)*

If this individual also provides contracted services to the provider, describe the types of services furnished *(e.g., managerial, billing, consultative, medical personnel staffing, etc.).*

☐ Limited Partnership interest

Effective Date of limited partnership interest *(mm/dd/yyyy)*

Exact percentage of limited partnership interest this individual has in the provider

If applicable, furnish this individual's title within the provider organization *(e.g., CEO, Board member, etc.)*

If this individual also provides contracted services to the provider, describe the types of services furnished *(e.g., managerial, billing, consultative, medical personnel staffing, etc.).*

SECTION 6: OWNERSHIP INTEREST AND/OR MANAGING CONTROL INFORMATION (INDIVIDUALS) *(Continued)*

☐ Officer

Effective Date of office *(mm/dd/yyyy)*

Exact percentage of control as an Officer this individual has in the provider

If applicable, furnish this individual's title within the provider organization *(e.g., CEO, Board member, etc.)*

If this individual also provides contracted services to the provider, describe the types of services furnished *(e.g., managerial, billing, consultative, medical personnel staffing, etc.).*

☐ Director

Effective Date as Director *(mm/dd/yyyy)*

Exact percentage of control as a Director this individual has in the provider

If applicable, furnish this individual's title within the provider organization *(e.g., CEO, Board member, etc.)*

If this individual also provides contracted services to the provider, describe the types of services furnished *(e.g., managerial, billing, consultative, medical personnel staffing, etc.).*

☐ W-2 Managing Employee

Effective Date of 5% or greater direct ownership interest *(mm/dd/yyyy)*

Exact percentage of management control this individual has in the provider

If applicable, furnish this manager's title within the provider organization *(e.g., CEO, Board member, etc.)*

If this individual also provides contracted services to the provider, describe the types of services furnished *(e.g., managerial, billing, consultative, medical personnel staffing, etc.).*

SECTION 6: OWNERSHIP INTEREST AND/OR MANAGING CONTROL INFORMATION (INDIVIDUALS) *(Continued)*

☐ Contracted Managing Employee

Effective Date of contract for managing employee *(mm/dd/yyyy)*

Exact percentage of this contracted managing employee's control in the provider

If applicable, furnish this individual's title within the provider organization *(e.g., CEO, Board member, etc.)*

If this individual also provides contracted services to the provider, describe the types of services furnished *(e.g., managerial, billing, consultative, medical personnel staffing, etc.).*

☐ Operational/Managerial Control

Effective Date of the operational/managerial control *(mm/dd/yyyy)*

Exact percentage of operational/managerial control this individual has in the provider

If applicable, furnish this individual's title within the provider organization *(e.g., CEO, Board member, etc.)*

If this individual also provides contracted services to the provider, describe the types of services furnished *(e.g., managerial, billing, consultative, medical personnel staffing, etc.).*

☐ Other ownership or control/interest (please specify): _____

Effective Date of other ownership or control/interest *(mm/dd/yyyy)*

Exact percentage of ownership or control/interest this individual has in the provider

If applicable, furnish this individual's title within the provider organization *(e.g., CEO, Board member, etc.)*

If this individual also provides contracted services to the provider, describe the types of services furnished *(e.g., managerial, billing, consultative, medical personnel staffing, etc.).*

SECTION 6: OWNERSHIP INTEREST AND/OR MANAGING CONTROL INFORMATION (INDIVIDUALS) *(Continued)*

B. Final Adverse Legal Action History

Complete this section for the individual reported in Section 6A above.

If you are changing information, check "change" box, furnish the effective date, and complete the appropriate fields in this section.

☐ Change ☐ Effective Date:_____

1. Has the individual in Section 6A, under any current or former name or business identity, ever had a final adverse legal action listed on page 16 of this application imposed against him/her?

   ☐ YES–Continue Below ☐ NO–Skip to Section 7

2. If YES, report each final adverse legal action, when it occurred, the Federal or State agency or the court/administrative body that imposed the action, and the resolution, if any.

   Attach a copy of the final adverse legal action documentation and resolution.

FINAL ADVERSE LEGAL ACTION	DATE	TAKEN BY	RESOLUTION

SECTION 7: CHAIN HOME OFFICE INFORMATION

This section captures information regarding chain organizations. This information will be used to ensure proper reimbursement when the provider's year-end cost report is filed with the Medicare fee-for-service contractor.

For more information on chain organizations, see 42 C.F.R. 421.404.

Check here ☐ if this section does not apply and skip to Section 8.

If you are changing, adding, or deleting information, check the applicable box, furnish the effective date, and complete the appropriate fields in this section.

CHECK ONE	☐ CHANGE	☐ ADD	☐ DELETE
DATE *(mm/dd/yyyy)*			

A. Type of Action this Provider is Reporting

CHECK ONE:	EFFECTIVE DATE	SECTIONS TO COMPLETE
☐ Provider in chain is enrolling in Medicare for the first time *(Initial Enrollment or Change of Ownership)*.		Complete all of Section 7.
☐ Provider is no longer associated with the chain		Complete Section 7 identifying the former chain home office.
☐ Provider has changed from one chain to another.		Complete Section 7 in full to identify the new chain home office.
☐ The name of provider's chain home office is changing *(all other information remains the same)*.		Complete Section 7C.

B. Chain Home Office Administrator Information

First Name of Home Office Administrator or CEO	Middle Initial	Last Name	Jr., Sr., etc.

Title of Home Office Administrator	Social Security Number	Date of Birth *(mm/dd/yyyy)*

SECTION 7: CHAIN HOME OFFICE INFORMATION *(Continued)*

C. Chain Home Office Information

1. Name of Home Office as Reported to the Internal Revenue Service

2. Home Office Business Street Address Line 1 *(Street Name and Number)*

Home Office Business Street Address Line 2 *(Suite, Room, etc.)*

City/Town	State	ZIP Code + 4

Telephone Number	Fax Number *(if applicable)*	E-mail Address *(if applicable)*

3. Home Office Tax Identification Number	Home Office Cost Report Year-End Date *(mm/dd)*
4. Home Office Fee-For-Service Contractor	Home Office Chain Number

D. Type of Business Structure of the Chain Home Office

Check one:

Voluntary:

☐ Non-Profit – Religious Organization

☐ Non-Profit – Other *(Specify)*:_____

Proprietary:

☐ Individual

☐ Corporation

☐ Partnership

☐ Other *(Specify)*: _____

Government:

☐ Federal

☐ State

☐ City

☐ County

☐ City-County

☐ Hospital District

☐ Other *(Specify)*: _____

E. Provider's Affiliation to the Chain Home Office

Check one:

☐ Joint Venture/Partnership ☐ Managed/Related ☐ Leased

☐ Operated/Related ☐ Wholly Owned ☐ Other *(Specify)*: _____

SECTION 8: BILLING AGENCY INFORMATION

Applicants that use a billing agency must complete this section. A billing agency is a company or individual that you contract with to process and submit your claims. If you use a billing agency, you are responsible for the claims submitted on your behalf.

☐ **Check here if this section does not apply and skip to Section 12.**

BILLING AGENCY NAME AND ADDRESS

If you are changing, adding, or deleting information, check the applicable box, furnish the effective date, and complete the appropriate fields in this section.

CHECK ONE	☐ CHANGE	☐ ADD	☐ DELETE
DATE *(mm/dd/yyyy)*			

Legal Business/Individual Name as Reported to the Social Security Administration or Internal Revenue Service

If Individual, Billing Agent Date of Birth *(mm/dd/yyyy)*

Tax Identification Number or Social Security Number *(required)*

"Doing Business As" Name *(if applicable)*

Billing Agency Address Line 1 *(Street Name and Number)*

Billing Agency Address Line 2 *(Suite, Room, etc.)*

City/Town		State	ZIP Code + 4
Telephone Number	Fax Number *(if applicable)*	E-mail Address *(if applicable)*	

SECTION 9: FOR FUTURE USE (THIS SECTION NOT APPLICABLE)

SECTION 10: FOR FUTURE USE (THIS SECTION NOT APPLICABLE)

SECTION 11: FOR FUTURE USE (THIS SECTION NOT APPLICABLE)

SECTION 12: SPECIAL REQUIREMENTS FOR HOME HEALTH AGENCIES (HHAS)

INSTRUCTIONS

All HHAs and HHA sub-units enrolling in the Medicare program must complete this section. HHAs and HHA sub-units initially enrolling in Medicare, Medicaid, or both programs on or after January 1, 1998 are required to provide documentation supporting that they have sufficient initial reserve operating funds (capitalization) to operate for the first three months in the Medicare and/or Medicaid program(s). The capitalization requirement applies to all HHAs and HHA sub-units enrolling in the Medicare program, including HHAs or HHA sub-units currently participating in the Medicare program that, as a result of a change of ownership, will be issued a new provider number. The capitalization requirement does not apply to a branch of an HHA. Regulations found at 42 C.F.R. 489.28 require that the fee-for-service contractor determine the required amount of reserve operating funds needed for the enrolling HHA or HHA sub-unit by comparing the enrolling HHA or HHA sub-unit to at least three other new HHAs that it serves which are comparable to the enrolling HHA or HHA sub-unit. Factors to be considered are geographic location, number of visits, type of HHA or HHA sub-unit and business structure of the HHA or HHA sub-unit. The fee-for-service contractor then verifies that the enrolling HHA or HHA sub-unit has the required funds. To assist the fee-for-service contractor in determining the amount of funds necessary, the enrolling HHA or HHA sub-unit should complete this section.

Check here ☐ if this section does not apply and skip to Section 13.

A. Type of Home Health Agency

1. CHECK ONE:

☐ Non-Profit Agency ☐ Proprietary Agency

2. PROJECTED NUMBER OF VISITS BY THIS HOME HEALTH AGENCY

How many visits does this HHA project it will make in the first:

three months of operation?_____

twelve months of operation? _____

3. FINANCIAL DOCUMENTATION

A) In order to expedite the enrollment process, the HHA may attach a copy of its most current savings, checking, or other financial statement(s) that verifies the initial reserve operating funds, accompanied by:

1) An attestation from an officer of the bank or other financial institution stating that the funds are in the account(s) and are immediately available for the HHA's use, and

2) Certification from the HHA attesting that at least 50% of the reserve operating funds are non-borrowed funds.

B) Will the HHA be submitting the above documentation with this application? ☐ YES ☐ NO

NOTE: The fee-for-service contractor may require a subsequent attestation that the funds are still available. If the fee-for-service contractor determines that the HHA requires funds in addition to those indicated on the originally submitted account statement(s), it will require verification of the additional amount as well as a new attestation statement.

SECTION 12: SPECIAL REQUIREMENTS FOR HOME HEALTH AGENCIES (HHAS) *(Continued)*

4. ADDITIONAL INFORMATION

Provide any additional documentation necessary to assist the fee-for-service contractor or State agency in properly comparing this HHA with other comparable HHAs. Use this space to explain or justify any unique financial situations of this HHA that may be helpful in determining the HHA's compliance with the capitalization requirements.

B. Nursing Registries

If you are changing, adding, or deleting information, check the applicable box, furnish the effective date, and complete the appropriate fields in this section.

CHECK ONE	☐ CHANGE	☐ ADD	☐ DELETE
DATE *(mm/dd/yyyy)*			

Does this HHA contract with a nursing registry whereby the latter furnishes personnel to perform HHA services on behalf of the provider?

☐ YES–Furnish the information below

☐ NO–Skip to Section 13

Legal Business/Individual Name as Reported to the Internal Revenue Service

Tax Identification Number *(required)*

"Doing Business As" Name *(if applicable)*

Billing Street Address Line 1 *(Street Name and Number)*

Billing Street Address Line 2 *(Suite, Room, etc.)*

City/Town	State	ZIP Code + 4

Telephone Number	Fax Number *(if applicable)*	E-mail Address *(if applicable)*

SECTION 13: CONTACT PERSON

If questions arise during the processing of this application, the fee-for-service contractor will contact the individual shown below. If the contact person is an authorized or delegated official, check the appropriate box below and skip to the section indicated.

☐ Contact an Authorized Official listed in Section 15

☐ Contact a Delegated Official listed in Section 16

First Name	Middle Initial	Last Name	Jr., Sr., etc.

Telephone Number	Fax Number *(if applicable)*

Address Line 1 *(Street Name and Number)*

Address Line 2 *(Suite, Room, etc.)*

City/Town	State	ZIP Code + 4

E-mail Address

SECTION 14: PENALTIES FOR FALSIFYING INFORMATION

This section explains the penalties for deliberately furnishing false information in this application to gain or maintain enrollment in the Medicare program.

1. 18 U.S.C. § 1001 authorizes criminal penalties against an individual who, in any matter within the jurisdiction of any department or agency of the United States, knowingly and willfully falsifies, conceals or covers up by any trick, scheme or device a material fact, or makes any false, fictitious, or fraudulent statements or representations, or makes any false writing or document knowing the same to contain any false, fictitious or fraudulent statement or entry. Individual offenders are subject to fines of up to $250,000 and imprisonment for up to five years. Offenders that are organizations are subject to fines of up to $500,000 (18 U.S.C. § 3571). Section 3571(d) also authorizes fines of up to twice the gross gain derived by the offender if it is greater than the amount specifically authorized by the sentencing statute.
2. Section 1128B(a)(1) of the Social Security Act authorizes criminal penalties against any individual who, "knowingly and willfully," makes or causes to be made any false statement or representation of a material fact in any application for any benefit or payment under a Federal health care program. The offender is subject to fines of up to $25,000 and/or imprisonment for up to five years.
3. The Civil False Claims Act, 31 U.S.C. § 3729, imposes civil liability, in part, on any person who:
   a) knowingly presents, or causes to be presented, to an officer or any employee of the United States Government a false or fraudulent claim for payment or approval;
   b) knowingly makes, uses, or causes to be made or used, a false record or statement to get a false or fraudulent claim paid or approved by the Government; or
   c) conspires to defraud the Government by getting a false or fraudulent claim allowed or paid.

   The Act imposes a civil penalty of $5,000 to $10,000 per violation, plus three times the amount of damages sustained by the Government
4. Section 1128A(a)(1) of the Social Security Act imposes civil liability, in part, on any person (including an organization, agency or other entity) that knowingly presents or causes to be presented to an officer, employee, or agent of the United States, or of any department or agency thereof, or of any State agency…a claim…that the Secretary determines is for a medical or other item or service that the person knows or should know:
   a) was not provided as claimed; and/or
   b) the claim is false or fraudulent.

   This provision authorizes a civil monetary penalty of up to $10,000 for each item or service, an assessment of up to three times the amount claimed, and exclusion from participation in the Medicare program and State health care programs.
5. 18 U.S.C. 1035 authorizes criminal penalties against individuals in any matter involving a health care benefit program who knowingly and willfully falsifies, conceals or covers up by any trick, scheme, or device a material fact; or makes any materially false, fictitious, or fraudulent statements or representations, or makes or uses any materially false fictitious, or fraudulent statement or entry, in connection with the delivery of or payment for health care benefits, items or services. The individual shall be fined or imprisoned up to 5 years or both.

SECTION 14: PENALTIES FOR FALSIFYING INFORMATION *(Continued)*

6. 18 U.S.C. 1347 authorizes criminal penalties against individuals who knowing and willfully execute, or attempt, to executive a scheme or artifice to defraud any health care benefit program, or to obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by or under the control of any, health care benefit program in connection with the delivery of or payment for health care benefits, items, or services. Individuals shall be fined or imprisoned up to 10 years or both. If the violation results in serious bodily injury, an individual will be fined or imprisoned up to 20 years, or both. If the violation results in death, the individual shall be fined or imprisoned for any term of years or for life, or both.
7. The government may assert common law claims such as "common law fraud," "money paid by mistake," and "unjust enrichment." Remedies include compensatory and punitive damages, restitution, and recovery of the amount of the unjust profit.

SECTION 15: CERTIFICATION STATEMENT

An **AUTHORIZED OFFICIAL** means an appointed official (for example, chief executive officer, chief financial officer, general partner, chairman of the board, or direct owner) to whom the organization has granted the legal authority to enroll it in the Medicare program, to make changes or updates to the organization's status in the Medicare program, and to commit the organization to fully abide by the statutes, regulations, and program instructions of the Medicare program.

A **DELEGATED OFFICIAL** means an individual who is delegated by an authorized official the authority to report changes and updates to the provider's enrollment record. A delegated official must be an individual with an "ownership or control interest in" (as that term is defined in Section 1124(a)(3) of the Social Security Act), or be a W-2 managing employee of, the provider.

Delegated officials may not delegate their authority to any other individual. Only an authorized official may delegate the authority to make changes and/or updates to the provider's Medicare status. Even when delegated officials are reported in this application, an authorized official retains the authority to make any such changes and/or updates by providing his or her printed name, signature, and date of signature as required in Section 15B.

> **NOTE:** Authorized officials and delegated officials must be reported in Section 6, either on this application or on a previous application to this same Medicare fee-for-service contractor. **If this is the first time an authorized and/or delegated official has been reported on the CMS-855A, you must complete Section 6 for that individual.**

By his/her signature(s), an authorized official binds the provider to all of the requirements listed in the Certification Statement and acknowledges that the provider may be denied entry to or revoked from the Medicare program if any requirements are not met. All signatures must be original and in ink. Faxed, photocopied, or stamped signatures will not be accepted.

Only an authorized official has the authority to sign (1) the initial enrollment application on behalf of the provider or (2) the enrollment application that must be submitted as part of the periodic revalidation process. A delegated official does not have this authority.

By signing this application, an authorized official agrees to immediately notify the Medicare fee-for-service contractor if any information furnished on this application is not true, correct, or complete. In addition, an authorized official, by his/her signature, agrees to notify the Medicare fee-for-service contractor of any future changes to the information contained in this form, after the provider is enrolled in Medicare, in accordance with the timeframes established in 42 C.F.R. 424.516(e).

The provider can have as many authorized officials as it wants. If the provider has more than two authorized officials, it should copy and complete this section as needed.

Each authorized and delegated official must have and disclose his/her social security number.

SECTION 15: CERTIFICATION STATEMENT *(Continued)*

A. Additional Requirements for Medicare Enrollment

These are additional requirements that the provider must meet and maintain in order to bill the Medicare program. Read these requirements carefully. By signing, the provider is attesting to having read the requirements and understanding them.

By his/her signature(s), the authorized official(s) named below and the delegated official(s) named in Section 16 agree to adhere to the following requirements stated in this Certification Statement:

1. I agree to notify the Medicare contractor of any future changes to the information contained in this application in accordance with the time frames established in 42 C.F.R. § 424.516(e). I understand that any change in the business structure of this provider may require the submission of a new application.
2. I have read and understand the Penalties for Falsifying Information, as printed in this application. I understand that any deliberate omission, misrepresentation, or falsification of any information contained in this application or contained in any communication supplying information to Medicare, or any deliberate alteration of any text on this application form, may be punished by criminal, civil, or administrative penalties including, but not limited to, the denial or revocation of Medicare billing privileges, and/or the imposition of fines, civil damages, and/or imprisonment.
3. I agree to abide by the Medicare laws, regulations and program instructions that apply to this provider. The Medicare laws, regulations, and program instructions are available through the Medicare contractor. I understand that payment of a claim by Medicare is conditioned upon the claim and the underlying transaction complying with such laws, regulations, and program instructions (including, but not limited to, the Federal anti-kickback statute and the Stark law), and on the provider's compliance with all applicable conditions of participation in Medicare.
4. Neither this provider, nor any physician owner or investor or any other owner, partner, officer, director, managing employee, authorized official, or delegated official thereof is currently sanctioned, suspended, debarred, or excluded by the Medicare or State Health Care Program, e.g., Medicaid program, or any other Federal program, or is otherwise prohibited from supplying services to Medicare or other Federal program beneficiaries.
5. I agree that any existing or future overpayment made to the provider by the Medicare program may be recouped by Medicare through the withholding of future payments.
6. I will not knowingly present or cause to be presented a false or fraudulent claim for payment by Medicare, and I will not submit claims with deliberate ignorance or reckless disregard of their truth or falsity.
7. I authorize any national accrediting body whose standards are recognized by the Secretary as meeting the Medicare program participation requirements, to release to any authorized representative, employee, or agent of the Centers for Medicare & Medicaid Services (CMS), a copy of my most recent accreditation survey, together with any information related to the survey that CMS may require (including corrective action plans).

SECTION 15: CERTIFICATION STATEMENT *(Continued)*

B. 1ST Authorized Official Signature

I have read the contents of this application. My signature legally and financially binds this provider to the laws, regulations, and program instructions of the Medicare program. By my signature, I certify that the information contained herein is true, correct, and complete, and I authorize the Medicare fee-for-service contractor to verify this information. If I become aware that any information in this application is not true, correct, or complete, I agree to notify the Medicare fee-for-service contractor of this fact in accordance with the time frames established in 42 C.F.R. § 424.516(e).

If you are changing, adding, or deleting information, check the applicable box, furnish the effective date, and complete the appropriate fields in this section.

CHECK ONE	☐ CHANGE	☐ ADD	☐ DELETE
DATE *(mm/dd/yyyy)*			

Authorized Official's Information and Signature

First Name	Middle Initial	Last Name	Suffix *(e.g., Jr., Sr.)*

Telephone Number	Title/Position
Authorized Official Signature *(First, Middle, Last Name, Jr., Sr., M.D., D.O., etc.)*	Date Signed *(mm/dd/yyyy)*

C. 2ND Authorized Official Signature

I have read the contents of this application. My signature legally and financially binds this provider to the laws, regulations, and program instructions of the Medicare program. By my signature, I certify that the information contained herein is true, correct, and complete, and I authorize the Medicare fee-for-service contractor to verify this information. If I become aware that any information in this application is not true, correct, or complete, I agree to notify the Medicare fee-for-service contractor of this fact in accordance with the time frames established in 42 C.F.R. § 424.516(e).

If you are changing, adding, or deleting information, check the applicable box, furnish the effective date, and complete the appropriate fields in this section.

CHECK ONE	☐ CHANGE	☐ ADD	☐ DELETE
DATE *(mm/dd/yyyy)*			

Authorized Official's Information and Signature

First Name	Middle Initial	Last Name	Suffix *(e.g., Jr., Sr.)*

Telephone Number	Title/Position
Authorized Official Signature *(First, Middle, Last Name, Jr., Sr., M.D., D.O., etc.)*	Date Signed *(mm/dd/yyyy)*

All signatures must be original and signed in ink. Applications with signatures deemed not original will not be processed. Stamped, faxed or copied signatures will not be accepted.

SECTION 16: DELEGATED OFFICIAL(S) *(Optional)*

- You are not required to have a delegated official. However, if no delegated official is assigned, the authorized official(s) will be the only person(s) who can make changes and/or updates to the provider's status in the Medicare program.
- The signature of a delegated official shall have the same force and effect as that of an authorized official, and shall legally and financially bind the provider to the laws, regulations, and program instructions of the Medicare program. By his or her signature, the delegated official certifies that he or she has read the Certification Statement in Section 15 and agrees to adhere to all of the stated requirements. The delegated official also certifies that he/she meets the definition of a delegated official. When making changes and/or updates to the provider's enrollment information maintained by the Medicare program, the delegated official certifies that the information provided is true, correct, and complete.
- Delegated officials being deleted do not have to sign or date this application.
- Independent contractors are not considered "employed" by the provider and, therefore, cannot be delegated officials.
- The signature(s) of an authorized official in Section 16 constitutes a legal delegation of authority to any and all delegated official(s) assigned in Section 16.
- If there are more than two individuals, copy and complete this section for each individual.

A. 1ST Delegated Official Signature

If you are changing, adding, or deleting information, check the applicable box, furnish the effective date, and complete the appropriate fields in this section.

CHECK ONE	☐ CHANGE	☐ ADD	☐ DELETE
DATE *(mm/dd/yyyy)*			

Delegated Official First Name	Middle Initial	Last Name	Suffix *(e.g., Jr., Sr.)*

Delegated Official Signature *(First, Middle, Last Name, Jr., Sr., M.D., D.O., etc.)*	Date Signed *(mm/dd/yyyy)*

☐ Check here if Delegated Official is a W-2 Employee	Telephone Number

Authorized Official Signature Assigning this Delegation *(First, Middle, Last Name, Jr., Sr., M.D., D.O., etc.)*	Date Signed *(mm/dd/yyyy)*

SECTION 16: DELEGATED OFFICIAL(S) *(Optional) (Continued)*

B. 2ND Delegated Official Signature

If you are changing, adding, or deleting information, check the applicable box, furnish the effective date, and complete the appropriate fields in this section.

CHECK ONE	☐ CHANGE	☐ ADD	☐ DELETE
DATE *(mm/dd/yyyy)*			

Delegated Official First Name	Middle Initial	Last Name	Suffix *(e.g., Jr., Sr.)*

Delegated Official Signature *(First, Middle, Last Name, Jr., Sr., M.D., D.O., etc.)*	Date Signed *(mm/dd/yyyy)*

☐ Check here if Delegated Official is a W-2 Employee	Telephone Number

Authorized Official Signature Assigning this Delegation *(First, Middle, Last Name, Jr., Sr., M.D., D.O., etc.)*	Date Signed *(mm/dd/yyyy)*

SECTION 17: SUPPORTING DOCUMENTS

This section lists the documents that, if applicable, must be submitted with this completed enrollment application. If you are newly enrolling, or are reactivating or revalidating your enrollment, you must provide all applicable documents. For changes, only submit documents that are applicable to that change. The enrolling provider may submit a notarized copy of a Certificate of Good Standing from the provider's State licensing/certification board or other medical associations in lieu of copies of the above-requested documents. This certification cannot be more than 30 days old.

The fee-for-service contractor may request, at any time during the enrollment process, documentation to support or validate information that you have reported in this application. The Medicare fee-for-service contractor may also request documents from you, other than those identified in this section 17, as are necessary to bill Medicare.

MANDATORY FOR ALL PROVIDER/SUPPLIER TYPES

Required documents that can only be obtained after a State survey are not required as part of the application submission but must be furnished within 30 days of the provider receiving them. The Medicare fee-for–service contractor will furnish specific licensing requirements for your provider type upon request.

- ☐ Licenses, certifications and registrations required by Medicare or State law.
- ☐ Federal, State, and/or local (city/county) business licenses, certifications and/or registrations required to operate a health care facility.
- ☐ Written confirmation from the IRS confirming your Tax Identification Number with the Legal Business Name (e.g., IRS CP 575) provided in Section 2.
- ☐ Completed Form CMS-588, Authorization Agreement for Electronic Funds Transfer.
  NOTE: If a provider already receives payments electronically and is not making a change to its banking information, the CMS-588 is not required.

MANDATORY FOR SELECTED PROVIDER/SUPPLIER TYPES

- ☐ Copy(s) of all bills of sale or sales agreements (CHOWS, Acquisition/Mergers, and Consolidations only).
- ☐ Copy(s) of all documents that demonstrate meeting capitalization requirements (HHAs only).

MANDATORY, IF APPLICABLE

- ☐ Statement in writing from the bank. If Medicare payment due a provider of services is being sent to a bank (or similar financial institution) with whom the provider has a lending relationship (that is, any type of loan), then the provider must provide a statement in writing from the bank (which must be in the loan agreement) that the bank has agreed to waive its right of offset for Medicare receivables.
- ☐ Copy(s) of all adverse legal action documentation (e.g., notifications, resolutions, and reinstatement letters).
- ☐ Copy of an attestation for government entities and tribal organizations
- ☐ Copy of HRSA Notice of Grant Award if that is a qualifying document for FQHC status
- ☐ Copy of IRS Determination Letter, if provider is registered with the IRS as non-profit
- ☐ Written confirmation from the IRS confirming your Limited Liability Company (LLC) is automatically classified as a Disregarded Entity. (e.g., Form 8832).
  NOTE: A disregarded entity is an eligible entity that is treated as an entity not separate from its single owner for income tax purposes.

MEDICARE SUPPLIER ENROLLMENT APPLICATION PRIVACY ACT STATEMENT

The Centers for Medicare & Medicaid Services (CMS) is authorized to collect the information requested on this form by sections 1124(a)(1), 1124A(a)(3), 1128, 1814, 1815, 1833(e), and 1842(r) of the Social Security Act [42 U.S.C. §§ 1320a-3(a)(1), 1320a-7, 1395f, 1395g, 1395(l)(e), and 1395u(r)] and section 31001(1) of the Debt Collection Improvement Act [31 U.S.C. § 7701(c)].

The purpose of collecting this information is to determine or verify the eligibility of individuals and organizations to enroll in the Medicare program as suppliers of goods and services to Medicare beneficiaries and to assist in the administration of the Medicare program. This information will also be used to ensure that no payments will be made to providers who are excluded from participation in the Medicare program. All information on this form is required, with the exception of those sections marked as "optional" on the form. Without this information, the ability to make payments will be delayed or denied.

The information collected will be entered into the Provider Enrollment, Chain and Ownership System (PECOS). The information in this application will be disclosed according to the routine uses described below.

Information from these systems may be disclosed under specific circumstances to:

1. CMS contractors to carry out Medicare functions, collating or analyzing data, or to detect fraud or abuse;
2. A congressional office from the record of an individual health care provider in response to an inquiry from the congressional office at the written request of that individual health care practitioner;
3. The Railroad Retirement Board to administer provisions of the Railroad Retirement or Social Security Acts;
4. Peer Review Organizations in connection with the review of claims, or in connection with studies or other review activities, conducted pursuant to Part B of Title XVIII of the Social Security Act;
5. To the Department of Justice or an adjudicative body when the agency, an agency employee, or the United States Government is a party to litigation and the use of the information is compatible with the purpose for which the agency collected the information;
6. To the Department of Justice for investigating and prosecuting violations of the Social Security Act, to which criminal penalties are attached;
7. To the American Medical Association (AMA), for the purpose of attempting to identify medical doctors when the National Plan and Provider System is unable to establish identity after matching contractor submitted data to the data extract provided by the AMA;
8. An individual or organization for a research, evaluation, or epidemiological project related to the prevention of disease or disability, or to the restoration or maintenance of health;
9. Other Federal agencies that administer a Federal health care benefit program to enumerate/enroll providers of medical services or to detect fraud or abuse;
10. State Licensing Boards for review of unethical practices or non-professional conduct;
11. States for the purpose of administration of health care programs; and/or
12. Insurance companies, self insurers, health maintenance organizations, multiple employer trusts, and other health care groups providing health care claims processing, when a link to Medicare or Medicaid claims is established, and data are used solely to process supplier's health care claims.

The supplier should be aware that the Computer Matching and Privacy Protection Act of 1988 (P.L. 100-503) amended the Privacy Act, 5 U.S.C. § 552a, to permit the government to verify information through computer matching.

Protection of Proprietary Information

Privileged or confidential commercial or financial information collected in this form is protected from public disclosure by Federal law 5 U.S.C. § 552(b)(4) and Executive Order 12600.

Protection of Confidential Commercial and/or Sensitive Personal Information

If any information within this application (or attachments thereto) constitutes a trade secret or privileged or confidential information (as such terms are interpreted under the Freedom of Information Act and applicable case law), or is of a highly sensitive personal nature such that disclosure would constitute a clearly unwarranted invasion of the personal privacy of one or more persons, then such information will be protected from release by CMS under 5 U.S.C. §§ 552(b)(4) and/or (b)(6), respectively.

NEWMAN DECLARATION: EXHIBIT B

DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR MEDICARE & MEDICAID SERVICES

FORM APPROVED
OMB No. 0938-0832

HEALTH INSURANCE BENEFIT AGREEMENT

(Agreement with Provider Pursuant to Section 1866 of the Social Security Act, as Amended and Title 42 Code of Federal Regulations (CFR) Chapter IV, Part 489)

AGREEMENT

between

THE SECRETARY OF HEALTH AND HUMAN SERVICES

and

_____

doing business as (D/B/A) _____

In order to receive payment under title XVIII of the Social Security Act,_____

_____

D/B/A _____ as the provider of services, agrees to conform to the provisions of section of 1866 of the Social Security Act and applicable provisions in 42 CFR.

This agreement, upon submission by the provider of services of acceptable assurance of compliance with title VI of the Civil Rights Act of 1964, section 504 of the Rehabilitation Act of 1973 as amended, and upon acceptance by the Secretary of Health and Human Services, shall be binding on the provider of services and the Secretary.

In the event of a transfer of ownership, this agreement is automatically assigned to the new owner subject to the conditions specified in this agreement and 42 CFR 489, to include existing plans of correction and the duration of this agreement, if the agreement is time limited.

ATTENTION: Read the following provision of Federal law carefully before signing.

Whoever, in any matter within the jurisdiction of any department or agency of the United States knowingly and willfully falsifies, conceals or covers up by any trick, scheme or device a material fact, or make any false, fictitious or fraudulent statement or representation, or makes or uses any false writing or document knowing the same to contain any false, fictitious or fraudulent statement or entry, shall be fined not more than $10,000 or imprisoned not more than 5 years or both (18 U.S.C. section 1001).

Name _____ Title _____

Date _____

ACCEPTED FOR THE PROVIDER OF SERVICES BY:

NAME *(signature)*

TITLE	DATE

ACCEPTED BY THE SECRETARY OF HEALTH AND HUMAN SERVICES BY:

NAME *(signature)*

TITLE	DATE

ACCEPTED FOR THE SUCCESSOR PROVIDER OF SERVICES BY:

NAME *(signature)*

TITLE	DATE

NEWMAN DECLARATION: EXHIBIT C

Idaho Vital Statistics Natality Dashboard

VS Natality - Introduction | VS Natality - Data Results, 2010-2020 | VS Natality - Rate Trends, 2010-2020 | VS Natality - Age Rate Trends, 2010-2020 | VS Natality - Technical Notes

Birth, Infant and Demographic Data

Category
Use this filter to select category
Maternal Pre-Pregnancy BMI

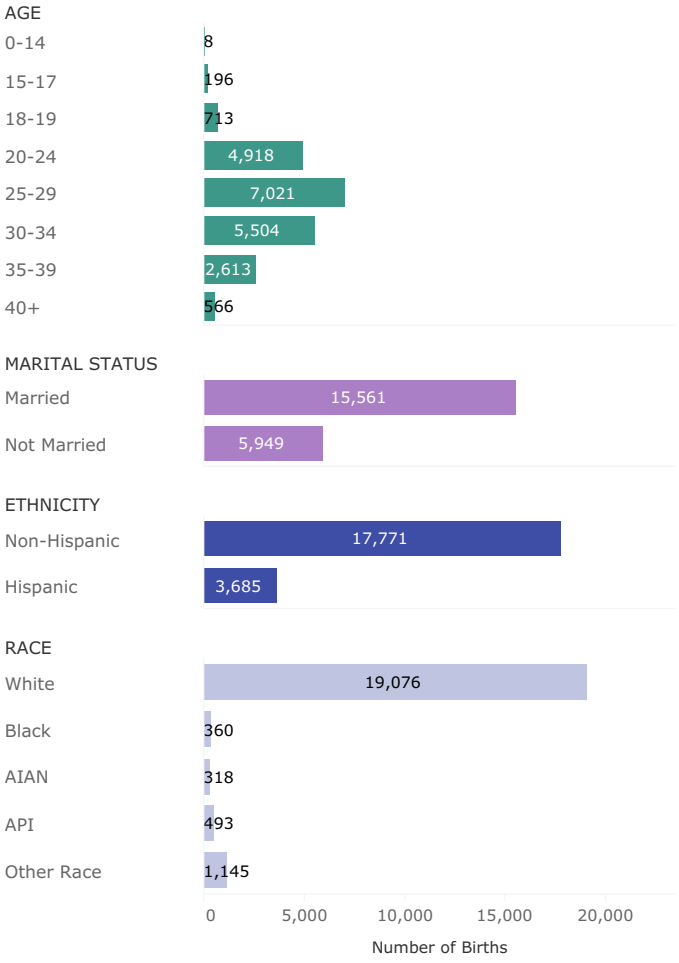
Year
Use this filter to select year
2020

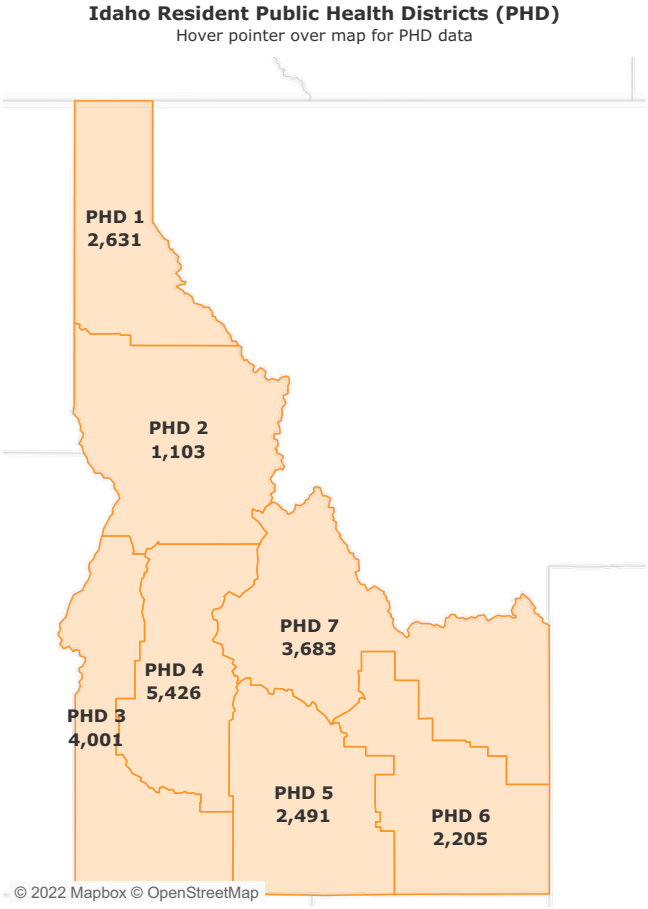
Location
Use this filter to select Idaho (All) or PHD
All

2020 All Idaho Resident Births: 21,540
Maternal Pre-Pregnancy BMI

Underweight	Normal weight	Overweight	Obese
572 2.7%	9,086 42.8%	5,662 26.7%	5,922 27.9%

Directions for using table filter: click on category value in table above to filter value into bar graph and Idaho PHD map data below; click on category value in table a second time to de-activate filter.





IDAHO DEPARTMENT OF HEALTH & WELFARE
DIVISION OF PUBLIC HEALTH

Idaho Vital Statistics Natality Dashboard

VS Natality - Introduction | VS Natality - Data Results, 2010-2020 | VS Natality - Rate Trends, 2010-2020 | VS Natality - Age Rate Trends, 2010-2020 | VS Natality - Technical Notes

Birth, Infant and Demographic Data

Category
Use this filter to select category
Maternal Pre-Pregnancy BMI

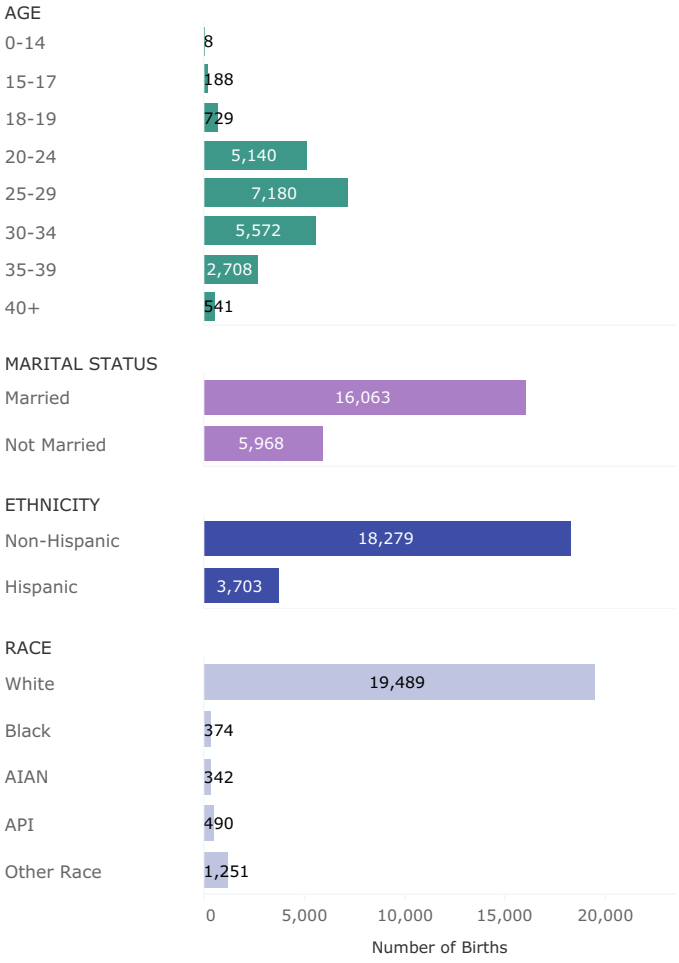
Year
Use this filter to select year
2019

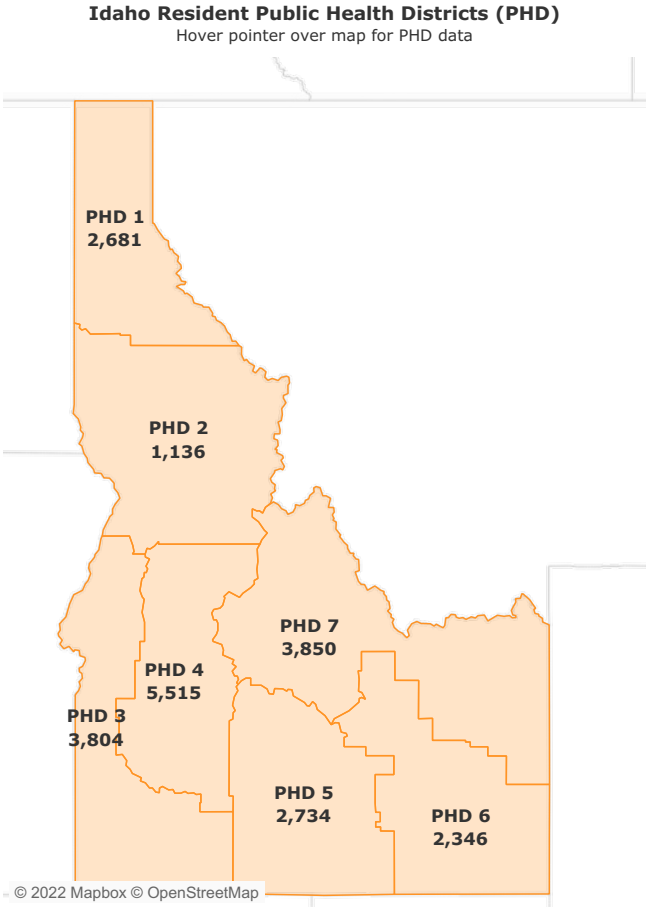
Location
Use this filter to select Idaho (All) or PHD
All

2019 All Idaho Resident Births: 22,066
Maternal Pre-Pregnancy BMI

Underweight	Normal weight	Overweight	Obese
595 2.7%	9,354 43.0%	5,849 26.9%	5,971 27.4%

Directions for using table filter: click on category value in table above to filter value into bar graph and Idaho PHD map data below; click on category value in table a second time to de-activate filter.





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DIVISION OF PUBLIC HEALTH

Idaho Vital Statistics Natality Dashboard

VS Natality - Introduction | VS Natality - Data Results, 2010-2020 | VS Natality - Rate Trends, 2010-2020 | VS Natality - Age Rate Trends, 2010-2020 | VS Natality - Technical Notes

Birth, Infant and Demographic Data

Category
Use this filter to select category
Maternal Pre-Pregnancy BMI

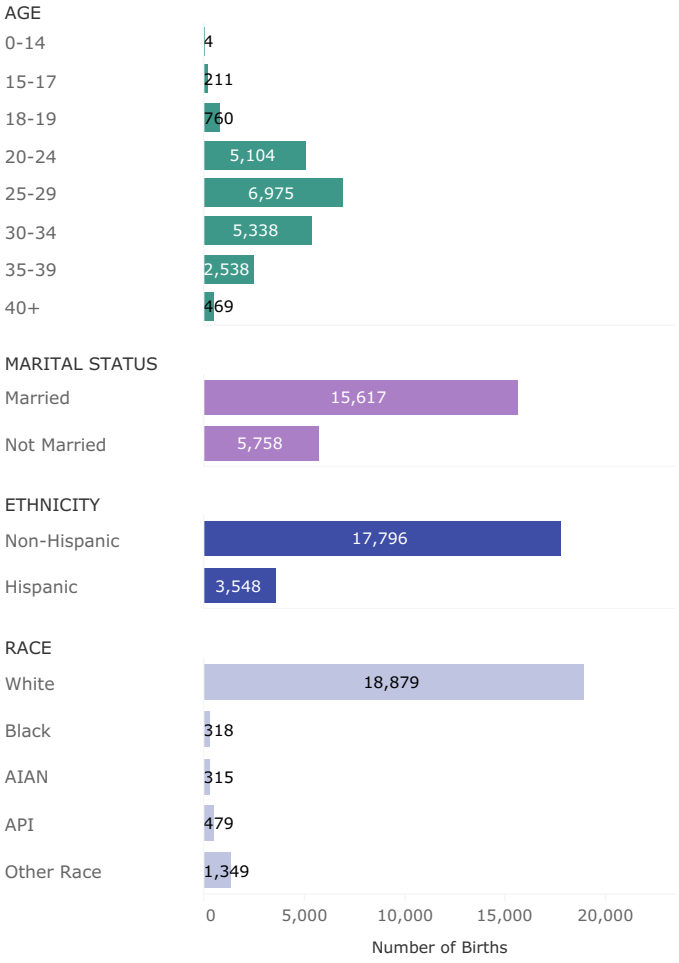
Year
Use this filter to select year
2018

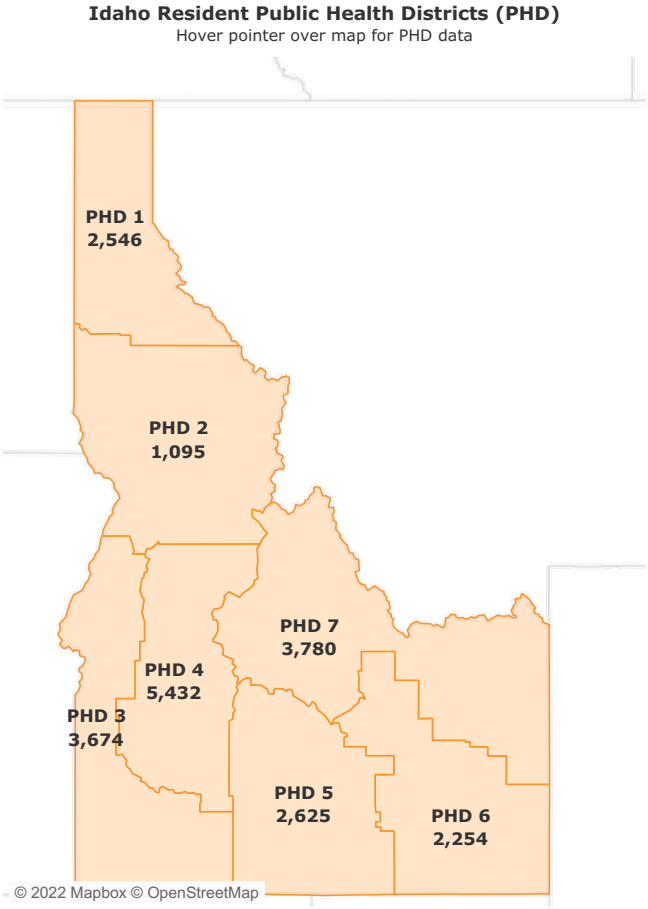
Location
Use this filter to select Idaho (All) or PHD
All

2018 All Idaho Resident Births: 21,406
Maternal Pre-Pregnancy BMI

Underweight	Normal weight	Overweight	Obese
617 2.9%	9,366 44.4%	5,542 26.2%	5,589 26.5%

Directions for using table filter: click on category value in table above to filter value into bar graph and Idaho PHD map data below; click on category value in table a second time to de-activate filter.





IDAHO DEPARTMENT OF HEALTH & WELFARE
DIVISION OF PUBLIC HEALTH

Idaho Vital Statistics Natality Dashboard

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Birth, Infant and Demographic Data

Category
Use this filter to select category
Maternal Pre-Pregnancy BMI

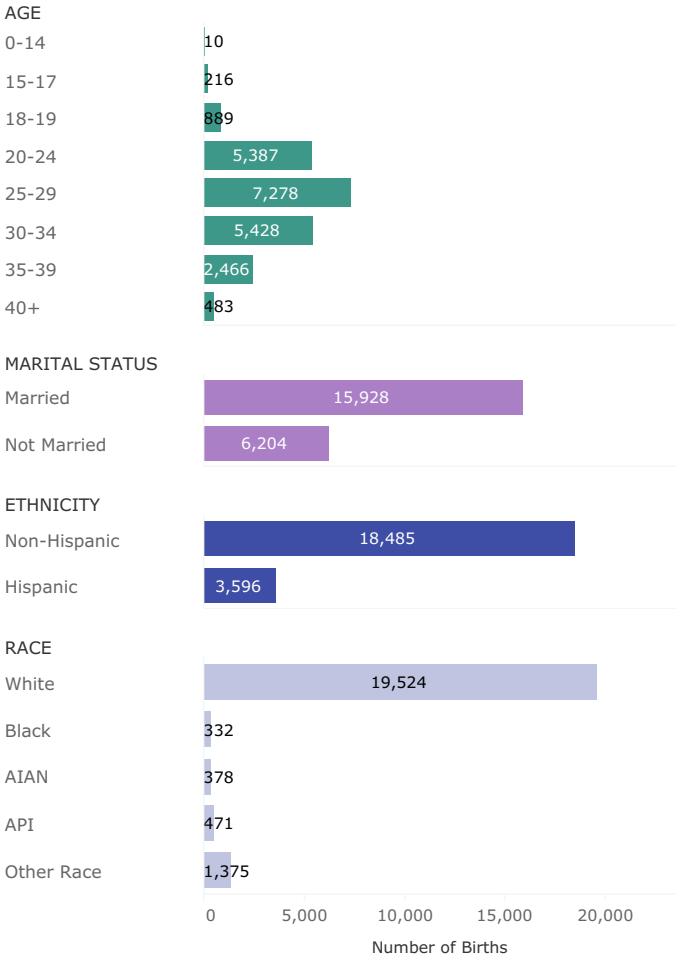
Year
Use this filter to select year
2017

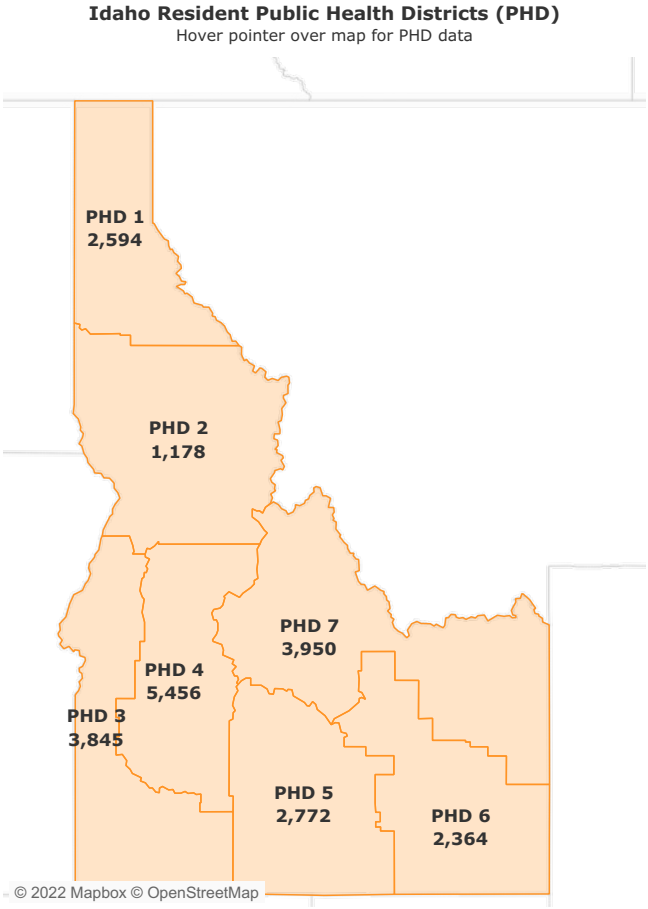
Location
Use this filter to select Idaho (All) or PHD
All

2017 All Idaho Resident Births: 22,159
Maternal Pre-Pregnancy BMI

Underweight	Normal weight	Overweight	Obese
682 3.1%	9,885 45.0%	5,674 25.9%	5,704 26.0%

Directions for using table filter: click on category value in table above to filter value into bar graph and Idaho PHD map data below; click on category value in table a second time to de-activate filter.





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DIVISION OF PUBLIC HEALTH

Idaho Vital Statistics Natality Dashboard

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Birth, Infant and Demographic Data

Category
Use this filter to select category
Maternal Pre-Pregnancy BMI

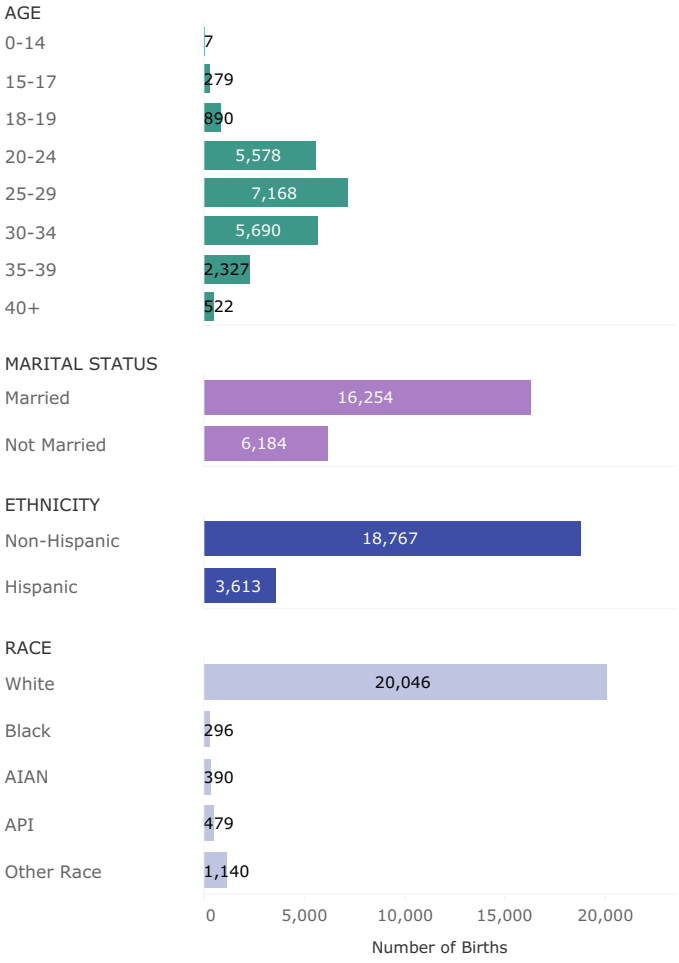
Year
Use this filter to select year
2016

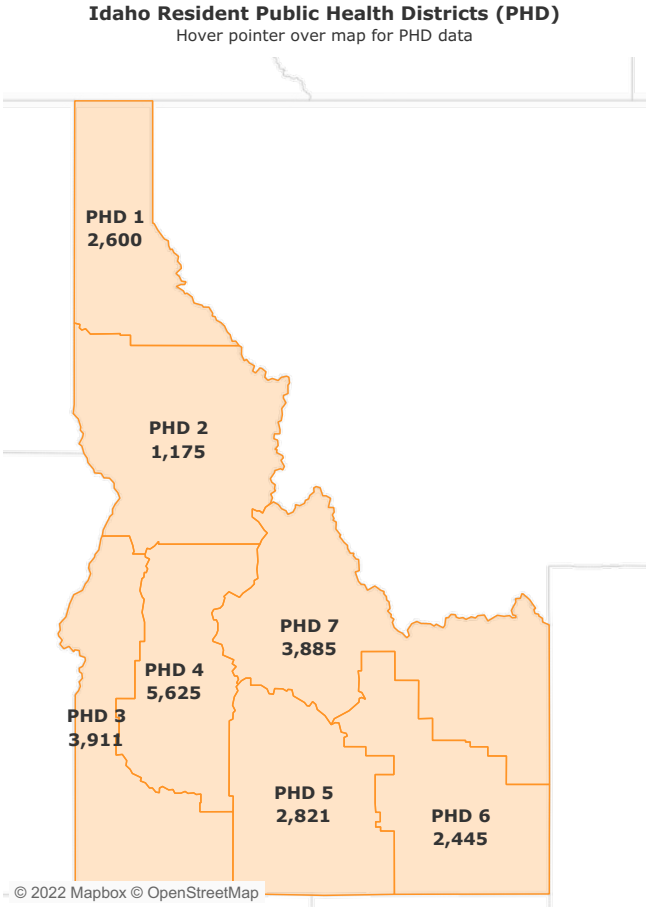
Location
Use this filter to select Idaho (All) or PHD
All

2016 All Idaho Resident Births: 22,462
Maternal Pre-Pregnancy BMI

Underweight	Normal weight	Overweight	Obese
707 3.2%	10,525 47.3%	5,536 24.9%	5,492 24.7%

Directions for using table filter: click on category value in table above to filter value into bar graph and Idaho PHD map data below; click on category value in table a second time to de-activate filter.





IDAHO DEPARTMENT OF HEALTH & WELFARE
DIVISION OF PUBLIC HEALTH

Idaho Vital Statistics Natality Dashboard

VS Natality - Introduction | VS Natality - Data Results, 2010-2020 | VS Natality - Rate Trends, 2010-2020 | VS Natality - Age Rate Trends, 2010-2020 | VS Natality - Technical Notes

Birth, Infant and Demographic Data

Category
Use this filter to select category
Maternal Pre-Pregnancy BMI

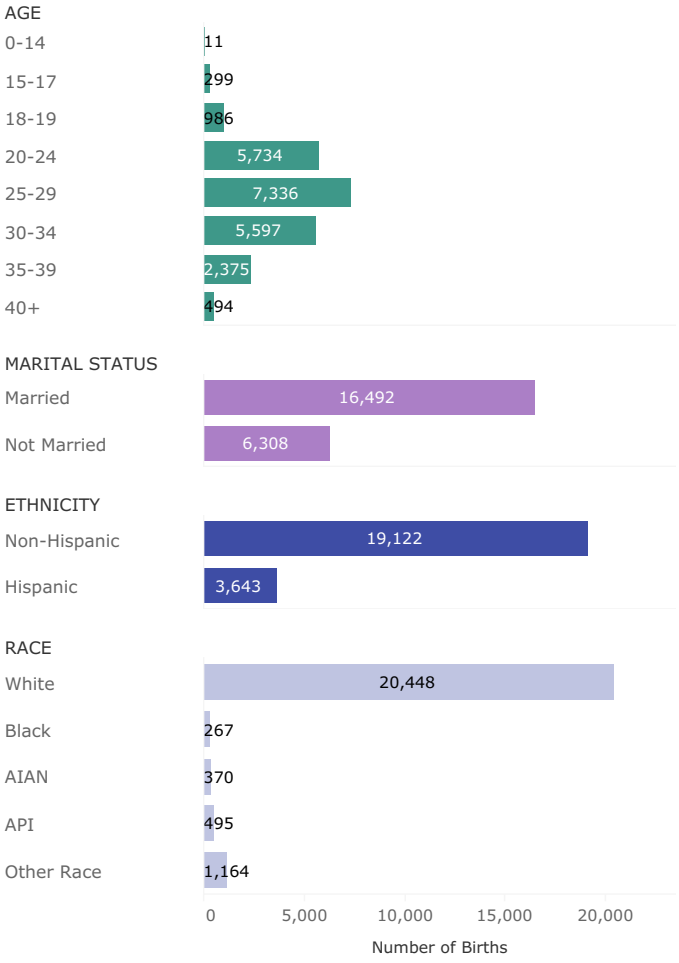
Year
Use this filter to select year
2015

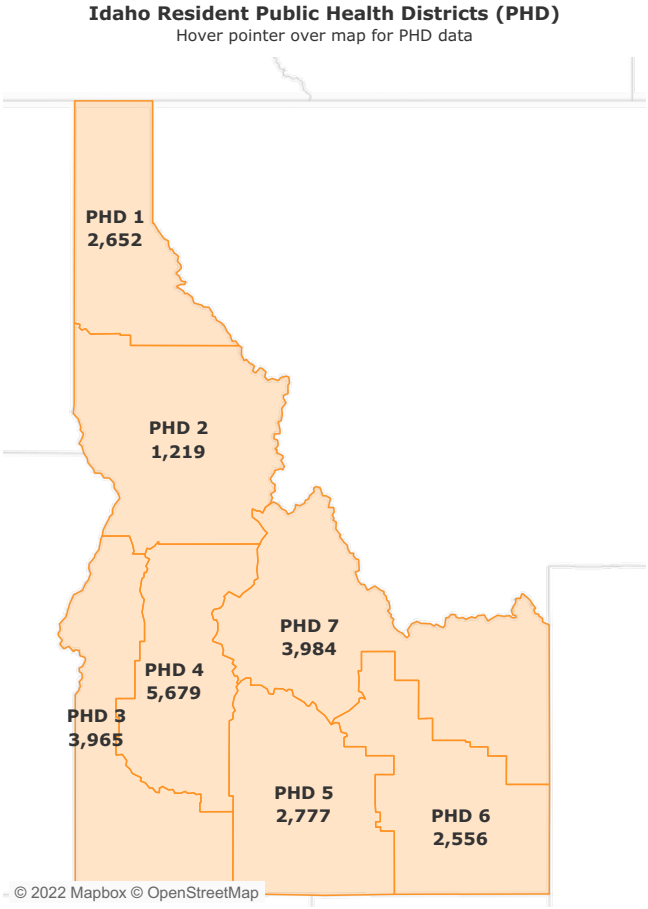
Location
Use this filter to select Idaho (All) or PHD
All

2015 All Idaho Resident Births: 22,832
Maternal Pre-Pregnancy BMI

Underweight	Normal weight	Overweight	Obese
733 3.2%	10,755 47.4%	5,734 25.2%	5,489 24.2%

Directions for using table filter: click on category value in table above to filter value into bar graph and Idaho PHD map data below; click on category value in table a second time to de-activate filter.





IDAHO DEPARTMENT OF HEALTH & WELFARE
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Idaho Vital Statistics Natality Dashboard

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Birth, Infant and Demographic Data

Category
Use this filter to select category
Maternal Pre-Pregnancy BMI

Year
Use this filter to select year
2014

Location
Use this filter to select Idaho (All) or PHD
All

2014 All Idaho Resident Births: 22,888
Maternal Pre-Pregnancy BMI

Underweight	Normal weight	Overweight	Obese
817 3.6%	11,055 48.4%	5,643 24.7%	5,317 23.3%

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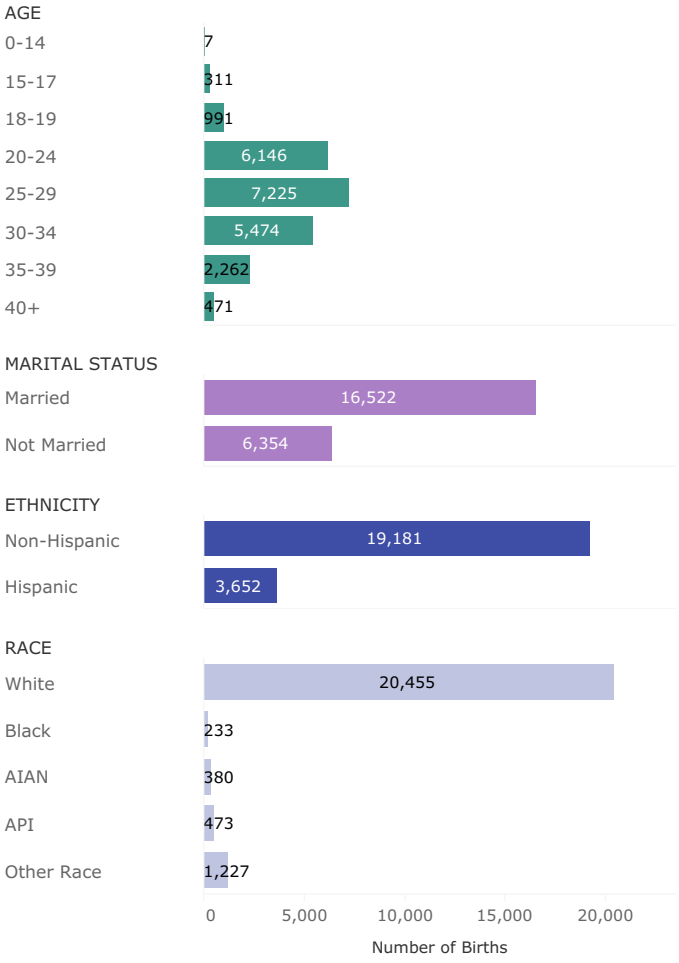
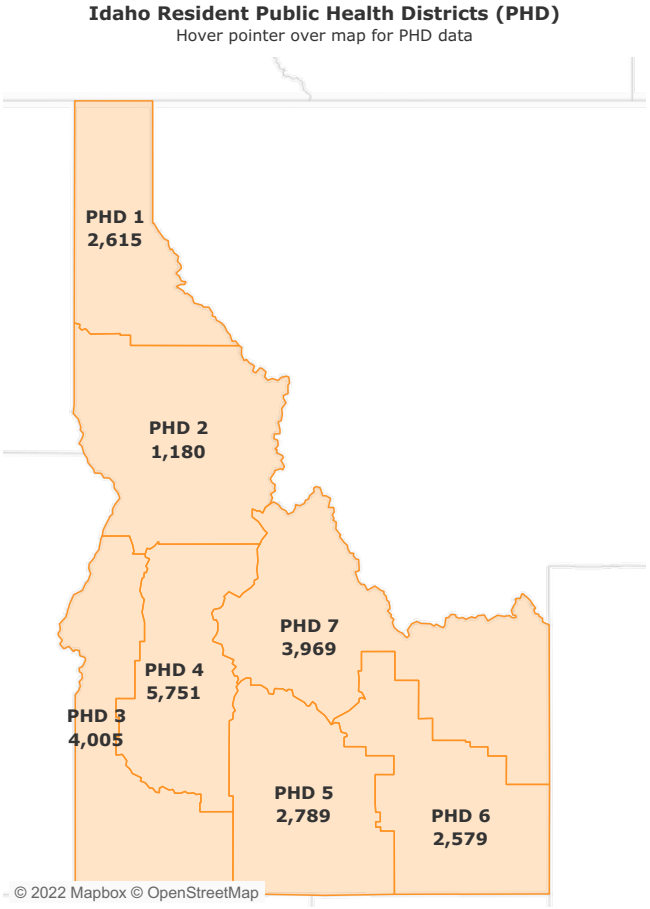




IDAHO DEPARTMENT OF HEALTH & WELFARE
DIVISION OF PUBLIC HEALTH

Idaho Vital Statistics Natality Dashboard

Birth, Infant and Demographic Data

Category
Use this filter to select category
Maternal Pre-Pregnancy BMI

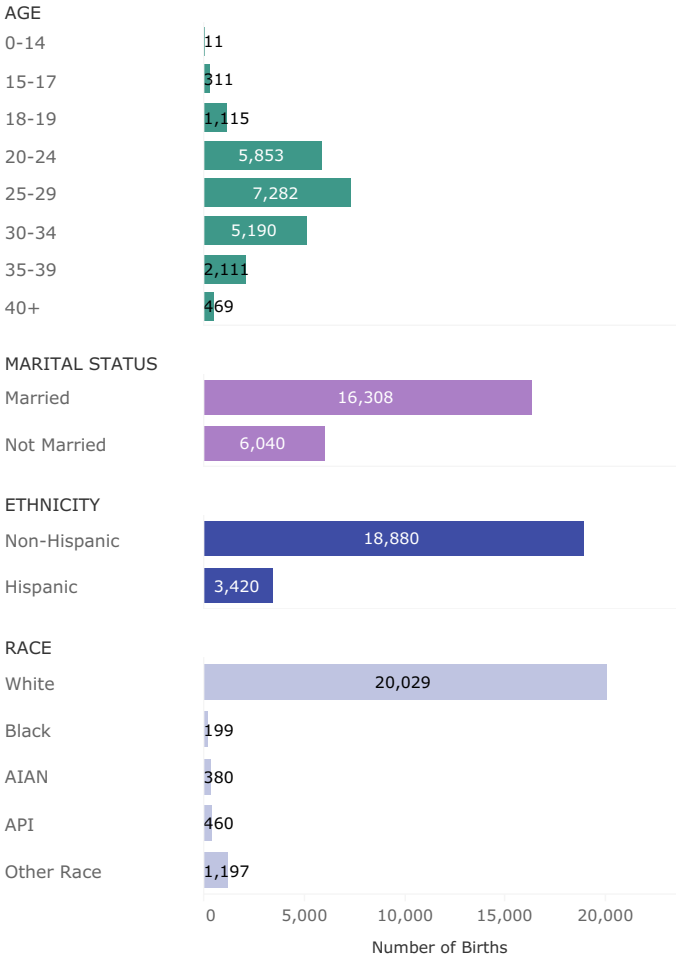
Year
Use this filter to select year
2013

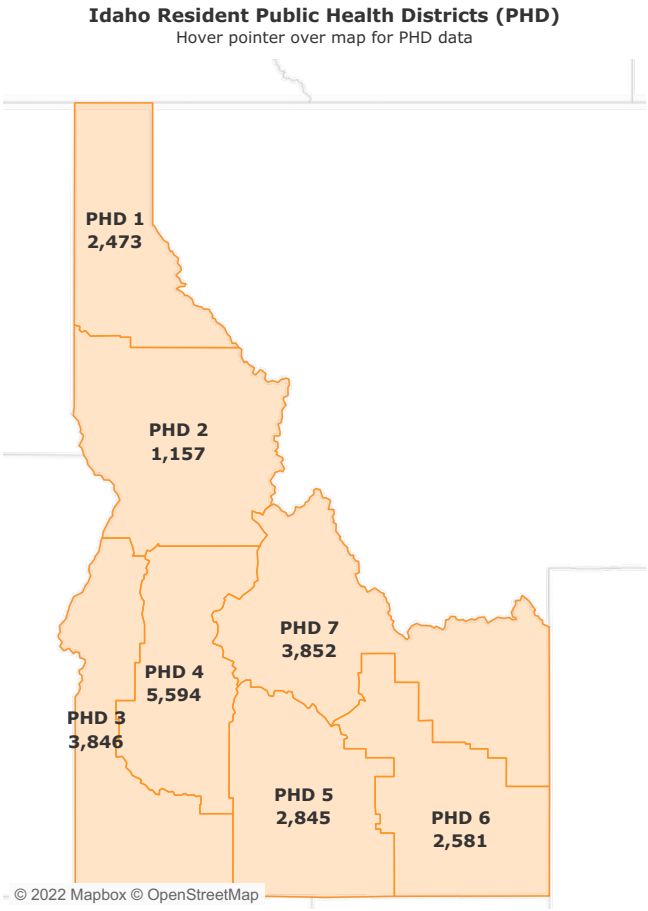
Location
Use this filter to select Idaho (All) or PHD
All

2013 All Idaho Resident Births: 22,348
Maternal Pre-Pregnancy BMI

Underweight	Normal weight	Overweight	Obese
764 3.4%	10,874 48.8%	5,585 25.1%	5,047 22.7%

Directions for using table filter: click on category value in table above to filter value into bar graph and Idaho PHD map data below; click on category value in table a second time to de-activate filter.





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Idaho Vital Statistics Natality Dashboard

VS Natality - Introduction | VS Natality - Data Results, 2010-2020 | VS Natality - Rate Trends, 2010-2020 | VS Natality - Age Rate Trends, 2010-2020 | VS Natality - Technical Notes

Birth, Infant and Demographic Data

Category
Use this filter to select category
Maternal Pre-Pregnancy BMI

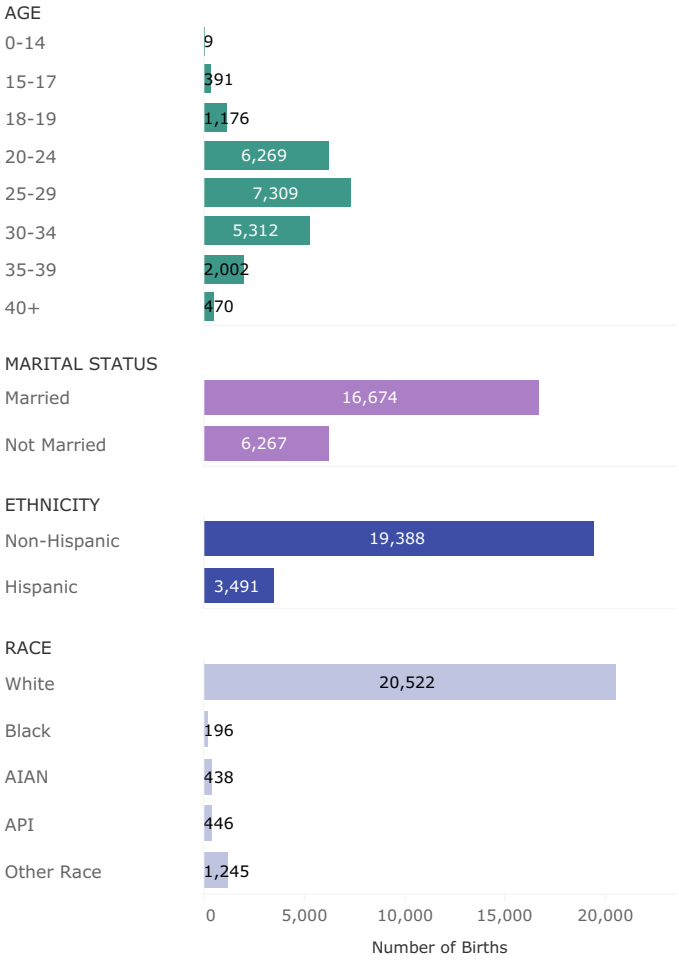
Year
Use this filter to select year
2012

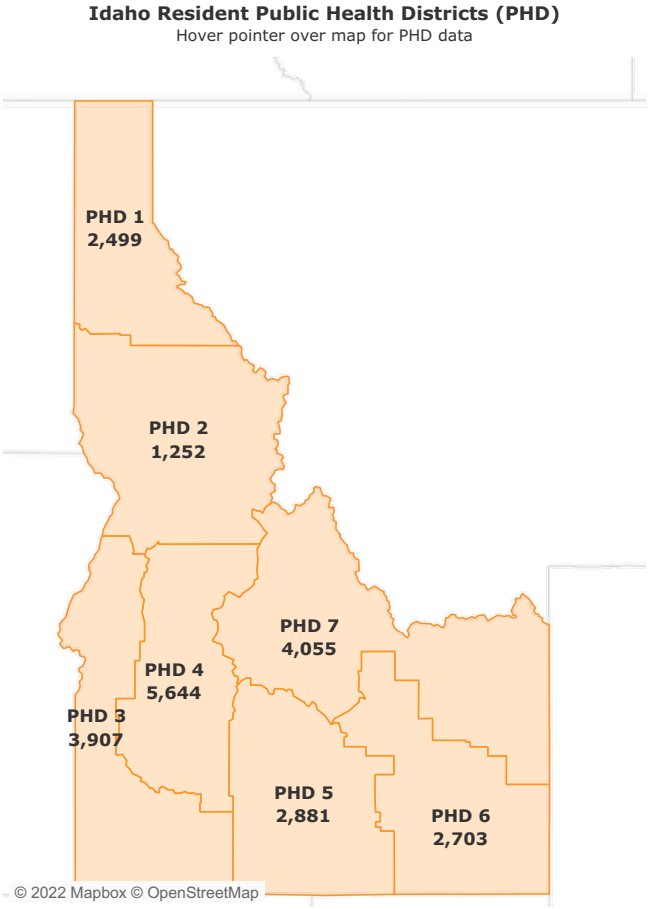
Location
Use this filter to select Idaho (All) or PHD
All

2012 All Idaho Resident Births: 22,941
Maternal Pre-Pregnancy BMI

Underweight	Normal weight	Overweight	Obese
770 3.4%	11,263 49.3%	5,663 24.8%	5,172 22.6%

Directions for using table filter: click on category value in table above to filter value into bar graph and Idaho PHD map data below; click on category value in table a second time to de-activate filter.





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Birth, Infant and Demographic Data

Category
Use this filter to select category
Maternal Pre-Pregnancy BMI

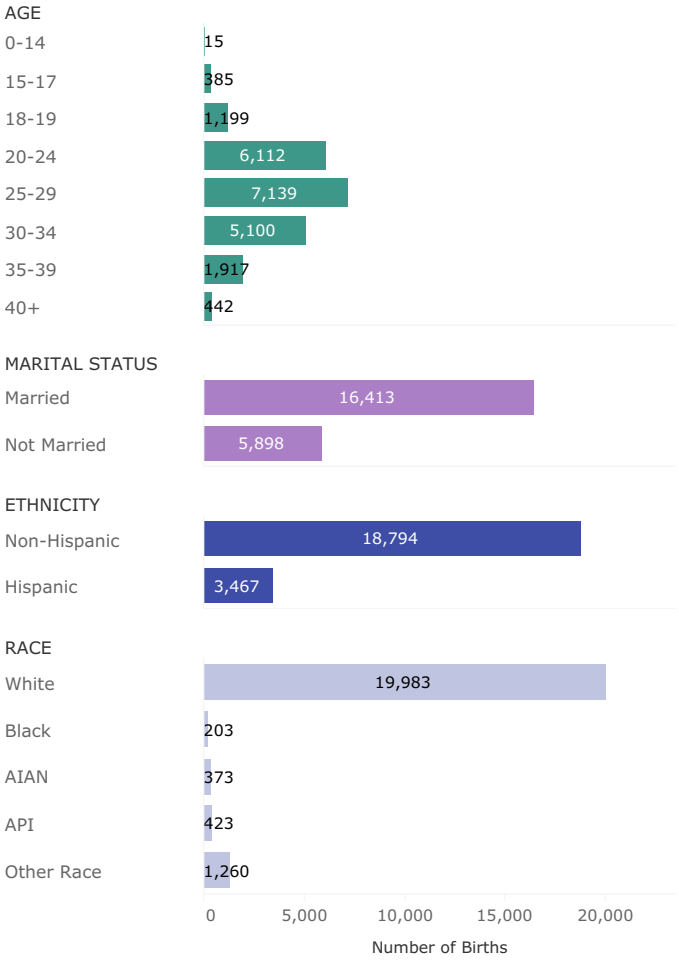
Year
Use this filter to select year
2011

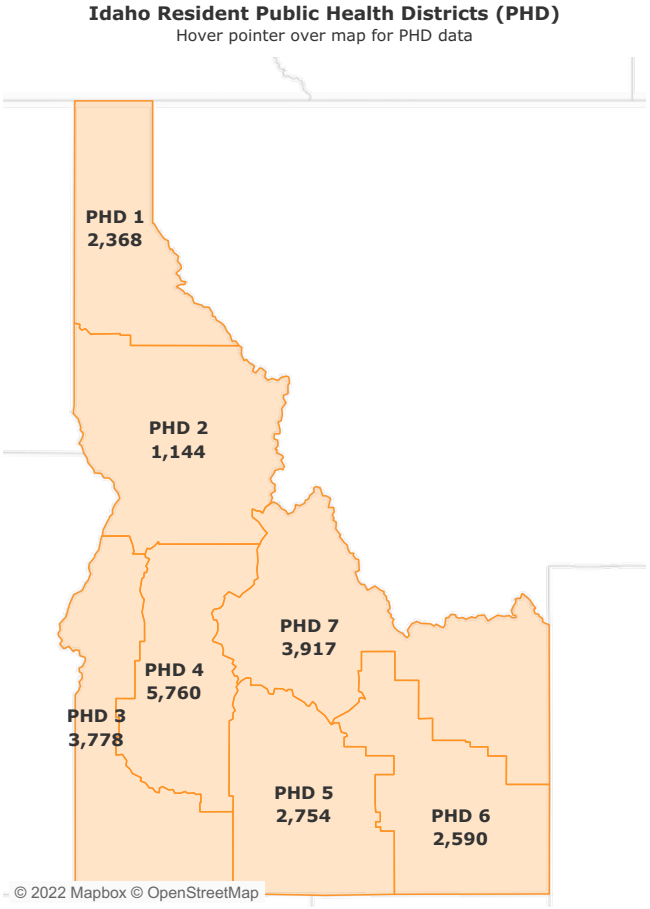
Location
Use this filter to select Idaho (All) or PHD
All

2011 All Idaho Resident Births: 22,311
Maternal Pre-Pregnancy BMI

Underweight	Normal weight	Overweight	Obese
745 3.3%	11,137 50.1%	5,522 24.8%	4,837 21.7%

Directions for using table filter: click on category value in table above to filter value into bar graph and Idaho PHD map data below; click on category value in table a second time to de-activate filter.





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Birth, Infant and Demographic Data

Category
Use this filter to select category
Maternal Pre-Pregnancy BMI

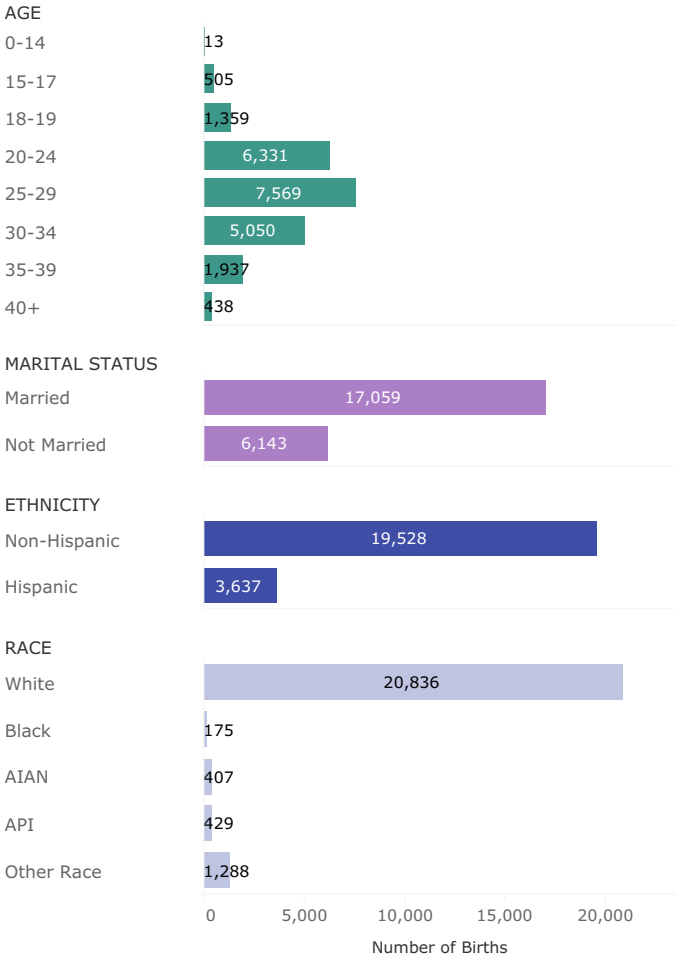
Year
Use this filter to select year
2010

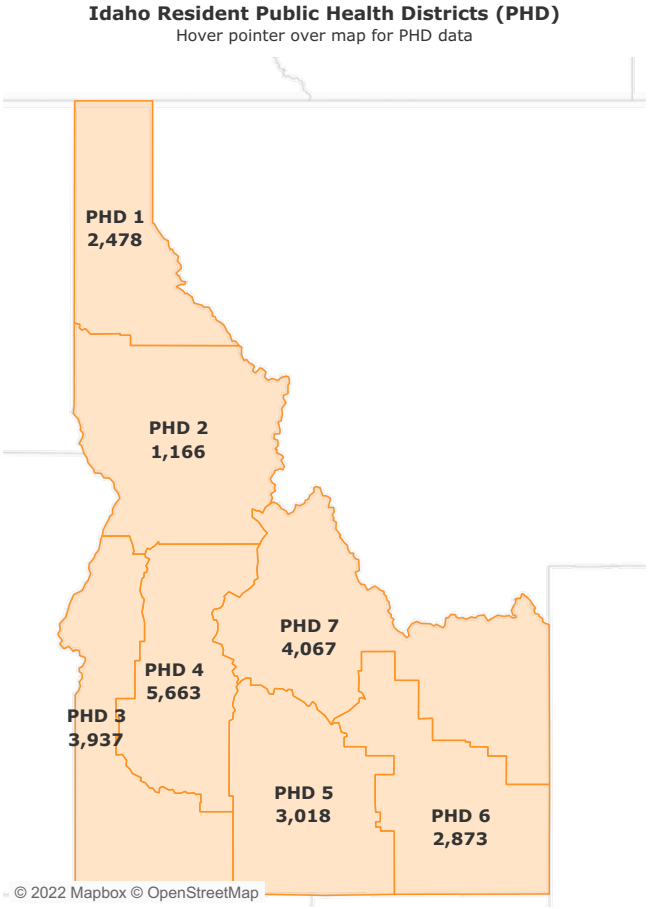
Location
Use this filter to select Idaho (All) or PHD
All

2010 All Idaho Resident Births: 23,202
Maternal Pre-Pregnancy BMI

Underweight	Normal weight	Overweight	Obese
826 3.6%	11,256 48.7%	5,852 25.3%	5,167 22.4%

Directions for using table filter: click on category value in table above to filter value into bar graph and Idaho PHD map data below; click on category value in table a second time to de-activate filter.





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