Health Evidence Review Commission's Value-based Benefits Subcommittee

May 16, 2019

8:00 AM - 1:00 PM

Clackamas Community College
Wilsonville Training Center, Room 111-112
29373 SW Town Center Loop E, Wilsonville, Oregon, 97070

Section 1.0

Call to Order

AGENDA
VALUE-BASED BENEFITS SUBCOMMITTEE
5/16/2019
8:00am - 1:00pm
Clackamas Community College
29373 SW Town Center Loop E,
Wilsonville Training Center, Rooms 111-112
Wilsonville, Oregon
A working lunch will be served at approximately 12 PM
All times are approximate

Note: public testimony on specific agenda topics will be taken when that agenda item is discussed

I. Call to Order, Roll Call, Approval of Minutes – Kevin Olson **8:00 AM**

II. Staff report – Ariel Smits, Cat Livingston, Darren Coffman **8:05 AM**

III. Straightforward/Consent agenda – Ariel Smits **8:10 AM**
- **A.** Consent table
- **B.** Straightforward guideline note corrections
- **C.** BAHA hearing aid HCPCS corrections
- **D.** Spinal artery compression syndromes
- **E.** Iontopheresis

IV. 2020 Biennial Review
- **A.** Reprioritization of certain chronic pain conditions **8:15 AM**
    - i. Presentation of independent review of proposal
    - ii. Review of work to date, current proposal for consideration
    - iii. Public testimony regarding chronic pain reprioritization **9:00 AM**
    - iv. Subcommittee discussion and recommendation **9:30 AM**
- **B.** Reprioritization of liver transplant for hepatic malignancies **10:45 AM**

V. New Discussion Items **11:15 AM**
- **A.** Functional MRI and epilepsy surgery
- **B.** Injections for plantar fasciitis
- **C.** Radiofrequency ablation for knee osteoarthritis
- **D.** Lymphedema
    - i. Non-LANA certification for lymphedema therapy
    - ii. Preventive treatment for high risk women
    - iii. Pneumatic compression devices

VI. Public comment for topics not on the agenda above **12:55 PM**

VII. Adjournment – Kevin Olson **1:00 PM**

Value-based Benefits Subcommittee Recommendations Summary
For Presentation to:
Health Evidence Review Commission on March 14, 2019

For specific coding recommendations and guideline wording, please see the text of the 3/14/2019 VbBS minutes.

RECOMMENDED CODE MOVEMENT (effective 10/1/2019 unless otherwise noted)

- Add the diagnosis code for posterior urethral valves to a covered line and leave it on two other covered lines
- Add procedure codes for treatment of arteriovenous malformations to a covered line
- Add two diagnosis codes to a covered line with a guideline specifying they are to be used for screening for ophthalmologic complications of high-risk medications
- Make various straightforward coding changes

RECOMMENDED GUIDELINE CHANGES (effective 10/1/2019 unless otherwise noted)

- Adopt a new guideline regarding pulmonary rehabilitation services
- Edit the guideline for menstrual bleeding disorders to exempt endometrial ablation from the requirement to demonstrate a hemoglobin level of less than 11, and to require only a pelvic ultrasound prior to that procedure
- Edit the guideline on noninvasive testing for liver fibrosis for hepatitis C to more broadly refer to testing for chronic liver disease
- Modify the guideline note on viscosupplementation for osteoarthritis of the knee to more broadly address newer interventions for osteoarthritis of the knee including glucosamine/chondroitin, whole body vibration, platelet-rich plasma, and TENS
- Edit two guidelines regarding breast imaging to refer to each other to increase clarity
- Edit the tonsillectomy guideline to reflect updated national expert guidelines
- Add a new guideline regarding when treatment of arteriovenous malformations are covered
- Add a new guideline specifying that shoulder decompression surgery is only covered when used as part of rotator cuff repair
- Make several guideline changes to the guidelines for lines 500 and 660 to help clarify HERC intent
- Make various straightforward guideline note changes

VALUE-BASED BENEFITS SUBCOMMITTEE
Human Services Building, Rooms 137 A-D
500 Summer Street NE
Salem Oregon
March 14, 2019
8:30 AM – 1:00 PM

Members Present: Kevin Olson, MD, Chair; Holly Jo Hodges, MD, Vice-Chair; Mark Gibson; Vern Saboe, DC; Gary Allen, DMD; Adriane Irwin, PharmD.

Members Absent: None

Staff Present: Darren Coffman; Ariel Smits, MD, MPH; Cat Livingston, MD, MPH; Dana Hargunani, MD; Jason Gingerich; Daphne Peck.

Also Attending: Renae Wentz, MD, and Trilby deJung (Oregon Health Authority); Billy Ray Pitt; Tracy Muday, MD; Kelly Howard; Larry and Wendy Gordon; Barry Schlansky, MD (Kaiser) via phone.

Ø **Roll Call/Minutes Approval/Staff Report**

The meeting of the Value-based Benefits Subcommittee (VbBS) was called to order at 8:35 am and roll was called. Minutes from the January 17, 2019 VbBS meeting were reviewed and approved unanimously. Smits reviewed the errata document; there were no questions.

Ø **Topic: Straightforward/Consent Agenda**

Discussion: There was no discussion about the consent agenda items.

Recommended Actions:

1) Remove ICD-10 Q66.21 (Congenital metatarsus primus varus) from line 359 DEFORMITY/CLOSED DISLOCATION OF JOINT AND RECURRENT JOINT DISLOCATIONS
2) Add ICD-10 Q66.21 (Congenital metatarsus primus varus) to line 540 DEFORMITIES OF FOOT
3) Remove CPT 28292 (Correction, hallux valgus (bunionectomy), with sesamoidectomy, when performed; with resection of proximal phalanx base, when performed, any method) from line 356 RHEUMATOID ARTHRITIS, OSTEOARTHRITIS, OSTEOCHONDRITIS DISSECANS, AND ASEPTIC NECROSIS OF BONE
4) Add ICD-10 R33.8 (Other retention of urine) to Line 327 FUNCTIONAL AND MECHANICAL DISORDERS OF THE GENITOURINARY SYSTEM INCLUDING BLADDER OUTLET OBSTRUCTION
    a. Keep ICD-10 R33.8 (Other retention of urine) on the Diagnostic Workup File
5) Add the ICD-10 H04.55 (Acquired stenosis of nasolacrimal duct) and H04.56 (Stenosis of right lacrimal punctum) code series to line 393 STRABISMUS WITHOUT AMBLYOPIA AND OTHER DISORDERS OF BINOCULAR EYE MOVEMENTS; CONGENITAL ANOMALIES OF EYE; LACRIMAL DUCT OBSTRUCTION IN CHILDREN
6) Add CPT 44186 (Laparoscopy, surgical; jejunostomy (eg, for decompression or feeding)) to line 157 CANCER OF COLON, RECTUM, SMALL INTESTINE AND ANUS
7) Modify Guideline Note 29 as shown in Appendix A

8) Modify the first clause of Diagnostic Guideline D1 as shown below
    a. Genetic tests are covered as diagnostic, unless they are listed below in section ~~F1~~ E1 as excluded or have other restrictions listed in this guideline…
9) Modify Guideline Note 36 as shown in Appendix A *[note: further revisions to this guideline discussed below]*
10) Add references to guideline notes 6, 64, and 65 to the new SI joint surgery line approved for the Biennial Review list effective 1/1/2020
11) Add references to guideline notes 64 and 65 to the new line for hidradenitis suppurativa approved for the Biennial Review list effective 1/1/2020

MOTION: To approve the recommendations stated in the consent agenda. CARRIES 6-0.

Ø **Topic: 2020 Biennial Review – Reprioritization of Certain Chronic Pain Conditions**

Discussion: Dr. Dana Hargunani, CMO of the Oregon Health Authority (OHA), stated that as transparency and integrity are key to the agency's work, OHA is requesting that the subcommittee table the discussion of this topic at this time, as potential conflicts of interest of a contracted medical consultant to HERC, Cat Livingston, recently became known. These potential conflicts involve two studies evaluating HERC's past decisions on the treatment of back pain that have been part of the discussions of the the Chronic Pain Task Force. This will give time for an independent review of the policy options in front of VbBS to ensure they are the appropriate options to be considered in light of the potential conflicts of interest. Further discussion could then occur at a special session of VbBS and HERC within the next month, if possible, and no later than the currently scheduled May 16th meeting if it was determined the biennial report to the legislature could still be transmitted in a timely fashion. Dr. Hargunani indicated that she will conduct a full review of the conflict of interest process to prevent this from happening in the future.

At this time, Vern Saboe, declared a potential conflict of interest. He is a paid consultant for a Kaiser Permanente study funded by a grant from the Patient Centered Outcomes Research Institute (PCORI) to evaluate the effects of the 2016 changes in OHP coverage of nonpharmacologic treatments for low back and spine pain and their impact on opioid prescribing. Written statements from both Dr. Livingston and Dr. Saboe on the potential conflicts of interest will be provided to HERC.

There was a brief discussion of making the public testimony time more immediately clear in the public notice and other meeting materials when it is taken for a specific topic rather than at the general public testimony time at 12:55 pm for topics not on the agenda.

Public testimony:

- Tracy Muday, MD: member of the Chronic Pain Task Force (CPTF) testified. The CPTF recommendation has been modified through the committee process. The goal was to add therapies to reduce the risk of harms. The evidence of benefit of these therapies are low, and there are unintended consequences of harm with reprioritizing these conditions. There is misunderstanding of the aims and scope of the process, among the public and even the task force members. Thoughtful, well intentioned people have pointed out the potential of harms of

the current proposal. These harms outweigh the benefits of the therapies, which themselves have low evidence.

- Kelly Howard: chronic pain patient testified. This process has been very difficult for patients to determine what is going on, and to understand the language used. Adding the alternative treatments under discussion is a great idea, but they are generally not very helpful. Concerned about removing opioid therapies. Baffled by VbBS attitude toward scientific literature. Evidence is low to very low for the therapies proposed to be added, but adding options is beneficial. However, evidence of opioid benefit, which is higher quality, was discounted. There are not studies of opioids longer than 3 months she acknowledged. Concerned about the ethics of tapering all chronic pain patients from their opioids. A lot of prejudice and bigotry about pain patients on opioids being "addicts." There is a difference between physiologic dependence and addiction.
- Shelley Latin: testified about concerns that the CPTF was "one-sided" and did not contain objective views about the best treatments for chronic pain patients. There should never be forced tapers; this is a medical decision between a doctor and patient. There has been a mountain of testimony about prominent pain physicians that tapers are harmful, including the testimony of Beth Darnell. She went to the Stanford pain program personally. She feels that the alternative treatments are not a replacement for opioids, which is supported by evidence. There is also inadequate infrastructure to provide these alternative treatments across the state, particularly places such as eastern Oregon. Please consider Dr. Darnell's offer to be included in her EMPOWER study.
- Larry Gordon: testified that Beth Darnell was an excellent addition to the committee and that he agreed with the previous testimony. Concerned that no one is on any of the task force/ committees that represents the chronic pain community. His wife is an example of the unintended consequences of forced tapering. Her family physician was afraid of the CDC guidelines and losing his license, so he abandoned her and sent her to another physician who did not know her. She is disabled and in chronic pain. She was sent to a pain specialist, who tapered her off her opioids. This was devastating to her and she wanted to commit suicide. The Department of Health and Human Services did a report on the CDC guidelines, and stated that these guidelines were not to be used for local jurisdictions to write laws or mandates. This policy will result in chronic pain patients being abandoned by their doctors. The doctors treating these patients should not be at risk for losing their license. Consider mitigating the unintended consequences.

Recommended Actions:

1) This topic was tabled until either a special VbBS/HERC meeting in April or the scheduled May meeting

Ø **Topic: Pulmonary rehabilitation**

Discussion: Smits reviewed the summary document. Hodges asked for clarification regarding whether the number of sessions of pulmonary rehabilitation should be limited to 36 visits per year or per lifetime. Gingerich noted that OHP cannot put in lifetime per the ACA. The question was raised regarding whether this is an overused treatment. Hodges noted that some CCOs are seeing overuse. Smits pointed out that repeat programs are limited in the last sentence of the guideline.

The subcommittee accepted the guideline note as proposed. The intent of VbBS is that coverage is limited to 36 lifetime sessions unless there is lung reduction surgery or lung transplant.

Recommended Actions:

1) Add pulmonary rehabilitation HCPCS codes to lines with chronic pulmonary disease diagnoses
    a. HCPCS codes:
        i. G0237 (Therapeutic procedures to increase strength or endurance of respiratory muscles, face to face, one on one, each 15 minutes (includes monitoring))
        ii. G0238 (Therapeutic procedures to improve respiratory function, other than described by G0237, one on one, face to face, per 15 minutes (includes monitoring))
        iii. G0239 (Therapeutic procedures to improve respiratory function or increase strength or endurance of respiratory muscles, two or more individuals (includes monitoring))
        iv. S9473 (Pulmonary rehabilitation program, non-physician provider, per diem)
        v. Note: G0424 (Pulmonary rehabilitation, including exercise (includes monitoring), one hour, per session, up to two sessions per day) is already on the lines below
    b. Lines:
        i. 9 ASTHMA
        ii. 58 BRONCHIECTASIS
        iii. 223 OCCUPATIONAL LUNG DISEASES
        iv. 234 ADULT RESPIRATORY DISTRESS SYNDROME; ACUTE RESPIRATORY FAILURE; RESPIRATORY CONDITIONS DUE TO PHYSICAL AND CHEMICAL AGENTS
        v. 241 CONDITIONS REQUIRING HEART-LUNG AND LUNG TRANSPLANTATION
        vi. 283 CHRONIC OBSTRUCTIVE PULMONARY DISEASE; CHRONIC RESPIRATORY FAILURE
2) Adopt a new guideline note as shown in Appendix B

MOTION: To recommend the code and guideline note changes as presented. CARRIES 6-0.

Ø **Topic: Non-invasive testing for liver fibrosis guideline**

Discussion: Livingston reviewed the summary document. Dr. Barry Schlansky was introduced as a content expert. He is the Chief of Hepatology at Kaiser and clinical assistant professor at OHSU and an Investigator at Kaiser Center for Health Research.

There were questions about the availability of proprietary versus non-proprietary blood testing. Schlansky discussed that non-proprietary tests are excellent and are readily available.

Members requested adding the specific proprietary and nonproprietary tests within the guideline note itself, for clarity.

The conversation turned to magnetic resonance elastography (MRE). One member suggested Line 500 was appropriate for MRE given the cost-effectiveness and thus perhaps the exceptions process could be used for allowing MRE in limited circumstances. However, Schlansky clarified that FibroScan® fails in 20% of patients, which was not a rare circumstance. If one is concerned about a patient without a reliable FibroScan, the choices are MRE or liver biopsy. When compared to the cost and potential complications of a liver biopsy, MRE is a reasonable choice.

Livingston asked about the clinical impact of patients in whom ultrasound-based screening are ineffective, such as due to obesity. The reason for this is that if cirrhosis is diagnosed, monitoring would then be with ultrasound, which was previously not an effective strategy. Schlansky discussed that evidence for HCC screening is based on a single RCT in China that has not been replicated in western populations because of equipoise. Therefore, the data is not based on an American population, which is very different than Chinese population. Most are thin and have hepatitis B. US is not as accurate at finding liver nodules in the setting of obesity. The strategy for follow-up of these patients would be to introduce CT alternating with ultrasound.

Wentz raised the concern about potential overuse of liver biopsy and the group then discussed the importance of having safer and cheaper alternatives. There was a clarifying question about what is the denominator of those we are getting screening with non-invasive liver testing. Schlansky discussed that there is a movement towards doing screening in those who are higher risk (obesity, diabetes, age over 50). He discussed some therapeutic options for fatty liver disease such as bariatric surgery, pioglitazone and vitamins. Livingston stated that as currently written, the proposed coverage policy is only for those with chronic liver disease, not for screening in an asymptomatic, but high-risk population.

Members discussed the importance of trying to ensure that access to services across the state is uniform. It can take a long time to get an answer on an exception request. In contrast, a concern was raised that to be more consistent with the evidence, noncoverage of MRE might be more appropriate.

Members debated the two options and ultimately a vote to move option 2 forward, which allows coverage of MRE in very specific circumstances, as an alternative to a medically-indicated liver biopsy.

Recommended Actions:

1) Retire the Coverage Guidance *Noninvasive Liver Testing for Liver Fibrosis in Patients with Hepatitis C.*
2) Modify Guideline Note 76 as shown in Appendix A.

MOTION: To approve the staff recommendations as amended, with coverage of magnetic resonance elastography in specific circumstances. CARRIES 6-0.

Ø **Topic: Endometrial ablation requirements for menstrual bleeding disorders**

Discussion: Smits reviewed the summary document. Wentz asked about the failure rate of endometrial ablation. Smits noted that there is a failure rate, but it is small. Hodges commented that the rate in her experience is small and when patients do continue to have bleeding after endometrial ablation, the bleeding is still lighter and more manageable.

Recommended Actions:

1) Modify Guideline Note 44 as shown in Appendix A

MOTION: To recommend the guideline note changes as presented. CARRIES 6-0.

Ø **Topic: Posterior urethral valves**

Discussion: Smits reviewed the summary document. There was no discussion.

Recommended Actions:
1) Add CPT 52400 (Cystourethroscopy with incision, fulguration, or resection of congenital posterior urethral valves, or congenital obstructive hypertrophic mucosal folds)) to line 87 CONGENITAL ANOMALIES OF GENITOURINARY SYSTEM

MOTION: To recommend the code change as presented. CARRIES 6-0.

Ø **Topic: Breast MRI for breast cancer screening in breast cancer survivors**

Discussion: Smits reviewed the summary document. Hodges noted that breast MRI CPT coding has changed recently, and computer aided diagnosis (CAD) is now included in the only CPT code available for billing breast MRI with contrast (without contrast still can be billed without CAD but is less frequently indicated than contrast MRI). The subcommittee struck the CAD reference from three locations in the diagnostic guideline note. It is the intent of VbBS that CAD should not be covered for breast MRI when and if coding for breast MRI without CAD again becomes available due to lack of benefit and possible harms of CAD.

Recommended Actions:
1) Modify diagnostic Guideline D6 as shown in Appendix A
2) Modify GN26 as shown in Appendix A

MOTION: To recommend the guideline note changes as presented. CARRIES 6-0.

Ø **Topic: Indications for adenotonsillectomy/tonsillectomy**

Discussion: Smits reviewed the summary document. Hodges asked whether a link to the ENT society article could be put into the tonsillectomy guideline; Smits replied that typically single articles are not referenced in guideline notes. Smits will ensure that the article citation is included in the minutes:

Mitchell, RB et al. Clinical Practice Guideline: Tonsillectomy in Children (Update). Otolaryngology–Head and Neck Surgery 2019, Vol. 160(1S) S1–S42. https://journals.sagepub.com/doi/pdf/10.1177/0194599818801757

Irwin pointed out that the number of episodes of strep infection should be modified with “or more” to indicate that the number of episodes is a minimum.

Recommended Actions:
1) Modify Guideline Note 36 as shown in Appendix A

MOTION: To recommend the guideline note changes as amended. CARRIES 6-0.

Ø **Topic: Embolization of vascular malformations**

Discussion: Smits reviewed the summary document. There was no discussion.

Recommended Actions:

1) Add CPT 37242 (Vascular embolization or occlusion, inclusive of all radiological supervision and interpretation, intraprocedural roadmapping, and imaging guidance necessary to complete the intervention; arterial, other than hemorrhage or tumor (e.g., congenital or acquired arterial malformations, arteriovenous malformations, arteriovenous fistulas, aneurysms, pseudoaneurysms)) to line 305 DISORDERS OF ARTERIES, OTHER THAN CAROTID OR CORONARY
2) Add a new guideline to line 305 as shown in Appendix B

MOTION: To recommend the code and guideline note changes as presented. CARRIES 6-0.

Ø **Topic: Injections for plantar fasciitis**

Discussion: This topic was tabled to the May, 2019 VbBS meeting at the request of the Oregon Podiatry Association.

Ø **Topic: Screening for ophthalmologic complications of high-risk drugs**

Discussion: Smits reviewed the summary document. Hodges requested that the ICD-10 code for high risk medication use be added to line 360 as well, as many ophthalmologists use that code for these types of screening. HERC staff identified that code as ICD-10 Z79.899 (Other long-term (current) drug therapy), which is currently on the Diagnostic Workup File. Livingston noted that H36 was the code used by many private insurers in this situation.

Recommended Actions:

1) Add ICD-10 H36 (Retinal disorders in diseases classified elsewhere) to line 360 CHORIORETINAL INFLAMMATION
2) Add ICD-10 Z79.899 (Other long-term (current) drug therapy) to line 360 CHORIORETINAL INFLAMMATION
    - Advise HSD to keep ICD-10 Z79.899 on the Diagnostic Workup File
3) Adopt a new guideline note for line 360 as shown in Appendix B

MOTION: To recommend the code and guideline note changes as amended. CARRIES 6-0.

Ø **Topic: Shoulder decompression surgery for shoulder impingement syndrome**

Discussion: Smits reviewed the summary document; there was no substantial discussion.

Recommended Actions:

1) A new guideline was added to lines 356,417,441 as shown in Appendix B

MOTION: To recommend the guideline note changes as presented. CARRIES 6-0.

Ø **Topic: Guideline note 172/173 modifications**

Discussion: Smits reviewed the summary document. There was no discussion.

Recommended Actions:

1) Remove CPT 88120 and 88121 (Cytopathology, in situ hybridization (eg, FISH), urinary tract specimen with morphometric analysis, 3-5 molecular probes) from line 271 CANCER OF BLADDER AND URETER
2) Modify GN 27 as shown in Appendix A
3) Modify GN 172 as shown in Appendix A
4) Modify GN 173 as shown in Appendix A

MOTION: To recommend the code and guideline note changes as presented. CARRIES 6-0.

Ø **Topic: Coverage Guidance—Newer interventions for osteoarthritis of the knee**

Discussion: Obley reviewed the evidence and policy background for the newer interventions for osteoarthritis of the knee. Livingston reviewed the other GRADE domains and the EbGS recommendations for noncoverage.

Members discussed these interventions as having few harms, but evidence of ineffectiveness. There was a suggestion posited that if something doesn't work, but has few harms, perhaps it has a role. An example was given of battlefield acupuncture. Others pointed out that in order for something to be covered, it would need to have evidence of benefit, not just lack of harm. The importance of harnessing the placebo was raised. Evidence of a placebo effect is possible to obtain. However, the evidence for TENS did not compare TENS to a non-sham TENS arm, therefore there was not proof of an effective placebo effect. Members agreed to adopt the suggested guidelines changes as recommended.

Recommended Actions:

1) Modify Guideline Note 104 as shown in Appendix A
2) Advise HSD to move A9270 (Non-covered item or service) from the Ancillary File to Excluded File

MOTION: To approve the recommended changes to the Prioritized List based on the draft Coverage Guidance on Newer Interventions for Osteoarthritis of the Knee scheduled for review by HERC at their March 14, 2019 meeting. CARRIES 6-0.

Ø **Public Comment:**

No additional public comment was received.

Ø **Issues for next meeting:**

- Reprioritization of certain chronic pain conditions
- Injections for plantar fasciitis

Ø **Next meeting:**

May 16, 2019 at Clackamas Community College, Wilsonville Training Center, Wilsonville Oregon, Rooms 111-112. *Note: a special meeting to discuss the chronic pain reprioritization topic may be held in April, 2019.*

Ø **Adjournment:**

The meeting adjourned at 12:50 PM.

Appendix A
Revised Guideline Notes

DIAGNOSTIC GUIDELINE D6, BREAST CANCER SCREENING IN ABOVE-AVERAGE RISK WOMEN

Annual screening mammography and annual screening MRI ~~without computer-aided detection (CAD)~~ are covered only for women at above-average risk of breast cancer. This coverage, beginning at 30 years of age, includes women who have one or more of the following:

- Greater than 20% lifetime risk of breast cancer
- BRCA1 or BRCA2 gene mutation, or who have not been tested for BRCA but have a first-degree relative who is a BRCA carrier
- A personal history or a first-degree relative diagnosed with Bannayan-Riley-Ruvalcaba syndrome, Cowden syndrome, or Li-Fraumeni syndrome
- Other germline gene mutations known to confer a greater than 20% lifetime risk of breast cancer

For women with a history of high dose chest radiation (≥ 20 Gray) before the age of 30, annual screening MRI ~~without computer-aided detection (CAD)~~ and annual screening mammography are covered beginning 8 years after radiation exposure or at age 25, whichever is later.

For women with both a personal history and a family history of breast cancer which give a greater than 20% lifetime risk of breast cancer, annual mammography, annual breast MRI ~~without computer-aided detection (CAD)~~ and annual breast ultrasound are covered.

For women with increased breast density, supplemental screening with breast ultrasound, MRI, or digital breast tomosynthesis is not covered.

Breast PET-CT scanning and breast-specific gamma imaging are not covered for breast cancer screening.

For surveillance for a treated breast cancer, see Guideline Note 26 BREAST CANCER SURVEILLANCE.

The development of this guideline note was informed by a HERC coverage guidance. See https://www.oregon.gov/oha/HPA/DSI-HERC/Pages/Evidence-based-Reports.aspx.

GUIDELINE NOTE 26, BREAST CANCER SURVEILLANCE

Line 191

A) History and physical exam is indicated every 3 to 6 months for the first three years after primary therapy, then every 6-12 months for the next 2 years, then annually thereafter.
B) Mammography is indicated annually, and patients treated with breast conserving therapy, initial mammogram of the affected breast should be 6 months after completion of radiotherapy.
C) No other surveillance testing is indicated

For ongoing screening for a new breast cancer, see Diagnostic Guideline D6 BREAST CANCER SCREENING IN ABOVE-AVERAGE RISK WOMEN.

Appendix A
Revised Guideline Notes

GUIDELINE NOTE 27, SLEEP APNEA

Line 203

CPAP is covered initially when all of the following conditions are met:

- 12 week 'trial' period to determine benefit. This period is covered if apnea-hypopnea index (AHI) or respiratory disturbance index (RDI) is greater than or equal to 15 events per hour; or if between 5 and 14 events with additional symptoms including one or more of the following:
  - excessive daytime sleepiness defined as either an Epworth Sleepiness Scale score>10 or daytime sleepiness interfering with ADLs that is not attributable to another modifiable sedating condition (e.g. narcotic dependence), or
  - documented hypertension, or
  - ischemic heart disease, or
  - history of stroke;
- Providers must provide education to patients and caregivers prior to use of CPAP machine to ensure proper use; and
- Positive diagnosis through polysomnogram (PSG) or Home Sleep Test (HST).

CPAP coverage subsequent to the initial 12 weeks is based on documented patient tolerance, compliance, and clinical benefit. Compliance (adherence to therapy) is defined as use of CPAP for at least four hours per night on 70% of the nights during a consecutive 30-day period.

Mandibular advancement devices (oral appliances) are covered for those for whom CPAP fails or is contraindicated.

Surgery for sleep apnea in adults is not included on this line (due to lack of evidence of efficacy). Surgical codes are included on this line only for children who meet criteria according to Guideline Note 118 OBSTRUCTIVE SLEEP APNEA DIAGNOSIS AND TREATMENT FOR CHILDREN.

Hypoglossal nerve stimulation for treatment of obstructive sleep apnea is not included on this line due to insufficient evidence of effectiveness and evidence of harm.

The development of this guideline note was informed by a HERC coverage guidance. See https://www.oregon.gov/oha/HPA/DSI-HERC/Pages/Evidence-based-Reports.aspx.

GUIDELINE NOTE 29, TYMPANOSTOMY TUBES IN ACUTE OTITIS MEDIA

Line 389

Tympanostomy tubes (CPT 69433, 69436) are only included on this line as treatment for:

A) recurrent acute otitis media (three or more well-documented and separate episodes in six months or four or more well-documented and separate episodes in the past 12 months with at least one episode in the past six months) in patients who have unilateral or bilateral middle ear effusion at the time of assessment for tube candidacy, or
B) patients with complicating conditions (immunocompromised host, meningitis by lumbar puncture, acute mastoiditis, sigmoid sinus/jugular vein thrombosis by CT/MRI/MRA, cranial

nerve paralysis, sudden onset dizziness/vertigo, need for middle ear culture, labyrinthitis, or brain abscess).

Patients with craniofacial anomalies, Down's syndrome, cleft palate, permanent hearing loss of 25dB or greater independent of otitis media with effusion, and patients with speech and language delay may be considered for tympanostomy if unresponsive to appropriate medical treatment or having recurring infections (without needing to meet the strict "recurrent" definition above).

Removal of retained tympanostomy tubes requiring anesthesia (CPT code 69424) or as an office visit, is included on Line 422 as a complication, pairing with ICD-10-CM H74.8.

The development of this guideline note was informed by a HERC coverage guidance. See https://www.oregon.gov/oha/HPA/DSI-HERC/Pages/Evidence-based-Reports.aspx.

GUIDELINE NOTE 36, ADENOTONSILLECTOMY FOR INDICATIONS OTHER THAN OBSTRUCTIVE SLEEP APNEA

Lines 42,47,368,548

Tonsillectomy/adenotonsillectomy is an appropriate treatment for patients with:

A) ~~Five~~ Seven or more documented attacks of strep tonsillitis in a year or ~~3~~ 5 or more documented attacks of strep tonsillitis in each of two consecutive years or 3 or more documented attacks of strep tonsillitis per year in each of the three consecutive years where an attack is considered a positive culture/screen and where an appropriate course of antibiotic therapy has been completed; or

B) ~~Peritonsillar abscess requiring surgical drainage~~ A history of two or more peritonsillar abscesses OR when general anesthesia is required for the surgical drainage of a peritonsillar abscess and tonsillectomy is performed at the time of the surgical drainage; or,

C) Unilateral tonsillar hypertrophy in adults; unilateral tonsillar hypertrophy in children with other symptoms suggestive of malignancy.

ICD-10-CM J35.1 and J35.3 are included on Line 368 only for 1) unilateral tonsillar hypertrophy in adults and 2) unilateral tonsillar hypertrophy in children with other symptoms suggestive of malignancy. Bilateral tonsillar hypertrophy and unilateral tonsillar hypertrophy in children without other symptoms suggestive of malignancy are included only on Line 548.

See Guideline Note 118 for diagnosis and treatment of obstructive sleep apnea in children.

GUIDELINE NOTE 44, MENSTRUAL BLEEDING DISORDERS

Line 420

Endometrial ablation or hysterectomy for abnormal uterine bleeding in premenopausal women may be indicated when all of the following are documented (A-C):

A) Patient history of (1, 2, 3, 4, and 5):
   1) Excessive uterine bleeding evidence by (a, b and c):

a) Profuse bleeding lasting more than 7 days or repetitive periods at less than 21-day intervals
b) Anemia due to acute or chronic blood loss (hemoglobin less than 10 or hemoglobin less than 11 g/dL if use of iron is documented) for hysterectomy. No documented hemoglobin level is required for endometrial ablation procedures.
c) Bleeding causes major impairment or interferes with quality of life

2) Failure of hormonal treatment for a six-month trial period or contraindication to hormone use (oral contraceptive pills or patches, progesterone-containing IUDs, injectable hormone therapy, or similar)
3) No current medication use that may cause bleeding, or contraindication to stopping those medications
4) Endometrial sampling performed
5) For hysterectomy, no evidence of treatable intrauterine conditions or lesions by (a, b or c):
   a) Sonohysterography
   b) Hysteroscopy
   c) Hysterosalpingography

   For endometrial ablation, a pre-operative ultrasound should be performed

B) Negative preoperative pregnancy test result unless patient has been previously sterilized
C) Nonmalignant cervical cytology, if cervix is present

~~**GUIDELINE NOTE 76, DIAGNOSTIC TESTING FOR LIVER FIBROSIS TO GUIDE TREATMENT OF HEPATITIS C IN NON-CIRRHOTIC PATIENTS**~~

~~*Line 199*~~

~~Given that a fibrosis score of ≥F2 is the threshold for antiviral treatment of Hepatitis C, the following are included on this line:~~

~~Imaging tests:~~
~~- Transient elastography (FibroScan®)~~
~~- Acoustic radiation force impulse imaging (ARFI) (Virtual Touch™ tissue quantification, ElastPQ)~~
~~- Shear wave elastography (SWE) (Aixplorer®)~~
~~Blood tests (only if imaging tests are unavailable):~~
~~- Enhanced Liver Fibrosis (ELF™)~~
~~- Fibrometer™~~
~~- FIBROSpect® II~~
~~- FibroSure® (FibroTest®) or ActiTest®~~

~~If a fibrosis score of ≥F3 is the threshold for antiviral treatment of Hepatitis C, one or more of the following are included on this line:~~

~~Imaging tests:~~
~~- Transient elastography (FibroScan®)~~
~~- Acoustic radiation force impulse imaging (ARFI)~~
~~- Shear wave elastography (SWE)~~

Appendix A
Revised Guideline Notes

~~Magnetic resonance elastography is included on this line for ≥F2 or ≥F3 only when at least one imaging test (FibroScan, ARFI, and SWE) has resulted in indeterminant results, a second one is similarly indeterminant, contraindicated or unavailable, and MRE is readily available.~~

~~The following tests are not included on this line (or any other line):~~

- ~~Real time tissue elastography~~
- ~~Hepascore (FibroScore)~~

~~Noninvasive tests are covered no more often than once per year.~~

~~The development of this guideline note was informed by a HERC coverage guidance. See https://www.oregon.gov/oha/HPA/DSI-HERC/Pages/Evidence-based-Reports.aspx.~~

GUIDELINE NOTE 76, DIAGNOSTIC TESTING FOR LIVER FIBROSIS TO GUIDE MANAGEMENT IN CHRONIC LIVER DISEASE

Line 199

The following tests are included on this line because of their ability to effectively distinguish F4 from lower levels of fibrosis:

Non-proprietary blood tests such as:

- Platelet count
- Hyaluronic acid
- Age-platelet index
- AST-platelet ratio
- FIB-4
- FibroIndex
- Forns index
- GUCI
- Lok index

Imaging tests:

- Transient elastography (FibroScan®)
- Acoustic radiation force impulse imaging (ARFI) (Virtual Touch™ tissue quantification, ElastPQ)
- Shear wave elastography (SWE) (Aixplorer®)

The following tests are not included on this line (or any other line):

- Real time tissue elastography
- Proprietary blood tests (such as):
  - EL

- Fibrometer
- FibroTest
- Hepascore
- FIBROSpect II

Noninvasive tests for liver fibrosis are only indicated for initial assessment or when monitoring progression from F3 to F4, no more than annually.
Magnetic resonance elastography is included on this line for patients when ALL of the following apply:

- In whom at least one imaging test (FibroScan, ARFI, and SWE) has resulted in indeterminant results, a second one is similarly indeterminant, contraindicated or unavailable
- The patient is suspected to have aggressive disease/advanced fibrosis (e.g. in NAFLD based on older age, diabetes, obesity, high FIB-4, or APRI)
- Cirrhosis is not identified on routine imaging (ultrasound, CT)
- A liver biopsy would otherwise be indicated, but MRE would be an appropriate alternative

Repeat MR elastography is not indicated.

GUIDELINE NOTE 104, ~~VISCOSUPPLEMENTATION~~ NEWER INTERVENTIONS FOR OSTEOARTHRITIS OF THE KNEE

Lines 430,461

The following treatments are not included on this line for osteoarthritis of the knee:

- Whole body vibration
- Glucosamine/chondroitin (alone, or in combination)
- Platelet rich plasma
- Viscosupplementation
- Transcutaneous electrical stimulation (TENS)

CPT 20610 and 20611 are included on these lines only for interventions other than viscosupplementation for osteoarthritis of the knee.

The development of this guideline note was informed by a HERC coverage guidance. See https://www.oregon.gov/oha/HPA/DSI-HERC/Pages/Evidence-based-Reports.aspx.

Appendix A
Revised Guideline Notes

GUIDELINE NOTE 172, INTERVENTIONS WITH MARGINAL CLINICAL BENEFIT OR LOW COST-EFFECTIVENESS FOR CERTAIN CONDITIONS

Line 500

The following interventions are prioritized on Line 500 CONDITIONS FOR WHICH INTERVENTIONS RESULT IN MARGINAL CLINICAL BENEFIT OR LOW COST-EFFECTIVENESS:

Procedure Code	Intervention Description	Rationale	Last Review
~~95250-95251~~	~~Retrospective (professional) continuous glucose monitoring~~	~~Limited evidence of clinical utility~~	~~August, 2017~~

GUIDELINE NOTE 173, INTERVENTIONS THAT ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS FOR CERTAIN CONDITIONS

Line 660

The following Interventions are prioritized on Line 660 CONDITIONS FOR WHICH CERTAIN INTERVENTIONS ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS:

Procedure Code	Intervention Description	Rationale	Last Review
~~64568~~	~~Incision for implantation of cranial nerve (eg, vagus nerve) neurostimulator electrode array and pulse generator for hypoglossal nerve stimulation for treatment of obstructive sleep apnea~~	~~Insufficient evidence of effectiveness and evidence of harm~~	~~May, 2018~~
~~79445~~ ~~C2616~~ ~~S2095~~	~~Radiopharmaceutical therapy, by intra-arterial particulate administration for use in treating cancers other than primary hepatocellular carcinoma or colorectal cancer metastatic to the liver~~ ~~Brachytherapy source, non-stranded, yttrium-90, per source in treating cancers other than primary hepatocellular carcinoma or colorectal cancer metastatic to the liver.~~ ~~Transcatheter occlusion or embolization for tumor destruction, percutaneous, any method, using yttrium-90~~	~~No evidence of effectiveness~~	~~March, 2018~~

Appendix A
Revised Guideline Notes

	~~microspheres, in treating cancers other than primary hepatocellular carcinoma or colorectal cancer metastatic to the liver~~		
81232~~, 81246~~	5-fluorouracil/5-FU and capecitabine drug metabolism	Insufficient evidence of effectiveness	November, 2017
~~90869~~	~~Therapeutic repetitive transcranial magnetic stimulation (TMS) treatment~~	~~No evidence of effectiveness~~	~~December, 2012~~
~~95012~~	~~Nitric oxide expired gas determination~~		~~August 2015~~

Appendix B
New Guideline Notes

GUIDELINE NOTE XXX, PULMONARY REHABILITATION

Lines 9,58,223,234,241,283

Pulmonary rehabilitation is included on these lines only for patients with all of the following (1-4):

1) Moderate to severe chronic pulmonary disease with dyspnea with exertion that reduces their ability to perform activities of daily living despite appropriate medical management
2) Moderate to severe pulmonary disability defined as either
    a. A maximal pulmonary exercise stress test under optimal bronchodilatory treatment which demonstrates a respiratory limitation to exercise with a maximal oxygen uptake (VO2max) equal to or less than 20 ml/kg/min, or about 5 metabolic equivalents (METS); *or*
    b. Pulmonary function tests showing that either the forced expiratory volume in one second (FEV1), forced vital capacity (FVC), FEV1/FVC ratio, or diffusion capacity for carbon monoxide (DlCO) is less than 60 % of that predicted
3) Physically able, motivated and willing to participate in the pulmonary rehabilitation program and be a candidate for self-care post program
4) No contraindications to pulmonary rehabilitation, including unstable cardiac disease, locomotor or neurological difficulties precluding exercise, significant cognitive or psychiatric impairment, or housebound due to the severity of disease.

Pulmonary rehabilitation is only covered for:

1) A multidisciplinary program with includes supervised exercise therapy, patient education, and smoking cessation (if applicable).
2) Up to 36 total sessions.

Repeat pulmonary rehabilitation programs should be limited to those patients who have had a subsequent lung reduction surgery or lung transplantation.

GUIDELINE NOTE XXX, EMBOLIZATION OF ARTERIAL MALFORMATIONS

Line 305

Vascular embolization or occlusion of arterial or arteriovenous malformations is included on this line only for Schobinger Class 3 or 4 lesions.

GUIDELINE NOTE XXX, SCREENING FOR OPHTHALMOLOGIC COMPLICATIONS OF HIGH-RISK MEDICATIONS

Lines 360, 632

ICD-10 H36 (Retinal disorders in diseases classified elsewhere) and/or Z79.899 (Other long term (current) drug therapy) are included on Line 360 only for ophthalmologic examinations and testing to screen for complications of high-risk medications. ICD-10 H36 is included on Line 632 for all other indications.

Appendix B
New Guideline Notes

GUIDELINE NOTE XXX, SHOULDER DECOMPRESSION SURGERY

Lines 356,417,441

CPT 29826 is only included on these lines as a component of rotator cuff repair surgery. CPT 29826 is not included on this line for pairing with shoulder impingement syndrome or adhesive capsulitis of shoulder.

Section 2.0

Staff Report

Errata
May 2019

1) Guideline Note 127 contains the CPT codes for physical therapy services that are no longer valid and were replaced with a new set of PT codes for 2019.

GUIDELINE NOTE 127, GENDER DYSPHORIA

Line 312

Hormone treatment with GnRH analogues for delaying the onset of puberty and/or continued pubertal development is included on this line for gender questioning children and adolescents. This therapy should be initiated at the first physical changes of puberty, confirmed by pubertal levels of estradiol or testosterone, but no earlier than Tanner stages 2-3. Prior to initiation of puberty suppression therapy, adolescents must fulfill eligibility and readiness criteria and must have a comprehensive mental health evaluation. Ongoing psychological care is strongly encouraged for continued puberty suppression therapy.

Cross-sex hormone therapy is included on this line for treatment of adolescents and adults with gender dysphoria who meet appropriate eligibility and readiness criteria. To qualify for cross-sex hormone therapy, the patient must:

A) have persistent, well-documented gender dysphoria
B) have the capacity to make a fully informed decision and to give consent for treatment
C) have any significant medical or mental health concerns reasonably well controlled
D) have a comprehensive mental health evaluation provided in accordance with Version 7 of the World Professional Association for Transgender Health (WPATH) Standards of Care (www.wpath.org).

Sex reassignment surgery is included for patients who are sufficiently physically fit and meet eligibility criteria. To qualify for surgery, the patient must:

A) have persistent, well documented gender dysphoria
B) for genital surgeries, have completed twelve months of continuous hormone therapy as appropriate to the member's gender goals unless hormones are not clinically indicated for the individual
C) have completed twelve months of living in a gender role that is congruent with their gender identity unless a medical and a mental health professional both determine that this requirement is not safe for the patient
D) have the capacity to make a fully informed decision and to give consent for treatment
E) have any significant medical or mental health concerns reasonably well controlled
F) for breast/chest surgeries, have one referral from a mental health professional provided in accordance with version 7 of the WPATH Standards of Care.
G) For genital surgeries, have two referrals from mental health professionals provided in accordance with version 7 of the WPATH Standards of Care.

Electrolysis (CPT 17380) and laser hair removal (CPT 17110,17111) are only included on this line as part of pre-surgical preparation for chest or genital surgical procedures also included on this line. These procedures are not included on this line for facial or other cosmetic procedures or as pre-surgical preparation for a procedure not included on this line

Mammoplasty (CPT 19316, 19324-19325, 19340, 19342, 19350) is only included on this line when 12 continuous months of hormonal (estrogen) therapy has failed to result in breast tissue growth of Tanner Stage 5 on the puberty scale OR there is any contraindication to, intolerance of or patient refusal of hormonal therapy.

Revisions to surgeries for the treatment of gender dysphoria are only covered in cases where the revision is required to address complications of the surgery (wound dehiscence, fistula, chronic pain directly related to the surgery, etc.). Revisions are not covered solely for cosmetic issues.

Pelvic physical therapy (CPT ~~97001, 97001,~~ 97110, 97140, 97161-97164, and 97530) is included on this line only for pre- and post-operative therapy related to genital surgeries also included on this line and as limited in Guideline Note 6 REHABILITATIVE AND HABILITATIVE THERAPIES.

2) HCPCS and CPT codes previously approved for addition to Guideline Note 173 or Line 660 but which were missing from the guideline note.
   a. New guideline note 173 entries (previously omitted):

D0422-D0423	Collection and preparation of genetic sample material for laboratory analysis and report Genetic test for susceptibility to diseases – specimen analysis	Insufficient evidence of effectiveness	October, 2018
81346	TYMS (thymidylate synthetase) (eg, 5-fluorouracil/5-FU drug metabolism), gene analysis, common variant(s) (eg, tandem repeat variant)	Insufficient evidence of effectiveness	November, 2017
62287, S2348	Percutaneous laser disc decompression Ozone therapy injections Radiofrequency denervation	Insufficient evidence of effectiveness	January, 2018 Coverage Guidance Blog
C2614	Probe, percutaneous lumbar discectomy	Insufficient evidence of effectiveness	May, 2018
C9745	Nasal endoscopy, surgical; balloon dilation of Eustachian tube	Insufficient evidence of effectiveness	May, 2018
G0481, G0482, G0843	Urine drug testing, definitive for >7 drug classes	No clinical benefit	August, 2018 Coverage Guidance Blog

b. Remove the following codes from Guideline note 173:

~~37212-37214~~	~~Transcatheter therapy, venous infusion for thrombolysis for treatment of peripheral deep vein thrombosis~~	~~Increased risk of harm compared to equally effective alternative therapy; significantly less cost effective~~	~~January, 2018~~
~~61863, 61864, 61867, 61868, 61880, 61886~~	~~Deep brain stimulation for any type of epilepsy~~	~~Evidence of no clinically significant effectiveness, evidence of harm~~	~~January, 2018~~

Section 3.0

Consent Agenda-

Straightforward Items

Consent Agenda Issues—May 2019

Code	Code Description	Line(s) Involved	Issue	Recommendation(s)
11971	Removal of tissue expander(s) without insertion of prosthesis	191 CANCER OF BREAST; AT HIGH RISK OF BREAST CANCER 285 COMPLICATIONS OF A PROCEDURE ALWAYS REQUIRING TREATMENT	A provider requested that CPT 11971 pair with ICD10 T85.79XA (Infection and inflammatory reaction due to other internal prosthetic devices, implants and graft) which is on line 285. 11971 is on 7 other lines. Another case reconsideration brought up that 11971 is used as part of breast reconstruction after breast cancer surgery and should be added to the breast cancer line.	Add 11971 to lines 191 and 285
96132 96133	Neuropsychological testing evaluation services by physician or other qualified health care professional, including integration of patient data, interpretation of standardized test results and clinical data, clinical decision making, treatment planning and report, and interactive feedback to the patient, family member(s) or caregiver(s), when performed; first hour Each additional hour	174 GENERALIZED CONVULSIVE OR PARTIAL EPILEPSY WITHOUT MENTION OF IMPAIRMENT OF CONSCIOUSNESS Treatment: SINGLE FOCAL SURGERY	Neuropsychological testing codes are generally diagnostic; however, 96132 and 96133 are on lines 92,173,193,202. These tests are used prior to epilepsy surgery to evaluate patients and the OHSU epilepsy surgery program has requested that they be paired on line 174 for pre-operative use. "…neuropsychological testing is mandatory before epilepsy surgery to address cognitive risk…This is a nationally recognized standard…"	Add 96132 and 96133 to line 174

Consent Agenda Issues—May 2019

Code	Code Description	Line(s) Involved	Issue	Recommendation(s)
M54.0	Panniculitis affecting regions of neck and back	401 CONDITIONS OF THE BACK AND SPINE 519 PANNICULITIS	The ICD-10 M54.0 family was mistakenly put on the medical back line when it needs to be put on the panniculitis line.	Remove M54.0 family from line 401 Add M54.0 family to line 519
19370 19371 19380	Open periprosthetic capsulotomy, breast Periprosthetic capsulectomy, breast Revision of reconstructed breast	191 CANCER OF BREAST; AT HIGH RISK OF BREAST CANCER	19370, 19371, and 19380 are used for revision of breast reconstructions, which might occur after a mastectomy for breast cancer. These codes are currently on line 634 GALACTORRHEA, MASTODYNIA, ATROPHY, BENIGN NEOPLASMS AND UNSPECIFIED DISORDERS OF THE BREAST and on a complications line. There is a guideline note that outlines when such revisions are covered. Other CPT codes used for revision of breast reconstruction appear on line 191.	Add 19370, 19371, and 19380 to line 191
G12.20	Motor neuron disease, unspecified	292 NEUROLOGICAL DYSFUNCTION IN POSTURE AND MOVEMENT CAUSED BY CHRONIC CONDITIONS	Provider requested consideration of coverage of PT/OT for G12.20, for use during the work-up of motor neuron diseases for education on fall prevention, coping skills, and other management techniques for the condition. Currently on the Undefined Diagnosis File.	Add G12.20 to line 292 Advise HSD to remove G12.20 from the Undefined Diagnosis File

Straightforward Guideline Note Changes
May 2019

1) The coding specification attached to line 292 NEUROLOGICAL DYSFUNCTION IN POSTURE AND MOVEMENT CAUSED BY CHRONIC CONDITIONS needs to be updated to include one additional CPT code (CPT 63650 Percutaneous implantation of neurostimulator electrode array, epidural):
    a. Spinal cord stimulation (63650 ~~63655~~-63688) is not included on this line when paired with ICD-10-CM category G90.5 Complex regional pain syndrome/reflex sympathetic dystrophy. Chemodenervation with botulinum toxin injection (CPT 64642-64647) is included on this line for treatment of upper and lower limb spasticity (ICD-10-CM codes G24.02, G24.1, G35, G36.0, I69.03- I69.06 and categories G71, and G80-G83.) CPT codes 62320-3 are only included on Lines 71 and 292 for trials of antispasmodics in preparation for placement of a baclofen pump. ICD-10-CM R62.0 is included on Lines 292, 345 and 377 for children 8 and under. ICD-10-CM F88 is included on these lines for developmental delay. When it is used to indicate sensory integration disorder or sensory processing disorder, it is included on Line 659.

BAHA Hearing Aids HCPCS Placement Correction

Issue: The HCPCS code for auditory osseointegrated devices were added to line 500 as part of a code clean up in November, 2017. However, these devices should be included on lines 311 HEARING LOSS - AGE 5 OR UNDER and 444 HEARING LOSS - OVER AGE OF FIVE and be governed by Guideline Note 103. CPT codes for the implantation of these devices (CPT 69714 and 60715 Implantation, osseointegrated implant, temporal bone…) are included on lines 311 and 444.

HCPCS Code	Code Description	Current Line Placement
L8690	Auditory osseointegrated device, includes all internal and external components	500 CONDITIONS FOR WHICH INTERVENTIONS RESULT IN MARGINAL CLINICAL BENEFIT OR LOW COST-EFFECTIVENESS
L8691	Auditory osseointegrated device, external sound processor, excludes transducer/actuator, replacement only, each	500
L8692	Auditory osseointegrated device, external sound processor, used without osseointegration, body worn, includes headband or other means of external attachment	500
L8693	Auditory osseointegrated device abutment, any length, replacement only	500
L8694	Auditory osseointegrated device, transducer/actuator, replacement only, each	New code

HERC staff recommendations:

1) Add L8690, L8691, L8693, and L8694 to lines 311 HEARING LOSS - AGE 5 OR UNDER and 444 HEARING LOSS - OVER AGE OF FIVE
2) Add HCPCS L8692 to line 311 HEARING LOSS - AGE 5 OR UNDER
    a. The headband device is only included for children under age 5 in GN 103
3) Modify GN103 as shown below
4) Modify GN173 as shown below

GUIDELINE NOTE 103, BONE ANCHORED HEARING AIDS

Lines 311,444

Bone anchored hearing aids (BAHA, CPT 69714, 69715; HCPCS L8690-8694) are included on these lines when the following criteria are met:

A) The patient is aged 5-20 years for implanted bone anchored hearing aids; headband mounted BAHA devices may be used for children under age 5
B) Treatment is for unilateral severe to profound hearing loss when the contralateral ear has normal hearing with or without a hearing aid
C) Traditional air amplification hearing aids and contralateral routing of signal (CROS) hearing aid systems are not indicated or have been tried and are found to be not effective
D) Implantation is unilateral.

Use of BAHA for treatment of tinnitus is not covered

GUIDELINE NOTE 172, INTERVENTIONS WITH MARGINAL CLINICAL BENEFIT OR LOW COST-EFFECTIVENESS FOR CERTAIN CONDITIONS

Line 500

The following interventions are prioritized on Line 500 CONDITIONS FOR WHICH INTERVENTIONS RESULT IN MARGINAL CLINICAL BENEFIT OR LOW COST-EFFECTIVENESS:

69710 ~~HCPCS L8690-L8693~~	Implantation or replacement of electromagnetic bone conduction hearing device in temporal bone ~~Auditory osseointegrated device~~	Less effective than other therapies	June, 2014, Aug. 2015

Spinal Artery Compression Syndromes

Question: Where should spinal cord compression syndromes be placed on the Prioritized List?

Question source: HERC staff

Issue: M47.01 family (Anterior spinal artery compression syndromes) and the M47.02 family (Vertebral artery compression syndromes) are currently on lines 346 CONDITIONS OF THE BACK AND SPINE WITH URGENT SURGICAL INDICATIONS and 401 CONDITIONS OF THE BACK AND SPINE (medical therapy line). Spinal compression syndromes are the most common cause of spinal cord infarctions. Clinical features include paraparesis or quadriparesis and impaired pain and temperature sensation.

Treatment of spinal artery compression syndromes is supportive. There are a few case reports on the literature of surgical procedures used to intervene early in the disease, but generally the spinal cord damage has already occurred, and these procedures have little impact on the outcome. These syndromes need the supportive care available on the dysfunction lines rather than the routine back pain interventions on the back lines.

HERC staff recommendation:

1) Remove ICD-10 M47.01 family (Anterior spinal artery compression syndromes) and the M47.02 family (Vertebral artery compression syndromes) from lines 346 CONDITIONS OF THE BACK AND SPINE WITH URGENT SURGICAL INDICATIONS and 401 CONDITIONS OF THE BACK AND SPINE
2) Add ICD-10 M47.01 family (Anterior spinal artery compression syndromes) and the M47.02 family (Vertebral artery compression syndromes) to line 292 NEUROLOGICAL DYSFUNCTION IN POSTURE AND MOVEMENT CAUSED BY CHRONIC CONDITIONS
    a. Similar spinal cord injury diagnoses are on this line

Iontophoresis

Issue: The procedure code for iontophoresis does not appear in any location in the HERC database and appears to have never been previously reviewed. Iontophoresis is a process of transdermal drug delivery by use of a voltage gradient on the skin. Molecules are transported across the stratum corneum by electrophoresis and electroosmosis and the electric field can also increase the permeability of the skin. Therapeutically, electromotive drug administration (EMDA) delivers a medicine or other chemical through the skin, thereby acting as a non-invasive way to "inject" medication. Iontophoresis of pilocarpine can be used as part of the diagnostic work up for cystic fibrosis and a reverse form of the procedure can be used for glucose monitoring in certain systems.

CPT codes in the same numerical series as CPT 97033 appear on the lines with PT services or on line 660/GN173.

CPT 97033 Application of a modality to 1 or more areas; iontophoresis, each 15 minutes

HERC staff recommendation:

1) Recommend HSD add CPT 97033 (Application of a modality to 1 or more areas; iontophoresis, each 15 minutes) to the Ancillary File
    a. Appears to be used for diagnostic and therapeutic indications, and for delivery of a variety of medications for a range of diagnoses

Section 4.0

Biennial Review

Value-based Benefits Subcommittee: Chronic Pain Reprioritization

May 16, 2019

Oregon Health Authority

Agenda

- Background
- Evidence summary
- Options for HERC consideration
  - No action
  - Prior modified CPTF proposal
  - Revised proposal—several options
- Public testimony
- Discussion and decision

Conditions under review

ICD-10 Code	Description
G89.21	Chronic pain due to trauma
G89.28	Other chronic postprocedural pain
G89.29	Other chronic pain
G89.4	Chronic pain syndrome
M79.7	Fibromyalgia

There is no proposal today to change **coverage** for other conditions associated with chronic pain other than these five specific conditions. The only other significant item under consideration is adjusting the back conditions opioid guideline taper language

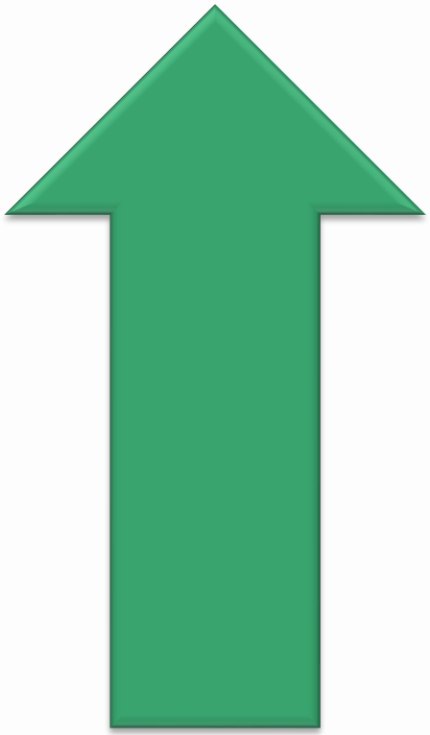
Current OHP Coverage for 5 Chronic Pain Conditions

Below funding Line (i.e. no treatment is intended to be covered)

CPTF's Chronic Care Paradigm: New Coverage of Therapies

Nonpharmacologic therapies:

- Pain education
- Cognitive behavioral therapy
- Yoga
- Tai Chi
- Mindfulness
- Massage
- Supervised exercise therapy
- Intensive interdisciplinary rehabilitation



Appropriate pharmacologic therapies

- Non-opioids such as pregabalin (Lyrica), gabapentin, duloxetine (Cymbalta)
- Opioids (subject to Oregon Prescribing Guidelines)

Oregon Health Authority

Today's major decision: Create and prioritize a new line for chronic pain?

Impact if funded

- Adds non-pharmacologic treatments and pharmacologic treatments
- For pharmacologic treatments, includes options for addition of chronic opioid coverage when prescribed according to statewide guidelines
- Possible taper plan for certain patients who fall outside guideline

Impact if unfunded

- No change in coverage: all five conditions remain below funding line
- Patients may continue to receive opioids if they have another funded painful condition (other than back pain), no PA requirement, or receiving through exception
- Still need to address back pain taper guideline

Evidence: Non-Pharmacologic Treatments

Treatment	Effect	Level of Evidence
Tai Chi	Small but clinically significant short term benefit in pain and function	Low
Yoga	Inconsistent evidence	Low
Exercise	Non-clinically significant improvement in pain (S) and function (S,I)	Low to Moderate
Acupuncture	Small, non-clinically significant improvement in function (S,I)	Low
Interdisciplinary rehab	Clinically meaningful improvement in function in the short, intermediate, and long term	Low
Mindfulness	No clear improvement in function or pain	Moderate
Massage/PT	Small, non-clinically significant impact on short term function; insufficient evidence of impact on pain	Low
CBT	Small, non-clinically significant effects on pain, function and mood immediately post-treatment but not intermediate or long term	Low
Pain Education	No improvement in pain or function	Low

Evidence: Non-Pharmacologic Treatments

	Function *Short-Term* *Effect Size SOE*	**Function** *Intermediate - Term* Effect Size SOE	**Function** *Long-Term* Effect Size SOE	**Pain** *Short-Term* Effect Size SOE	**Pain** *Intermediate-Term* Effect Size SOE	**Pain** *Long-Term* Effect Size SOE
Exercise	slight +	slight ++	none +	slight ++	none ++	none ++
Psychological Therapies: CBT	slight +	slight +	insufficient evidence	slight +	none +	insufficient evidence
Psychological Therapies: Biofeedback, Imagery	insufficient evidence	insufficient evidence	insufficient evidence	insufficient evidence	insufficient evidence	insufficient evidence
Physical Modalities: Magnetic Pads	insufficient evidence	none +	no evidence	insufficient evidence	none +	no evidence
Manual Therapies: Massage (Myofascial Release)	no evidence	slight +	none +	insufficient evidence	insufficient evidence	slight +
Mindfulness Practices: MBSR	none ++	no evidence	no evidence	none ++	no evidence	no evidence
Mind-Body Practices: Qigong, Tai Chi	slight +	no evidence	no evidence	moderate +	no evidence	no evidence
Acupuncture	slight ++	slight ++	no evidence	none +	none +	no evidence
Multidisciplinary Rehabilitation	slight +	slight +	slight +	none +	slight +	none +

Short-Term: 1 to <6 months; Intermediate-Term: ≥6 to <12 months; Long-Term: ≥12 months
Effect Size: none, slight/small, moderate, or large improvement
Strength of Evidence: + = low, ++ = moderate, +++ = high
CBT = cognitive-behavioral therapy; MBSR = mindfulness-based stress reduction; none = no effect/no statistically significant effect; SOE = strength of evidence

Oregon Health Authority

Evidence: Non-Opioid Medications

Drug	Effect	Level of Evidence
Milnacipran (Savella)	Improves pain and function by 30% or more (NNT 5-11)	Low
Duloxetine (Cymbalta)	Improves pain and function by 30% or more (NNT 5-11)	Low
Pregabalin (Lyrica)	Improves pain 30-50% (NNT 7-22)	Low

Harms: Sedation, weight gain, nausea

Evidence: Opioid Therapy

- Small, non-clinically significant short-term improvement in pain and functioning
- Risk of adverse events (Constipation, fatigue)
- Risk of any harm 78%; serious adverse events 7.5%
- Increased opioid prescribing in recent decades associated with increased overdoses and deaths

Evidence: Opioid taper

- Overall quality of the evidence is very low
- Findings suggested that pain, function, and quality of life might improve during and after opioid discontinuation or dose reduction
- Scant evidence on harms associated with tapering strategies
- Not able to draw any conclusions regarding rate of tapering or final goal of tapering (i.e., goal of zero vs. other dose)
- Very little information found on this issue. In almost all of the studies included in the previous MED report and in this update, patients had some autonomy in the decision to taper their opioids.

Coverage Questions -- Opioids
(Initiation of therapy < 90d, not on long-term opioids)

- Based on available expert opinion and low quality evidence, does the balance of benefit and harms support coverage for new initiations of acute/subacute opioid therapy for these five conditions (<90 days)?
- Based on expert opinion alone: Should fibromyalgia be treated differently (e.g., no new short-term opioids for patients with fibromyalgia)?
- Should coverage require prescribing aligned with Oregon Chronic Opioid Prescribing Guidelines and Oregon Acute Opioid Prescribing Guidelines?

Coverage Question -- Opioids
(Initiation of therapy >= 90 days, not currently on long-term opioids)

- Based on available expert opinion and low quality evidence, does the balance of benefit and harms support coverage for new initiations of long-term opioid therapy for these five conditions (>=90 days)?
- Based on expert opinion/international guidelines (suggesting opioids may be harmful for patients with fibromyalgia): should fibromyalgia be treated differently than the other four conditions?
- Should coverage require prescribing aligned with CPTF prescribing criteria or just the Oregon Prescribing Guidelines?

Coverage Question -- Opioids
(Patients already taking long-term opioids)

- For patients already on long-term opioid therapy, when not in alignment with the preceding decisions (i.e., long-term therapy deemed not covered or not covered for specific conditions), which option is appropriate for coverage:
  - "Grandfathering": allow continued coverage as long as it is aligned with Oregon Chronic Opioid Prescribing Guidelines; when not in alignment, require taper as below.
  - Require an individualized taper
    - With goal to zero (no evidence to support)
    - Without goal to zero

Options for HERC Consideration

- ***OPTION 1: Do not reprioritize chronic pain syndrome, fibromyalgia and related conditions due to lack of evidence of effectiveness of available treatment modalities. Consider readdressing the prioritization of these conditions as part of the 2022 or 2024 Biennial Review.***
  - Rationale:
    - Low level of evidence of small, non-clinically significant effectiveness of various therapies
    - Wait for studies on back line changes and AHRQ reviews
  - Impact:
    - Continued HERC intent of non-coverage for various treatments and medications (including opioids) for these 5 conditions

Options for HERC Consideration

- ***OPTION 2: Adopt the CPTF proposal with minor edits***
  - ***Rationale:*** Chronic pain patients would have access to alternative therapies to opioids (physical treatments, pharmaceutical options). The Chronic Pain Taskforce felt these were beneficial treatments in their expert opinion.
  - ***Impact:*** New coverage would be created for nonpharmacologic and pharmacologic treatments for patients with these specific chronic pain conditions, including new coverage of long-term opioid therapy if patients meet certain criteria.
  - OHA's Actuarial Services Unit (ASU) estimates the cost of the nonpharmacologic therapies to be $10.8 to $17.3 million for all of the Oregon Health Plan in 2020.

Options for HERC Consideration

- ***OPTION 3: Adopt the CPTF informed proposal with consideration of staff suggested edits based on AAI and other feedback***
  - ***Rationale:*** Chronic pain patients would have access to alternative therapies to opioids (other pharmaceutical options plus non-pharmaceutical options). Restrictions on opioids have limited evidence.
  - ***Impact:*** New coverage would be created for nonpharmacologic and pharmacologic treatments for patients with these specific chronic pain conditions, including new coverage of long-term opioid therapy which may be for some or all of the 5 conditions under consideration. This will have cost implications which will require actuarial analysis.

Options Review

- Option 1: Make no changes; wait for further evidence and readdress at future biennial review
- Option 2: Adopt modified CPTF recommendation
  - Adds coverage for various non-pharmacologic therapies and non-opioid pharmacologic therapies
  - Adds coverage for opioid therapy for 4 of the 5 conditions for appropriate patients
- Option 3: Staff modified recommendation choices
  - Adds coverage from #2, plus short term opioids for fibromyalgia
  - Removes “practice guideline” type language from guideline
  - Amends taper language and includes 3 options for long-term opioids:
    - No new starts for fibromyalgia
    - No new starts for any of the 5 conditions
    - New long-term opioids covered for all patients with these five conditions who meet Oregon statewide opioid prescribing guideline criteria

New Line

- ***Create a new line for five chronic pain conditions including fibromyalgia for the 2020 Biennial Review***

CONDITION: FIBROMYALGIA, CHRONIC PAIN SYNDROME AND RELATED CONDITIONS

TREATMENT: LIMITED PHYSICAL MODALITIES, COGNITIVE BEHAVIORAL THERAPY, MEDICAL THERAPY

Diagnoses:

- Chronic pain due to trauma
- Other chronic postprocedural pain
- Other chronic pain
- Chronic pain syndrome
- Fibromyalgia

Procedures:

- Standard outpatient codes
- Psychotherapy (for CBT/ACT)
- Physical therapy
- Occupational therapy
- Acupuncture
- Health and behavior assessment

New Line Prioritization

Line Scoring if Reprioritized

Line 401 CONDITIONS OF THE BACK AND SPINE
Line XXX FIBROMYALGIA, CHRONIC PAIN SYNDROME AND RELATED CONDITIONS [proposed]
Line 528 FIBROMYALGIA, CHRONIC FATIGUE SYNDROME, AND RELATED DISORDERS [current]

	Line 401	Line XXX	Line 528
Category (Non-Fatal Condition)	7	7	7
Healthy Life (0-10)	5	TBD	4
Suffering (0-5)	3	TBD	3
Population effects (0-5)	0	0	0
Vulnerable population (0-5)	0	0	0
Tertiary prevention (0-5)	2	TBD	0
Effectiveness (0-5)	3	TBD	1
Need for service (0-1)	0.8	TBD	0.8
Net cost	2	2	2
Score	432	TBD	112
Approximate line	401	TBD	528

Scoring Examples

HLY Score	Line Examples
5	Arthritis, back conditions
4	Migraine, persistent depression
Tertiary Prevention	
2	Strep throat, back conditions
1	Anxiety, Vestibular conditions
0	Arthritis, migraines
Effectiveness	
3	Back conditions, anxiety, arthritis
2	Peripheral nerve disorder, prostate disorders
1	Pelvic pain syndrome, colitis

Line 528 Revision

Line:	**528**
Condition:	~~FIBROMYALGIA,~~ CHRONIC FATIGUE SYNDROME~~, AND RELATED DISORDERS~~ (See Guideline Notes 64,65~~,135~~)
Treatment:	MEDICAL THERAPY
ICD-10:	~~G89.21,G89.28-G89.29,G89.4,M79.7,~~R53.82
CPT:	90785,90832-90840,90846-90853,93792,93793,98966-98969,99051, 99060,99070,99078,99201-99215,99281-99285,99341-99378,99381-99404,99408-99449,99487-99490,99495-99498,99605-99607
HCPCS:	G0248-G0250,G0396,G0397,G0463-G0467,G0490,G0511,G0513, G0514

Other Proposed Changes

- Back conditions guideline note edits (GN 56)
  - Wording changes to tie into new chronic pain line/guideline
  - Deletion of obsolete table
- Opioids for back condition guideline note edits (GN 60)
  - Removes “flare” as indication for short-term opioids (expert input)
  - Tapering section revised to align with recommended language for chronic pain line proposal (see next slide)
- Acupuncture guideline note edit (GN 92)
  - Adds entry for new line
- Delete fibromyalgia guideline note (GN 135)

Back Conditions Opioid Guideline Coverage Questions
(For patients currently taking long-term opioids)

- Question: how should the existing taper requirement for long-term opioids prescribed for back and neck conditions be modified?

Discussion and Decision

Executive Summary: HERC Biennial Review of Certain Chronic Pain Conditions

Every two years (each biennium) the Health Evidence Review Commission (HERC) can recommend updates to the prioritization of condition/treatment pairs on Oregon's Prioritized List of Health Services. In the past two years, a focus has been given to five chronic pain-related conditions and their treatments (chronic pain due to trauma, other chronic postprocedural pain, other chronic pain, chronic pain syndrome and fibromyalgia), currently on the unfunded region of the Prioritized List, with attention to whether there is sufficient evidence to consider their reprioritization. Because these conditions are currently "unfunded" or "below the (funding) line", neither pharmacologic or non-pharmacologic treatments are intended to be covered services for Oregon Health Plan members with these conditions unless they have another qualifying condition or individual exceptions are made.

Considerations for the reprioritization of the five chronic pain conditions has been informed by numerous efforts, including but not limited to:

- Recommendations by the Chronic Pain Taskforce which convened in 2017-2018
- Public, CCO, and expert input
- A third-party appraisal of the evidence by Washington-based Aggregate Analytics, Inc. (AAI)

HERC staff now submits three options for HERC's consideration regarding the potential reprioritization of these conditions as part of the next biennium, starting January 1, 2020, including:

- **Option 1:** Make no prioritization changes to the coverage for five chronic pain conditions and their treatments due to insufficient evidence of effectiveness.
    - No change to current non-coverage of both non-pharmacologic and pharmacologic therapies
    - Readdress at a future biennial review once new studies and evidence reviews currently in process are available to inform the decision
- **Option 2**: Adopt the modified Chronic Pain Task Force proposal for reprioritization of the five conditions and their treatments, as presented at the March 2019 Value-based Benefits Subcommittee (VbBS)/HERC meetings
    - Adds coverage for various non-pharmacologic therapies such as cognitive behavioral therapy, physical therapy and acupuncture
    - Adds coverage for non-opioid pharmacologic therapies such as gabapentin, pregabalin and duloxetine
    - Adds coverage for opioid therapy for 4 of the 5 conditions for appropriate patients
- **Option 3:** Adopt a further revised proposal for reprioritization, informed by the recent AAI evidence appraisal and public input, as modified by HERC staff.
    - Adds all benefits from option 2
    - Additional options for consideration related to long-term opioid therapy coverage, including for fibromyalgia.

Background

The Chronic Pain Task Force

To inform the possible reprioritization of the five chronic pain conditions, OHA convened a Chronic Pain Taskforce (CPTF) to review the evidence for treatments of these chronic pain conditions including pharmacologic and non-pharmacologic benefits. The CPTF met multiple times in 2017 and 2018.

One of the initial recommendations of the CPTF was the addition of a statement of intent (SOI) regarding chronic pain care. This SOI was approved at the May 2018 VbBS/HERC meetings, and added to the Prioritized List with the October 1, 2018 version:

> STATEMENT OF INTENT 5: TREATMENT OF CHRONIC PAIN
> It is the intent of the Commission that covered chronic pain conditions be treated in a multidisciplinary fashion, with a focus on active therapies, improving function, and demedicalizing the condition. Care should include education on sleep, nutrition, stress reduction, mood, exercise, and knowledge of pain. All providers seeing chronic pain patients should be trained in pain science (e.g., a contemporary understanding of the central and peripheral nervous system in chronic pain), motivational interviewing, culturally sensitive care, and trauma-informed care. Care should be provided as outlined in the Oregon Pain Management Commission pain management module: https://www.oregon.gov/oha/HPA/DSI-PMC/Pages/module.aspx.

In addition, the CPTF developed a proposal for coverage of the five chronic pain conditions based on review of the evidence, public input and expert input. The in-process CPTF proposal was reviewed in detail at the August 2018 and January 2019 VbBS meetings and was briefly discussed at the August 2018 and January 2019 HERC meetings. Ultimately, while the CPTF found limited evidence to support various therapies, its members recommended coverage of these therapies based on expert opinion of effectiveness. These therapies include pain education, cognitive behavioral therapy, yoga, mindfulness training, supervised exercise therapy, physical therapy and acupuncture. The CPTF also recommended coverage for certain pharmaceutical treatments including pregabalin, gabapentin, and duloxetine. Patients with four of these conditions would also have new coverage for opioid medications in many cases. Members with fibromyalgia would not gain coverage, based on expert opinion and guidelines indicating low effectiveness with risks of harm.

INTERVAL WORK SINCE JANUARY 2019

January VbBS meeting

At the January 2019 VbBS meeting, HERC staff presented proposed Prioritized List changes regarding coverage of certain chronic pain conditions, as informed by the CPTF and extensive public comment to date. HERC staff were directed to work on several sections of the proposal and bring it back for further consideration at the March 2019 VbBS and HERC meetings.

VbBS and HERC concerns to be addressed by HERC staff included:

1) Clarification of wording for the portion of the proposed new guideline regarding pain education:

   a. …. All providers ~~seeing~~ managing *[staff to propose improved wording here]* chronic pain patients should be trained in pain science (e.g., a contemporary understanding of the central and peripheral nervous system in chronic pain)…
2) Clarifications or modifications to the section of the proposed new guideline referring to opioid prescribing:
   a. Clarification regarding what (if any) circumstances would allow co-prescribing opioids with benzodiazepines
   b. Consideration for adding a requirement for co-prescribing naloxone for patients prescribed over 50 MED of opioids
   c. Suggestion to group provider qualifications together and patient requirements together for improved clarity
3) Clarify or modify the section of the proposed new guideline referring to opioid tapering:
   a. Remove the title of the section as it is confusing
   b. Clarify that the opioid taper requirement in fibromyalgia is for "when prescribed for fibromyalgia"
   c. Clarify whether "evidence of harm" should be removed from the section when referring to opioid use in fibromyalgia

CCO Pharmacy Director Feedback

Following the January 2019 VbBS meeting, HERC staff solicited feedback regarding the draft reprioritization proposal from Coordinated Care Organization (CCO) Pharmacy Directors during their monthly public meetings. A summary of CCO Pharmacy Directors input includes:

1) High level of concern that the overall effect of this proposal would be to increase access to opioids
2) Appreciation of the VbBS/HERC goal to reduce opioid reliance for these conditions by offering alternative treatments, but unanimous concern that the other services and medications proposed for these conditions will have costs that outweigh any benefits
3) Many CCOs have implemented opioid controls for prescribing related to a broad range of conditions. There was general concern that the current proposed new guideline wording would require coverage of a second taper when the CCOs have already covered a taper for a patient
4) Concern about the ability to track whether a provider or patient has completed the required pain education component of the opioid portion of the guideline
5) The high cost of the non-opioid medications used to treat fibromyalgia
   a. *Note: Per OHA Pharmacy Team, duloxetine and amitriptyline are mental health carve-out drugs covered by FFS. Gabapentin is currently frequently covered without prior authorization. The only high cost drug added for coverage for fibromyalgia in this proposal would be pregabalin [Lyrica], which could have a substantial financial impact on the CCOs. However, pregabalin is scheduled to become generic in mid-2019, which could substantially reduce the cost of this drug over the next few years. A new drug, milnacipran (brand name Savella), has received FDA approval for treatment of fibromyalgia but has only very limited use to date.*
6) The proposed new guideline as written would add a significant prior authorization burden for CCOs, providers and patients
7) Concern that the magnitude of benefit and level of evidence for all the drugs used to treat fibromyalgia is low

March VbBS/HERC Meetings

At the March 2019 VbBS and HERC meetings, the Director of the Oregon Health Authority (OHA) requested that the HERC pause deliberation of the proposal for reprioritization of the five chronic pain conditions due to newly identified potential conflict of interest among a contracted medical consultant to the HERC, a member of VbBS, and a Chronic Pain Task Force member. In response, the OHA hired Washington-based Aggregate Analytics, Inc. (AAI) to conduct a third-party review of the chronic pain reprioritization proposal to determine whether it reasonably aligns with the clinical evidence that informed its development. AAI's report was completed on May 6.

Aggregate Analytics Inc Report: Key Findings

Key findings from the AAI appraisal of the evidence for the five chronic pain conditions include:

1. Overall, the HERC evidence summary was well done; a vast amount of literature was summarized by HERC staff
2. The evidence review conducted by HERC staff was limited to adults, but children and adolescents with these conditions may be included in the coverage under consideration.
3. In some cases, effectiveness of an intervention was extrapolated from literature regarding other chronic pain conditions (e.g., back pain or osteoarthritis) due to limited evidence across the range of diagnoses that could be studied as "chronic pain."
4. The overall evidence to support many of the interventions for chronic pain is sparse.
5. The cited evidence is inadequate to support the exclusion of fibromyalgia for the use of opioids either in the short or long term.
6. There is very low evidence on opioid tapering.
7. An expanded search for high quality systematic reviews and evidence-based clinical guidelines may be of benefit.
8. High quality evidence reviews on the treatment of chronic pain are currently underway by the Agency for Healthcare Research and Quality (AHRQ)

Many of the key findings from the AAI report have previously been discussed at VbBS and HERC meetings or represent challenges that the HERC must frequently consider in face of limited evidence. The AAI report and its key findings will need to be considered closely by the HERC during their final consideration of the proposal.

Since receiving the AAI report, HERC staff have reviewed the additional literature noted by AAI through review of public and expert comment and summarized this review in a separate disposition of the literature document. No identified article or study identified in the AAI report changes the previous HERC staff summary of the evidence or the recommendations in the overall chronic pain proposal. In addition, HERC staff have summarized the previous evidence reviews and discussions regarding the considered exclusion of opioids for treatment of fibromyalgia, including tramadol. This is included as Appendix A.

Finally, after review of the AAI report as well as public and expert input, HERC staff have created a modified proposal for HERC consideration (Option 3) regarding prioritization of certain chronic pain conditions; specifically, this option removes "practice guideline" type language and, instead, refers to Oregon's statewide opioid prescribing guidelines. It also includes consideration of long-term opioid use for current OHP members with fibromyalgia, with variable options as to whether or not "new opioid

starts" would be allowed for those members who have never received opioids. Finally, Option 3 includes language updates regarding opioid tapering to ensure a focus on individualized approaches to care.

EVIDENCE SUMMARY

Note: Please see Appendix B for a more detailed summary of previously reviewed evidence

A HERC staff summary of the overall evidence for non-pharmacologic interventions for the five, chronic pain conditions under consideration includes:

1) **Tai chi**: small but clinically significant benefit in pain and function in the short term but not intermediate or long term (SOE: low)
2) **Yoga**: inconsistent evidence (SOE: low)
3) **Exercise**: short-term non-clinically significant improvement in pain and function (SOE: low to moderate); intermediate term non-clinically significant improvement in function (SOE: moderate); no long-term impact on pain (SOE: moderate)
4) **Acupuncture:** small, short to intermediate term, non-clinically significant improvement in function (SOE: moderate); no improvement in pain (SOE: low)
5) **Interdisciplinary rehabilitation**: clinically meaningful improvement in function in the short, intermediate, and long term based on one poor quality study (SOE: low). No clinically meaningful impact on pain (SOE: low)
6) **Mindfulness**: no clear improvement in function or pain (SOE: moderate)
7) **Massage/PT with myofascial release**: small, non-clinically significant impact on short-term function (SOE: low); insufficient evidence of impact on pain
8) **Cognitive behavioral therapy**: small, non-clinically significant effects on pain, function and mood immediately post-treatment that is not sustained in the intermediate or long term (SOE: low)
9) **Pain education**: no improvement in pain or disability (SOE: low)

Summary of evidence for non-pharmacological treatments for fibromyalgia from AHRQ review article (2018) compared with usual care, placebo, sham, attention control, or waitlist:

	Function *Short-Term* *Effect Size SOE*	**Function** *Intermediate - Term* Effect Size SOE	**Function** *Long-Term* Effect Size SOE	**Pain** *Short-Term* Effect Size SOE	**Pain** *Intermediate-Term* Effect Size SOE	**Pain** *Long-Term* Effect Size SOE
Exercise	slight +	slight ++	none +	slight ++	none ++	none ++
Psychological Therapies: CBT	slight +	slight +	insufficient evidence	slight +	none +	insufficient evidence
Psychological Therapies: Biofeedback, Imagery	insufficient evidence	insufficient evidence	insufficient evidence	insufficient evidence	insufficient evidence	insufficient evidence
Physical Modalities: Magnetic Pads	insufficient evidence	none +	no evidence	insufficient evidence	none +	no evidence
Manual Therapies: Massage (Myofascial Release)	no evidence	slight +	none +	insufficient evidence	insufficient evidence	slight +
Mindfulness Practices: MBSR	none ++	no evidence	no evidence	none ++	no evidence	no evidence
Mind-Body Practices: Qigong, Tai Chi	slight +	no evidence	no evidence	moderate +	no evidence	no evidence
Acupuncture	slight ++	slight ++	no evidence	none +	none +	no evidence
Multidisciplinary Rehabilitation	slight +	slight +	slight +	none +	slight +	none +

Short-Term: 1 to <6 months; Intermediate-Term: ≥6 to <12 months; Long-Term: ≥12 months
Effect Size: none, slight/small, moderate, or large improvement
Strength of Evidence: + = low, ++ = moderate, +++ = high
CBT = cognitive-behavioral therapy; MBSR = mindfulness-based stress reduction; none = no effect/no statistically significant effect; SOE = strength of evidence

For comparison, a summary of the evidence for non-pharmacologic therapies for back and neck pain (used to inform the development of the 2016 Back Pain Guidelines) is included in the following table:

Treatment	Strength of Evidence	Magnitude of Benefit
Spinal manipulation	Good	Small to moderate short-term benefit
Yoga (viniyoga)	Fair	Moderate benefit
Acupuncture	Fair	Moderate benefit
Cognitive behavioral therapy	Good	Moderate benefit
Exercise therapy	Good	Moderate benefit
Intensive interdisciplinary rehabilitation	Good	Moderate benefit
Massage therapy	Fair	Moderate benefit
Progressive relaxation	Fair	Moderate benefit

Note: This evidence table was previously reviewed by the HERC when considering coverage for back pain. The back pain interventions summarized above are abstracted from Chou 2007 and may not be directly comparable to the same treatment summarized by HERC staff above for chronic pain conditions

Evidence for Non-opioid Pharmacologic Therapy

Pharmacy and Therapeutics (P&T) Committee review of non-opioid pharmacologic interventions for fibromyalgia

Note: Chronic pain was too undefined a condition for P&T to conduct a meaningful literature review on the broader topic

- There is no moderate or high strength evidence for any pharmacological treatment compared to placebo or other therapy. Like many other conditions for chronic pain, evidence supporting benefit of long-term pharmacological treatment for fibromyalgia is limited, efficacy of pharmacotherapy is relatively modest, and clinical trials often document a large placebo response upon evaluation of symptom improvement. Pharmacological interventions with the most evidence of benefit include duloxetine, milnacipran, and pregabalin, but applicability to a broader population is limited.
- There is low strength evidence that milnacipran and duloxetine may improve pain symptoms as evaluated by patient global impression of improvement or change (PGI-I or PGIC) of much or very much improved, 30% improvement in pain, pain intensity, and disability, but have no clinical improvement for pain relief of 50% or more, sleep, fatigue, depression, cognitive disturbances, anxiety or quality of life. The number needed to treat (NNT) for pain improvement ranged from 5-11 depending on the outcome evaluated.
- There is low strength evidence that, compared to placebo, pregabalin may improve outcomes of pain relief of more than 50%, pain relief of more than 30%, and pain improvement as evaluated by a PGIC score of much or very much improved. The estimated NNT varied depending on dose and outcome but ranged from 7 to 22.
- Adverse effects are more common with pregabalin compared to placebo and included somnolence (number needed to harm [NNH] 7), dizziness (NNH 3), weight gain (NNH 18) and peripheral edema (NNH 19; low strength evidence). SNRIs (duloxetine, milnacipran and desvenlafaxine) were associated with an increased incidence of nausea (NNH 6) and somnolence (NNH 20).
- Evidence of benefit or harms for other pharmacological treatments was insufficient.

Update of Evidence for Opioid Therapy

Since the last review by VbBS/HERC in January, several studies were identified by HERC staff as providing high quality evidence regarding opioid therapy for chronic non-cancer pain. Please see Appendix C for detailed summaries of these studies. Briefly, Busse et al (2018) completed a systematic review and meta-analysis of 96 studies (26,196 patients) that found that compared to placebo, opioids were associated with small improvements in pain, physical functioning, and sleep quality; there were no improvements in social functioning, emotional functioning or role functioning. Compared with placebo, opioids were associated with increased vomiting, drowsiness, constipation, dizziness, nausea, dry mouth, and pruritus. Els et al (2018) published a Cochrane review of the harms of intermediate and long-term opioid therapy for chronic non-cancer pain, including 16 reviews. Based on short duration studies, there was a significantly increased risk of experiencing any adverse event with opioids compared to placebo or non-opioid therapy. Specific adverse events included were constipation, dizziness, drowsiness, fatigue, hot flushes, increased sweating, nausea, pruritus, and vomiting; no data was found on other adverse events. Opioids can cause serious adverse events, including death.

According to the CDC, in 2017 prescription opioids were involved in more than 35% of all opioid overdose deaths.

FDA Drug Safety Communication April 9, 2019:

The U.S. Food and Drug Administration (FDA) has received reports of serious harm in patients who are physically dependent on opioid pain medicines suddenly having these medicines discontinued or the dose rapidly decreased. These include serious withdrawal symptoms, uncontrolled pain, psychological distress, and suicide.

According to the FDA, rapid discontinuation can result in uncontrolled pain or withdrawal symptoms. In turn, these symptoms can lead patients to seek other sources of opioid pain medicines, which may be confused with drug-seeking for abuse. Patients may attempt to treat their pain or withdrawal symptoms with illicit opioids, such as heroin, and other substances.

The FDA recommends that health care professionals should not abruptly discontinue opioids in a patient who is physically dependent. When the provider and their patient have agreed to taper the dose of opioid analgesic, it is recommended that they consider a variety of factors, including the dose of the drug, the duration of treatment, the type of pain being treated, and the physical and psychological attributes of the patient. No standard opioid tapering schedule exists that is suitable for all patients. Patient-specific plans should be created to gradually taper the dose of the opioid and ensure ongoing monitoring and support, as needed, to avoid serious withdrawal symptoms, worsening of the patient's pain, or psychological distress.

Full notice available at https://www.fda.gov/media/122935/download.

HERC Staff Evidence Summary: Overall evidence for pharmacologic and non-pharmacologic treatments for certain chronic pain conditions

Of the various non-pharmacologic interventions proposed for the new chronic pain line, only Tai Chi and interdisciplinary rehabilitation resulted in clinically meaningful but small improvements in short-term function. This improvement only continued into the intermediate and long term for interdisciplinary rehabilitation. Tai Chi and possibly massage/PT with myofascial release had clinically meaningful improvement in short-term pain, but this improvement did not continue to the intermediate or long term. The strength of evidence for all these findings is low. Topic experts making up the Chronic Pain Taskforce recommended inclusion of these therapies because, in their experience, these therapies can be helpful for certain patients and have low level of risk. Overall, there was a significantly higher level of evidence that non-pharmacological therapies had a clinically significant impact on back pain (which informed the HERC's 2016 Back Pain Guideline) as compared to the chronic pain conditions under current coverage consideration.

The pharmacologic interventions indicated for fibromyalgia included only 3 medications with low evidence of effectiveness (duloxetine [Cymbalta], milnacipran [Savella], and pregabalin [Lyrica]). All other medications reviewed had insufficient evidence of effectiveness. Non-opioid pharmacologic interventions had evidence of adverse effects, including weight gain, nausea and somnolence. Opioid therapy has no to minimal evidence of long-term clinically significant benefit for chronic pain conditions for improvement of pain function, or role functioning; there is evidence of harms associated with long-term opioid therapy including fatigue, constipation, and nausea. Opioids have also been associated with risks of dependence, overdose, opioid-induced hyperalgesia, and death. There is limited evidence on the benefits or harms of opioid tapering, although early studies indicate that tapering long-term opioid therapy may improve pain, function, and quality of life.

OPTIONS FOR HERC CONSIDERATION:

Note: the HERC can adopt one of these options, a combination of elements of several options, or a completely different option of their own development

Option 1
NO CHANGE

Do not reprioritize chronic pain syndrome, fibromyalgia and related conditions due to lack of evidence of effectiveness of available treatment modalities. Consider readdressing the prioritization of these conditions as part of the 2022 or 2024 Biennial Review after expected forthcoming evidence is available.

Note: if this option is adopted, the HERC will still need to discuss any changes required to the chronic back line opioid guideline (see below)

Rationale: There is limited evidence that the proposed interventions have meaningful clinical impact on fibromyalgia and chronic pain syndrome; these interventions will have costs associated with them. The revised proposal may have the effect of increasing access to opioid medications which have limited evidence for effectiveness for long-term pain treatment for these conditions. The decision regarding reprioritization of certain chronic pain conditions can be delayed until the 2022 or 2024 Biennial Review, to allow this decision to be informed by emerging evidence, including the impacts of the 2016 changes in coverage for back conditions. As noted by AAI, AHRQ is currently undertaking a review of opioid, non-opioid pharmacologic, and non-pharmacologic therapies for treatment of both short term and chronic pain. These studies will provide relevant evidence to inform future proposed policies related to coverage for these chronic pain conditions.

Impact: Making no change in the prioritization of the five chronic pain conditions including fibromyalgia will continue the status quo. As "unfunded" conditions, treatments such as pharmacologic and non-pharmacologic treatments are not intended to be covered for Oregon Health Plan members except when a member has a covered comorbid condition (e.g. arthritis) or has gone through an exceptions process.

Option 2
ADOPT MODIFIED CPTF PROPOSAL INCLUDING NO LONG-TERM OPIOID USE FOR FIBROMYALGIA

Adopt the modified CPTF proposal with minor changes based on January VbBS input

Note: No longer recommended for consideration by HERC staff

Key elements:

- Adds coverage for various pharmacologic and non-pharmacologic treatments for individuals with five specific chronic pain conditions.
- Adds new coverage for opioid medications for four of these specific chronic pain conditions, except under certain circumstances, and not including OHP members with fibromyalgia

- Includes coverage for opioid tapering with a goal of zero for members who do not meet coverage criteria

Rationale: Currently, OHP members with these five chronic pain conditions (and who do not have co-morbid covered conditions) do not have access to any therapies except for pharmacologic agents in circumstances when they are not subject to prior authorization controls. Such medications may include opioids and gabapentin. In the face of the opioid epidemic, alternative non-pharmacologic therapies for these conditions would be covered for OHP members. The Chronic Pain Taskforce recommended these changes based on their expert opinion and experience.

Impact: New coverage will be created for non-pharmacologic and pharmacologic treatments for patients with these specific chronic pain conditions, including new coverage of long-term opioid therapy for these conditions if patients meet certain criteria. This will have cost implications that have initially been estimated by the Actuarial Services Unit to be between $10.8-$17.3 million/year starting in 2020. For patients with fibromyalgia, opioids will continue to not be covered, although an opioid taper for patients with fibromyalgia would be newly covered.

Option 3

ADOPT NEWLY MODIFIED PROPOSAL INCLUDING OPTIONS FOR COVERAGE OF LONG-TERM OPIOIDS

Informed by AAI Report and public input

Key elements:

- Removes details included in prior proposals representative of "practice guideline" type language and replaces with reference to Oregon's statewide opioid prescribing guidelines
- Includes three options for coverage of long-term opioids:
    A. No new starts for fibromyalgia
    B. No new starts for any of the 5 conditions
    C. New long-term opioids for all patients with these five conditions who meet Oregon statewide opioid prescribing guideline criteria
- Updates language related to opioid tapering to ensure focus on individualized approach

Rationale: As in Option #2, this option would allow patients with these five specific chronic pain conditions to have access to various pharmaceutical and non-pharmaceutical therapies which are not currently available to them, including cognitive behavioral therapy, physical therapy, acupuncture, and various mind-body treatments. All three versions include new coverage for short-term opioid therapy for all five chronic pain conditions, including fibromyalgia. In **Option 3A**, there will be no coverage of newly initiated long-term opioid therapy for fibromyalgia based on expert/expert guideline recommendations, but patients already receiving long-term opioid therapy (despite explicit lack of coverage on the Prioritized List) will be "grandfathered" in to coverage. In **Option 3B**, there will be no coverage of newly initiated long-term opioid therapy for any of these five chronic pain conditions due to lack of evidence of benefit and risks of harm, but patients already receiving long-term opioid therapy will be "grandfathered" in to coverage. In **Option 3C**, new coverage for short and long-term opioid therapy would be added for any of the five chronic pain conditions under consideration. This option is

based on the lack of evidence to exclude fibromyalgia for short- or long-term opioid therapy as identified in the AAI report, as well as lack of evidence pertaining to the tapering of opioids for any condition. All three proposals include removal of certain parameters related to opioid tapering, as well as removal of "prescriber guideline language" and instead reference to Oregon statewide prescribing guidelines.

Impact: New coverage will be created for non-pharmacologic and pharmacologic treatments for patients with these specific chronic pain conditions, including new coverage of long-term opioid therapy for these conditions if patients meet certain criteria (depending on the option for long-term opioid coverage adopted). The Actuarial Services Unit has not estimated the cost of this option, but it would presumably be slightly higher due to a subset of patients choosing to use long-term opioid therapy who previously did not qualify for coverage.

If the HERC adopts either option 2 or 3 (or a variation of those options), the following Prioritized List edits are recommended:

a. Create a new line for five chronic pain conditions including fibromyalgia for the 2020 Biennial Review Prioritized List as shown below
b. Adopt a new guideline for this line as shown below
    i. Different versions are shown below for "Option 2" and "Option 3"
c. Determine scoring for this new line
d. Modify line 528 FIBROMYALGIA, CHRONIC FATIGUE SYNDROME AND RELATED CONDITIONS as shown below
    i. Remove all diagnoses other than chronic fatigue syndrome and modify line title
    ii. Rescore this line if necessary
e. Modify GUIDELINE NOTE 56, NON-INTERVENTIONAL TREATMENTS FOR CONDITIONS OF THE BACK AND SPINE as shown below
    i. Matches changes in the new chronic pain conditions guideline
    ii. Removes obsolete table
f. Modify GUIDELINE NOTE 92, ACUPUNCTURE as shown below
    i. Adds the new chronic pain line to the guideline
g. Delete GUIDELINE NOTE 135, FIBROMYALGIA
    i. Components are all incorporated into the new guideline

LINE: XXX
CONDITION: FIBROMYALGIA, CHRONIC PAIN SYNDROME AND RELATED CONDITIONS
TREATMENT: LIMITED PHYSICAL MODALITIES, COGNITIVE BEHAVIORAL THERAPY, MEDICAL THERAPY
ICD-10: G89.21 (Chronic pain due to trauma), G89.28 (Other chronic postprocedural pain), G89.29 (Other chronic pain), G89.4 (Chronic pain syndrome), M79.7 (fibromyalgia)
CPT: 90785, 90832-90840, 90853 (psychotherapy—for CBT and ACT), 96150-96155 (Health and behavior assessment and intervention), 97110-97124, 97140-97168, 97530, 97535 (PT/OT), 97810-97814 (acupuncture), 98966-98969, 99051, 99060,99070,99078,99201-99215,99281-99285,99304-99337,99340-99404,99408-99449,99487-99490,99495,99496,99605-99607 (medical office visits, including ER and SNF)
HCPCS: G0157-G0160 (PT/OT assistant), G0396-G0397 (alcohol and substance abuse screening), G0463-G0467,G0469,G0470 (FQHC care), G0490, G0511-G0513 (RFQHC care), G0514 (prolonged office visit)

Proposed Prioritized List Guideline Note edits related to OPTION #2
Note: This includes modifications as requested by the VbBS in January 2019

GUIDELINE NOTE XXX, TREATMENT OF FIBROMYALGIA, CHRONIC PAIN SYNDROME AND RELATED CONDITIONS

Line XXX

Chronic pain syndrome (ICD-10 G89.4), chronic pain due to trauma (ICD-10 G89.21), other chronic postprocedural pain (ICD-10 G89.28), other chronic pain (ICD-10 G89.29), and fibromyalgia (ICD-10 M79.7) are included on line XXX when symptoms have been present for at least 3 months.

The following treatments are included on line XXX:

- Office evaluation, consultation and education.
    - Pain education, if done, should include but not be limited to sleep, nutrition, stress reduction/mood, exercise, and knowledge of pain as a biopsychosocial phenomenon. All providers with primary responsibility for managing fibromyalgia, chronic pain syndrome and related conditions ~~patients~~ should be trained in pain science (e.g., a contemporary understanding of the central and peripheral nervous system in chronic pain), motivational interviewing, culturally sensitive care, and trauma informed care. Care should be multidisciplinary and focus on active therapies.
- Cognitive behavioral therapy (CBT). The necessity for CBT should be re-evaluated every 90 days and coverage will only be continued if there is documented evidence of decreasing depression or anxiety symptomatology, improved ability to work/function, increased self-efficacy, or other clinically significant, objective improvement.
- The following therapies, when available, may be provided: adaptive and restorative yoga, Tai Chi, mindfulness training, massage, supervised exercise therapy (land based and aquatic), intensive interdisciplinary rehabilitation. HCPCS S9451 is only included on Line XXX for the provision of yoga, Tai Chi, or supervised exercise therapy.
- A total of 30 visits per year of any combination of the following therapies when available and medically appropriate. These therapies are only included on these lines if provided by a provider licensed to provide the therapy and when there is documentation of measurable clinically significant progress toward the therapy plan of care goals and objectives using evidence-based objective tools. Once the pre-determined goals of care have been achieved, an additional two visits may be authorized for maintenance therapy to maintain these improvements. These 30 visits count toward the visit totals in GUIDELINE NOTE 56 NON-INTERVENTIONAL TREATMENTS FOR CONDITIONS OF THE BACK AND SPINE if the patient has comorbid back or spine conditions.
    1) Rehabilitative therapy (physical and/or occupational therapy), if provided according to Guideline Note 6 REHABILITATIVE AND HABILITATIVE THERAPIES. Rehabilitation services provided under this guideline also count towards visit totals in Guideline Note 6. CPT 97124 is included in this category.
    2) Acupuncture

Non-opioid medications are only included on line XXX if all of the following apply:

1) The patient is also being treated with active therapy (e.g., physical therapy, CBT) or is continuing maintenance of self-management strategies learned from such therapy.
2) The benefit of non-opioid medication is re-evaluated at least every 90 days and medications are only continued if there is documented evidence of initial improvement of function of at least fifteen percent as compared to baseline based on a validated tool (e.g., "Pain average, interference with Enjoyment of life, and interference with General activity" (PEG) Assessment Scale, Oswestry, SF-MPQ, MSPQ), and function is maintained thereafter. Less frequent monitoring may be appropriate for certain medications after safety and efficacy are established.

Short-term opioid therapy (<90 days) is included on these lines only for chronic pain syndrome (ICD-10 G89.4), chronic pain due to trauma (ICD-10 G89.21), other chronic postprocedural pain (ICD-10 G89.28), and other chronic pain (ICD-10 G89.29), and only when prescribed in alignment with the Oregon Acute Opioid Prescribing Guideline (2018 version)
https://www.oregon.gov/oha/PH/PREVENTIONWELLNESS/SUBSTANCEUSE/OPIOIDS/Documents/Acute-Prescribing-Guidelines.pdf

and the Oregon Chronic Opioid Prescribing Guideline (2017-2018 version) https://www.oregon.gov/oha/PH/PREVENTIONWELLNESS/SUBSTANCEUSE/OPIOIDS/Documents/Chronic-Opioid-Prescribing-Guidelines.pdf

Long-term opioid therapy (>90 days) is included on these lines only for chronic pain syndrome (ICD-10 G89.4), chronic pain due to trauma (ICD-10 G89.21), other chronic postprocedural pain (ICD-10 G89.28), and other chronic pain (ICD-10 G89.29) when all of the following criteria are met:

- In alignment with the Oregon Opioid Prescribing Guideline (2017-2018 version) https://www.oregon.gov/oha/PH/PREVENTIONWELLNESS/SUBSTANCEUSE/OPIOIDS/Documents/taskforce/oregon-opioid-prescribing-guidelines.pdf
    - No illicit drug use or active substance use disorder (excluding tobacco)
    - The patient has been prescribed the patient pain education module through OPMC when it becomes available
    - Verification that the patient is not high risk for opioid misuse or abuse
        - Appropriate risk assessment has been performed [strike from previous CPTF recommendation as tool is not evidence based]
        - PDMP checked at least annually and shows no aberrant behavior
        - Urine drug testing is performed at least once per year and is appropriate
- Prescribing criteria
    - Initial functional improvement has been documented of at least 30%, and function is maintained throughout the prescribing period
    - When prescribed with nonpharmacologic treatment options for managing pain
    - Careful reassessment of the evidence of individual benefits and risks should be undertaken for dosages > 50 MED. Dosages >90 MED should be avoided or carefully justified. When dosages > 50 MED are prescribed, naloxone should also be prescribed to the patient.
    - Patient and provider have assessed the relative risks and benefits of therapy and agree benefits outweigh risks, and have completed a material risk notice https://www.oregon.gov/omb/OMBForms1/material-risk-notice.pdf
    - No additional opioids are prescribed for flares of the chronic pain condition, although opioids may be prescribed separately for other acute injuries or surgeries as clinically appropriate
    - Comorbid mental health disorders are appropriately addressed
    - ~~No concurrent prescribing of benzodiazepines without extenuating circumstances~~ [strike from previous CPTF recommendation as this is included in the Oregon Opioid Prescribing Guideline]
- ~~Prescriber criteria~~
    - ~~Prescriber has updated opioid prescribing CME and ideally has completed the Oregon Pain Management Commission (OPMC) pain module~~
    - ~~[strike this language from previous recommendation as it would not be implementable]~~

~~Opioid tapering for fibromyalgia and patients failing to meet the opioid prescribing criteria above:~~
Opioid therapy is not included on this line for the following conditions/situations due to the evidence for harm:

- When prescribed for fibromyalgia

- For patients who fail to meet the guideline requirements regarding opioids above who have chronic pain syndrome, chronic pain due to trauma, other chronic postprocedural pain, and other chronic pain conditions included on this line

If a patient is already receiving long-term opioid therapy for these conditions/situations, then tapering is indicated. Opioid tapering should be done on an individualized basis which includes a taper goal of zero. Tapering should be unidirectional with a shared goal set by the patient and provider, generally with a 5-10% decrease monthly, and can be paused or slowed if the prescriber believes this is medically appropriate based on the patient's overall status. Taper plans should include nonpharmacological treatment strategies for managing the patient's pain. During the taper, behavioral health conditions need to be regularly assessed and appropriately managed. In some situations (e.g., in the setting of active substance use disorder, history of opioid overdose, aberrant behavior), more rapid tapering or transition to medication assisted treatment may be appropriate and should be directed by the prescribing provider. If a patient has developed opioid use disorder, treatment is included on Line 4 SUBSTANCE USE DISORDER**.**

Proposed Prioritized List Guideline Note edits related to OPTION #3

GUIDELINE NOTE XXX, TREATMENT OF FIBROMYALGIA, CHRONIC PAIN SYNDROME AND RELATED CONDITIONS

Line XXX

Chronic pain syndrome (ICD-10 G89.4), chronic pain due to trauma (ICD-10 G89.21), other chronic postprocedural pain (ICD-10 G89.28), other chronic pain (ICD-10 G89.29), and fibromyalgia (ICD-10 M79.7) are included on line XXX when symptoms have been present for at least 3 months.

The following treatments are included on line XXX:

- Office evaluation, consultation and education.
    - Pain education, if done, should include but not be limited to sleep, nutrition, stress reduction/mood, exercise, and knowledge of pain as a biopsychosocial phenomenon. All providers with primary responsibility for managing fibromyalgia, chronic pain syndrome and related conditions should be trained in pain science (e.g., a contemporary understanding of the central and peripheral nervous system in chronic pain), motivational interviewing, culturally sensitive care, and trauma informed care. Care should be multidisciplinary and focus on active therapies.
- Cognitive behavioral therapy (CBT). The necessity for CBT should be re-evaluated every 90 days and coverage will only be continued if there is documented evidence of decreasing depression or anxiety symptomatology, improved ability to work/function, increased self-efficacy, or other clinically significant, objective improvement.
- The following therapies, when available, may be provided: adaptive and restorative yoga, Tai Chi, mindfulness training, massage, supervised exercise therapy (land based and aquatic), intensive interdisciplinary rehabilitation. HCPCS S9451 is only included on Line XXX for the provision of yoga, Tai Chi, or supervised exercise therapy.
- A total of 30 visits per year of any combination of the following therapies when available and medically appropriate. These therapies are only included on these lines if provided by a provider licensed to provide the therapy and when there is documentation of measurable clinically significant progress toward the therapy plan of care goals and objectives using evidence-based

objective tools. Once the pre-determined goals of care have been achieved, an additional two visits may be authorized for maintenance therapy to maintain these improvements. These 30 visits count toward the visit totals in GUIDELINE NOTE 56 NON-INTERVENTIONAL TREATMENTS FOR CONDITIONS OF THE BACK AND SPINE if the patient has comorbid back or spine conditions.

3) Rehabilitative therapy (physical and/or occupational therapy), if provided according to Guideline Note 6 REHABILITATIVE AND HABILITATIVE THERAPIES. Rehabilitation services provided under this guideline also count towards visit totals in Guideline Note 6. CPT 97124 is included in this category.
4) Acupuncture

Non-opioid medications are only included on line XXX if all of the following apply:

1) The patient is also being treated with active therapy (e.g., physical therapy, CBT) or is continuing maintenance of self-management strategies learned from such therapy.
2) The benefit of non-opioid medication is re-evaluated at least every 90 days and medications are only continued if there is documented evidence of initial improvement of function of at least fifteen percent as compared to baseline based on a validated tool (e.g., "Pain average, interference with Enjoyment of life, and interference with General activity" (PEG) Assessment Scale, Oswestry, SF-MPQ, MSPQ), and function is maintained thereafter. Less frequent monitoring may be appropriate for certain medications after safety and efficacy are established.

Short-term opioid therapy (<90 days) is included on these lines only when prescribed in alignment with the Oregon Acute Opioid Prescribing Guideline (2018 version) https://www.oregon.gov/oha/PH/PREVENTIONWELLNESS/SUBSTANCEUSE/OPIOIDS/Documents/Acute-Prescribing-Guidelines.pdf and the Oregon Chronic Opioid Prescribing Guideline (2017-2018 version) https://www.oregon.gov/oha/PH/PREVENTIONWELLNESS/SUBSTANCEUSE/OPIOIDS/Documents/Chronic-Opioid-Prescribing-Guidelines.pdf.

Three options for long-term opioids:

A. No new starts for fibromyalgia, coverage for other conditions
B. No new starts for any of the 5 conditions
C. New long-term opioid coverage for all patients with these five conditions who meet the Oregon statewide opioid prescribing guideline criteria

Long-term opioid therapy:

Option 3A: *No new starts of long-term opioid therapy for fibromyalgia (based on expert opinion and expert guidelines), continues long-term coverage for the other 4 chronic pain conditions and "grandfathered" fibromyalgia patients*

Long-term opioid therapy (>90 days) is included on these lines only for chronic pain syndrome (ICD-10 G89.4), chronic pain due to trauma (ICD-10 G89.21), other chronic postprocedural pain (ICD-10 G89.28), and other chronic pain (ICD-10 G89.29) and for patients currently receiving long-term opioid therapy for fibromyalgia (ICD-10 M79.7) when prescribed In alignment with the Oregon Opioid Prescribing Guideline (2017-2018 version)

https://www.oregon.gov/oha/PH/PREVENTIONWELLNESS/SUBSTANCEUSE/OPIOIDS/Documents/taskforce/oregon-opioid-prescribing-guidelines.pdf

Opioid therapy is not included on this line for the following conditions/situations:

- When long-term opioid therapy is newly prescribed for fibromyalgia
- For patients who fail to meet the guideline requirements regarding opioids above who have chronic pain syndrome, chronic pain due to trauma, other chronic postprocedural pain, and other chronic pain conditions included on this line

If a patient is receiving long-term opioid therapy not meeting the criteria above, or the patient's status falls out of alignment with the Oregon Opioid Prescribing Guidelines, then tapering is indicated. Opioid tapering should be done on an individualized basis with a shared goal set by the patient and provider based on the patient's overall status. Taper plans should include nonpharmacological treatment strategies for managing the patient's pain. During the taper, behavioral health conditions need to be regularly assessed and appropriately managed. In some situations (e.g., in the setting of active substance use disorder, history of opioid overdose, aberrant behavior), more rapid tapering or transition to medication assisted treatment may be appropriate and should be directed by the prescribing provider. If a patient has developed opioid use disorder, treatment is included on Line 4 SUBSTANCE USE DISORDER**.**

Option 3B: *No new long-term opioids for any of the 5 conditions (based on expert opinion and evidence of harm/lack of evidence of clinically-significant benefit). Allow continued prescribing ("grandfathering") for patients already on long-term opioid therapy.*

For patients currently receiving long-term opioid therapy (>90 days) for conditions included on this line, continued opioid therapy is included on these lines when prescribed In alignment with the Oregon Opioid Prescribing Guideline (2017-2018 version)
https://www.oregon.gov/oha/PH/PREVENTIONWELLNESS/SUBSTANCEUSE/OPIOIDS/Documents/taskforce/oregon-opioid-prescribing-guidelines.pdf

Opioid therapy is not included on this line for the following conditions/situations:

- When long-term opioid therapy is newly prescribed for chronic pain syndrome (ICD-10 G89.4), chronic pain due to trauma (ICD-10 G89.21), other chronic postprocedural pain (ICD-10 G89.28), other chronic pain (ICD-10 G89.29) and fibromyalgia (ICD-10 M79.7)
- For patients who fail to meet the guideline requirements regarding opioids above who have chronic pain syndrome, chronic pain due to trauma, other chronic postprocedural pain, and other chronic pain conditions included on this line

If a patient is receiving long-term opioid therapy not meeting the criteria above, or the patient's status falls out of alignment with the Oregon Opioid Prescribing Guidelines, then tapering is indicated. Opioid tapering should be done on an individualized basis with a shared goal set by the patient and provider based on the patient's overall status. Taper plans should include nonpharmacological treatment strategies for managing the patient's pain. During the taper, behavioral health conditions need to be regularly assessed and appropriately managed. In some situations (e.g., in the setting of active substance use disorder, history of opioid overdose, aberrant behavior), more rapid tapering or transition to medication assisted treatment may be appropriate and should be directed by the prescribing

provider. If a patient has developed opioid use disorder, treatment is included on Line 4 SUBSTANCE USE DISORDER**.**

Option 3C: *Allow new and continued long-term opioid coverage for all five chronic pain conditions*

Long-term opioid therapy is included on these lines when prescribed In alignment with the Oregon Opioid Prescribing Guideline (2017-2018 version)
https://www.oregon.gov/oha/PH/PREVENTIONWELLNESS/SUBSTANCEUSE/OPIOIDS/Documents/taskforce/oregon-opioid-prescribing-guidelines.pdf

Line Scoring if Reprioritized

	Line 401	Line XXX	Line 528
Category (Non-Fatal Condition)	7	7	7
Healthy Life (0-10)	5	TBD	4
Suffering (0-5)	3	TBD	3
Population effects (0-5)	0	0	0
Vulnerable population (0-5)	0	0	0
Tertiary prevention (0-5)	2	TBD	0
Effectiveness (0-5)	3	TBD	1
Need for service (0-1)	0.8	TBD	0.8
Net cost	2	2	2
Score	432	TBD	112
Approximate line	401	TBD	528

Line 401 CONDITIONS OF THE BACK AND SPINE
Line XXX FIBROMYALGIA, CHRONIC PAIN SYNDROME AND RELATED CONDITIONS [proposed]
Line 528 FIBROMYALGIA, CHRONIC FATIGUE SYNDROME, AND RELATED DISORDERS [current]

Scoring comparators

Healthy Life (0-10)

- Score = 5
    - 356 RHEUMATOID ARTHRITIS, OSTEOARTHRITIS AND ASEPTIC NECROSIS OF BONE/JOINT REPLACEMENT
    - 361 SCOLIOSIS
    - 395 ENDOMETRIOSIS AND ADENOMYOSIS
    - 401 CONDITIONS OF THE BACK AND SPINE/MEDICAL THERAPY
    - 526 DISORDERS OF FUNCTION OF STOMACH AND OTHER FUNCTIONAL DIGESTIVE DISORDERS
- Score = 4
    - 409 MIGRAINE HEADACHES
    - 421 LYMPHEDEMA
    - 431 PERSISTENT DEPRESSIVE DISORDER
    - 527 CONDITIONS OF THE BACK AND SPINE WITHOUT URGENT SURGICAL INDICATIONS/SURGERY
    - 529 CHRONIC PELVIC INFLAMMATORY DISEASE, PELVIC PAIN SYNDROME, DYSPAREUNIA

Tertiary prevention (0-5)

- Score = 2
    - 368 STREPTOCOCCAL SORE THROAT AND SCARLET FEVER; VINCENT'S DISEASE; ULCER OF TONSIL; UNILATERAL HYPERTROPHY OF TONSIL
    - 387 ANOGENITAL VIRAL WARTS
    - 395 ENDOMETRIOSIS AND ADENOMYOSIS
    - 401 CONDITIONS OF THE BACK AND SPINE/MEDICAL THERAPY
    - 420 MENSTRUAL BLEEDING DISORDERS
    - 421 LYMPHEDEMA

- Score = 1
    - 376 DISRUPTIONS OF THE LIGAMENTS AND TENDONS OF THE ARMS AND LEGS, EXCLUDING THE KNEE, RESULTING IN SIGNIFICANT INJURY/IMPAIRMENT
    - 413 OVERANXIOUS DISORDER; GENERALIZED ANXIETY DISORDER; ANXIETY DISORDER, UNSPECIFIED
    - 431 PERSISTENT DEPRESSIVE DISORDER
    - 510 VERTIGINOUS SYNDROMES AND OTHER DISORDERS OF VESTIBULAR SYSTEM
    - 534 PERIPHERAL NERVE DISORDERS/SURGERY
- Score = 0
    - 356 RHEUMATOID ARTHRITIS, OSTEOARTHRITIS AND ASEPTIC NECROSIS OF BONE/JOINT REPLACEMENT (surgical line)
    - 409 MIGRAINE HEADACHES
    - 461 OSTEOARTHRITIS AND ALLIED DISORDERS
    - 507 PERIPHERAL NERVE DISORDERS
    - 522 UNCOMPLICATED HERNIA AND VENTRAL HERNIA (OTHER THAN INGUINAL HERNIA IN CHILDREN AGE 18 AND UNDER OR DIAPHRAGMATIC HERNIA)
    - 538 TENSION HEADACHES

Effectiveness (0-5)

- Score = 3
    - 395 ENDOMETRIOSIS AND ADENOMYOSIS
    - 401 CONDITIONS OF THE BACK AND SPINE/MEDICAL THERAPY
    - 413 OVERANXIOUS DISORDER; GENERALIZED ANXIETY DISORDER; ANXIETY DISORDER, UNSPECIFIED
    - 461 OSTEOARTHRITIS AND ALLIED DISORDERS
    - 494 RAYNAUD'S SYNDROME
    - 538 TENSION HEADACHES
    - 549 SOMATIC SYMPTOMS AND RELATED DISORDERS
- Score = 2
    - 431 PERSISTENT DEPRESSIVE DISORDER
    - 507 PERIPHERAL NERVE DISORDERS
    - 510 VERTIGINOUS SYNDROMES AND OTHER DISORDERS OF VESTIBULAR SYSTEM
    - 513 CHRONIC PROSTATITIS, OTHER DISORDERS OF PROSTATE
- Score = 1
    - 489 SPASTIC DIPLEGIA/RHIZOTOMY
    - 529 CHRONIC PELVIC INFLAMMATORY DISEASE, PELVIC PAIN SYNDROME, DYSPAREUNIA
    - 534 PERIPHERAL NERVE DISORDERS/SURGERY
    - 550 OTHER NONINFECTIOUS GASTROENTERITIS AND COLITIS

Reprioritization of Certain Chronic Pain Conditions
May 2019

Rescoring remainder of line 528

Line:	528
Condition:	~~FIBROMYALGIA,~~ CHRONIC FATIGUE SYNDROME~~, AND RELATED DISORDERS~~ (See Guideline Notes 64,65~~,135~~)
Treatment:	MEDICAL THERAPY
ICD-10:	~~G89.21,G89.28-G89.29,G89.4,M79.7,~~R53.82
CPT:	90785,90832-90840,90846-90853,93792,93793,98966-98969,99051,99060,99070,99078, 99201-99215,99281-99285,99341-99378,99381-99404,99408-99449,99487-99490,99495-99498,99605-99607
HCPCS:	G0248-G0250,G0396,G0397,G0463-G0467,G0490,G0511,G0513,G0514

Maintain the 2014 prioritization for Chronic Fatigue Syndrome line as shown below

	Current Line 528	Chronic Fatigue Syndrome
Category (Non-Fatal Condition)	7	7
Healthy Life Years (0-10)	4	4
Suffering (0-5)	3	3
Population effects (0-5)	0	0
Vulnerable population (0-5)	0	0
Tertiary prevention (0-5)	0	0
Effectiveness (0-5)	1	1
Need for service (0-1)	0.8	0.8
Net cost	2	2
Score	112	112
Approximate line	528	528

Accompanying guideline note changes

GUIDELINE NOTE 56, NON-INTERVENTIONAL TREATMENTS FOR CONDITIONS OF THE BACK AND SPINE

Lines 361,401

Patients seeking care for back pain should be assessed for potentially serious conditions ("red flag" symptoms requiring immediate diagnostic testing), as defined in Diagnostic Guideline D4. Patients lacking red flag symptoms should be assessed using a validated assessment tool (e.g. STarT Back Assessment Tool) in order to determine their risk level for poor functional prognosis based on psychosocial indicators.
For patients who are determined to be low risk on the assessment tool, the following services are included on these lines:

- Office evaluation and education,
- Up to four total visits, consisting of the following treatments: OMT/CMT, acupuncture, and PT/OT. Massage, if available, may be provided as part of these four total visits.
- First line medications: NSAIDs, acetaminophen, and/or muscle relaxers. Opioids may be considered as a second line treatment, subject to the limitations on coverage of opioids in Guideline Note 60 OPIOIDS FOR CONDITIONS OF THE BACK AND SPINE. ~~See evidence table.~~

For patients who are determined to be medium- or high risk on the validated assessment tool, as well as patients undergoing opioid tapers as in Guideline Note 60 OPIOIDS FOR CONDITIONS OF THE BACK AND SPINE, the following treatments are included on these lines:

- Office evaluation, consultation and education
- Cognitive behavioral therapy (CBT). The necessity for CBT should be re-evaluated every 90 days and coverage will only be continued if there is documented evidence of decreasing depression or anxiety symptomatology, improved ability to work/function, increased self-efficacy, or other clinically significant, objective improvement.
- Prescription and over-the-counter medications; opioid medications subject to the limitations on coverage of opioids in Guideline Note 60 OPIOIDS FOR CONDITIONS OF THE BACK AND SPINE. ~~See evidence table.~~
- The following evidence-based therapies, when available, may be provided: yoga, massage, supervised exercise therapy, intensive interdisciplinary rehabilitation. HCPCS S9451 is only included on Line 401 for the provision of yoga or supervised exercise therapy.
- A total of 30 visits per year of any combination of the following evidence-based therapies when available and medically appropriate. These therapies are only included on these lines if provided by a provider licensed to provide the therapy and when there is documentation of measurable clinically significant progress toward the therapy plan of care goals and objectives using evidence based objective tools (e.g. Oswestry, Neck Disability Index, SF-MPQ, and MSPQ). These 30 visits count toward the visit totals in GUIDELINE NOTE XXX TREATMENT OF FIBROMYALGIA, CHRONIC PAIN SYNDROME AND RELATED CONDITIONS if the patient has one or more of these comorbid chronic pain conditions.
    5) Rehabilitative therapy (physical and/or occupational therapy), if provided according to Guideline Note 6 REHABILITATIVE AND HABILITATIVE THERAPIES. Rehabilitation services provided under this guideline also count towards visit totals in Guideline Note 6. CPT 97124 is included in this category.
    6) Chiropractic or osteopathic manipulation
    7) Acupuncture

Mechanical traction (CPT 97012) is not included on these lines, due to evidence of lack of effectiveness for treatment of back and neck conditions.

The development of this guideline note was informed by HERC coverage guidances on Low Back Pain Non-Pharmacologic, Non-Invasive Intervention, Low Back Pain, Pharmacological and Herbal Therapies. See http://www.oregon.gov/oha/HPA/CSI-HERC/Pages/Evidence-based-Reports.aspx.

[delete the table below]

~~**Evidence Table of Effective Treatments for the Management of Low Back Pain**~~

Intervention Category*	Intervention	Acute < 4 Weeks	Subacute & Chronic > 4 Weeks
Self-care	Advice to remain active	•	•
	Books, handout	•	•
	Application of superficial heat	•	
Nonpharmacologic therapy	Spinal manipulation	•	•
	Exercise therapy		•
	Massage		•
	Acupuncture		•
	Yoga		•
	Cognitive-behavioral therapy		•
	Progressive relaxation		•
Pharmacologic therapy (Carefully consider risks/harms)	Acetaminophen	•	•
	NSAIDs	•(▲)	•(▲)
	Skeletal muscle relaxants	•	
	Antidepressants (TCA)		•
	*Benzodiazepines***	•(▲)	•(▲)
	*Tramadol, opioids***	•(▲)	•(▲)
Interdisciplinary therapy	Intensive interdisciplinary rehabilitation		•

- Interventions supported by grade B evidence (at least fair-quality evidence of moderate benefit, or small benefit but no significant harms, costs, or burdens). No intervention was supported by grade "A" evidence (good-quality evidence of substantial benefit).

▲ *Carries greater risk of harms than other agents in table.*

NSAIDs = nonsteroidal anti-inflammatory drugs; TCA = tricyclic antidepressants.

*These are general categories only. Individual care plans need to be developed on a case by case basis. For more detailed information please see: http://www.annals.org/content/147/7/478.full.pdf

**Associated with significant risks related to potential for abuse, addiction and tolerance. This evidence evaluates effectiveness of these agents with relatively short term use studies. Chronic use of these agents may result in significant harms.

GUIDELINE NOTE 60, OPIOIDS FOR CONDITIONS OF THE BACK AND SPINE

Lines 346,361,401,527

Opioid medications are only included on these lines under the following criteria:

For acute injury, ~~acute flare of chronic pain,~~ or after surgery:

1) During the first 6 weeks opioid treatment is included on these lines ONLY:
   a) When each prescription is limited to 7 days of treatment, AND
   b) For short acting opioids only, AND
   c) When one or more alternative first line pharmacologic therapies such as NSAIDs, acetaminophen, and muscle relaxers have been tried and found not effective or are contraindicated, AND
   d) When prescribed with a plan to keep active (home or prescribed exercise regime) and with consideration of additional therapies such as spinal manipulation, physical therapy, yoga, or acupuncture, AND
   e) There is documented verification that the patient is not high risk for opioid misuse or abuse.
2) Treatment with opioids after 6 weeks, up to 90 days after the initial injury/~~flare/~~surgery is included on these lines ONLY:
   a) With documented evidence of improvement of function of at least thirty percent as compared to baseline based on a validated tools (e.g. Pain average, interference with Enjoyment of life, and interference with General activity" (PEG) Assessment Scale, Oswestry, Neck Disability Index, SF-MPQ, and MSPQ).
   b) When prescribed in conjunction with therapies such as spinal manipulation, physical therapy, yoga, or acupuncture.
   c) With verification that the patient is not high risk for opioid misuse or abuse. Such verification may involve
      i) Documented verification from the state's prescription monitoring program database that the controlled substance history is consistent with the prescribing record
      ii) Use of a validated screening instrument to verify the absence of a current substance use disorder (excluding nicotine) or a history of prior opioid misuse or abuse
      iii) Administration of a baseline urine drug test to verify the absence of illicit drugs and non-prescribed opioids.
   d) Each prescription must be limited to 7 days of treatment and for short acting opioids only
3) Long-term opioid treatment (>90 days) after the initial injury~~/flare/~~surgery is not included on these lines except for the taper process described below.

~~Transitional coverage for patients on long-term opioid therapy as of July 1, 2016:~~
~~For patients on covered chronic opioid therapy as of July 1, 2016, opioid medication is included on these lines only from July 1, 2016 to December 31, 2016. During the period from January 1, 2017 to December 31, 2017, continued coverage of opioid medications requires an individual treatment plan developed by January 1, 2017 which includes a taper with an end to opioid therapy no later than January 1, 2018 and include a taper goal to zero. Tapering should be unidirectional, generally with a 5-10% decrease monthly and can be paused or slowed if the prescriber believes this is medically appropriate. Taper plans must include nonpharmacological treatment strategies for managing the patient's pain based on Guideline Note 56 NON-INTERVENTIONAL TREATMENTS FOR CONDITIONS OF THE BACK AND SPINE. If a~~

~~patient has developed dependence and/or addiction related to their opioids, treatment is available on Line 4 SUBSTANCE USE DISORDER.~~

Transitional coverage for patients on long-term opioid therapy:
For patients receiving long-term opioid therapy (>90 days) for conditions of the back and spine, continued coverage of opioid medications requires an individual treatment plan which includes a taper plan. Opioid tapering should be done on an individualized basis with a shared goal set by the patient and provider based on the patient's overall status. Taper plans should include nonpharmacological treatment strategies for managing the patient's pain. During the taper, behavioral health conditions need to be regularly assessed and appropriately managed. In some situations (e.g., in the setting of active substance use disorder, history of opioid overdose, aberrant behavior), more rapid tapering or transition to medication assisted treatment may be appropriate and should be directed by the prescribing provider. If a patient has developed opioid use disorder, treatment is included on Line 4 SUBSTANCE USE DISORDER.

GUIDELINE NOTE 92, ACUPUNCTURE

Lines 1,5,202,361,401,409,461,538

Inclusion of acupuncture (CPT 97810-97814) on the Prioritized List has the following limitations:

Line 1 PREGNANCY

Acupuncture pairs on Line 1 for the following conditions and codes.

Hyperemesis gravidarum

ICD-10-CM: O21.0, O21.1

Acupuncture pairs with hyperemesis gravidarum when a diagnosis is made by the maternity care provider and referred for acupuncture treatment for up to 12 sessions of acupressure/acupuncture per pregnancy.

Breech presentation

ICD-10-CM: O32.1

Acupuncture (and moxibustion) is paired with breech presentation when a referral with a diagnosis of breech presentation is made by the maternity care provider, the patient is between 33 and 38 weeks gestation, for up to 6 sessions per pregnancy.

Back and pelvic pain of pregnancy

ICD-10-CM: O99.89

Acupuncture is paired with back and pelvic pain of pregnancy when referred by maternity care provider/primary care provider for up to 12 sessions per pregnancy.

Line 5 TOBACCO DEPENDENCE

Acupuncture is included on this line for a maximum of 12 sessions per quit attempt up to two quit attempts per year; additional sessions may be authorized if medically appropriate.

Line 202 CHRONIC ORGANIC MENTAL DISORDERS INCLUDING DEMENTIAS

Acupuncture is paired with the treatment of post-stroke depression only. Treatments may be billed to a maximum of 30 minutes face-to-face time and limited to 12 total sessions per year, with documentation of meaningful improvement; patients may have additional visits authorized beyond these limits if medically appropriate.

Line 361 SCOLIOSIS

Acupuncture is included on this line with visit limitations as in Guideline Note 56 NON-INTERVENTIONAL TREATMENTS FOR CONDITIONS OF THE BACK AND SPINE.

Line 401 CONDITIONS OF THE BACK AND SPINE

Acupuncture is included on this line with visit limitations as in Guideline Note 56 NON-INTERVENTIONAL TREATMENTS FOR CONDITIONS OF THE BACK AND SPINE.

Line 409 MIGRAINE HEADACHES

Acupuncture pairs on Line 409 for migraine (ICD-10-CM G43.0, G43.1, G43.5, G43.7, G43.8, G43.9), for up to 12 sessions per year.

Line XXX FIBROMYAGIA, CHRONIC PAIN SYNDROME AND RELATED CONDITIONS

Acupuncture is included on this line with visit limitations as in Guideline Note XXX TREATMENT OF FIBROMYAGIA, CHRONIC PAIN SYNDROME AND RELATED CONDITIONS

Line 461 OSTEOARTHRITIS AND ALLIED DISORDERS

Acupuncture pairs on Line 461 for osteoarthritis of the knee only (ICD-10-CM M17), for up to 12 sessions per year.

*Line 538 TENSION HEADACHES

Acupuncture is included on Line 538 for treatment of tension headaches (ICD-10-CM G44.2), for up to 12 sessions per year.

The development of this guideline note was informed by a HERC coverage guidance. See http://www.oregon.gov/oha/HPA/CSI-HERC/Pages/Evidence-based-Reports.aspx.

*Below the current funding line

~~**GUIDELINE NOTE 135, FIBROMYALGIA**~~

~~*Line 528*~~

~~Fibromyalgia (ICD-10-CM M79.7) treatment should consist of a multi-modal approach, which should include two of more of the following:~~

~~A) medications other than opioids~~
~~B) exercise advice/programs~~
~~C) cognitive behavioral therapy.~~

~~Care should be provided in the primary care setting. Referrals to specialists are generally not required. Use of opioids should be avoided due to evidence of harm in this condition~~

Appendix A
Previous Evidence Reviews for Fibromyalgia and Opioids

2010 Biennial Review
Fibromyalgia was discussed at the May 2008 HOSC meeting; there was no specific discussion of opioids although the articles noted in the 2013 evidence review below were also included in the 2008 evidence review and included lack of evidence of effectiveness of opioids for this condition. The HOSC/HSC decision was to not reprioritize fibromyalgia due to lack of evidence of effective treatments.

2014 Biennial Review
Fibromyalgia was proposed for reprioritization to a funded line by a group of providers as part of the 2014 Biennial Review. This topic was discussed at three meetings in 2013 and 2014.

1) 2013 evidence review
    a. **EULAR 07** (European League Against Rheumatism) systematic review and treatment guidelines [reviewed in 2008]
        i. Simple analgesics such as paracetamol and other weak opioids can also be considered in the treatment of fibromyalgia. Corticosteroids and strong opioids are not recommended. SOE: D
        ii. See update from 2016
    b. **Goldenberg 04**: Literature review and treatment guidelines
        i. No Evidence for Efficacy
            1. Opioids, corticosteroids, nonsteroidal anti-inflammatory drugs, benzodiazepine and nonbenzodiazepene hypnotics, melatonin, calcitonin, thyroid hormone, guaifenesin, dehydroepiandrosterone, magnesium.

A further extensive evidence review done in 2013 and 2014 did not find further evidence on opioids; this evidence review focused on non-opioid pharmaceutical and non-pharmaceutical therapies.

The outcome of the 2014 Biennial Review was the creation of a new line for fibromyalgia, separate from conditions like conversion disorder. This new line was scored to approximately the current line position, well below the funding line. A new guideline was added regarding treatments for fibromyalgia that explicitly stated that opioids were not included on that line for fibromyalgia. This clause was added by VbBS members due to concerns for lack of evidence of effectiveness for opioids, and evidence of harms, for the treatment of fibromyalgia.

October 2017 P&T review on pharmacologic therapy for fibromyalgia
1) Evidence of benefit or harms for other pharmacological treatments (including tricyclic antidepressants, gabapentin, and tramadol) was insufficient
2) Overall, evidence for other pharmacological treatments [including tramadol and opioids] was limited by significant risk of bias, small sample sizes, and/or limited applicability to patients with comorbid medical conditions
3) Russell 2000 was described, RCT of tramadol vs placebo for fibromyalgia

a. Outcome was rate of discontinuation due to side effects; not relevant to current question

2019 guideline review:
A review of the efficacy of opioids or tramadol for fibromyalgia is the purview of the P&T committee. HERC staff have compiled expert guidelines which comment on opioid use for treatment of fibromyalgia. These guidelines recommend weak opioids (specifically tramadol) based on low level evidence, and recommend against use of stronger opioids, particularly long term, due to lack of evidence of efficacy and evidence of harms.

1) **MacFarlane 2017**, reviewed EULAR recommendations for management of fibromyalgia
    a. Systematic review and expert guidelines
    b. Weak recommendations for: tramadol
    c. Strong recommendations against: opioids (other than tramadol)
    d. Opioid evidence:
        i. Tramadol: 2 reviews found to mention; only one study cited (see below)
            1. Roskell et al identified a single study of tramadol with paracetamol. Those in the active arm were more likely to have 30% improvement in pain (RR 1.77, 95% CI 1.26 to 2.48).
        ii. Other opioids:
            1. The literature search did not identify any reviews on corticosteroids, strong opioids, cannabinoids and antipsychotics. The committee made a 'strong against' evaluation (100% agreement) regarding the use of strong opioids and corticosteroids in patients with fibromyalgia on the basis of lack of evidence of efficacy and high risk of side effects/addiction reported in individual trials.
2) **Fitzcharles 2012**, Canadian guidelines for management of fibromyalgia
    a. A trial of opioids, beginning with a weak opioid such as tramadol, should be reserved for treatment of patients with moderate to severe pain that is unresponsive to other treatment modalities [*Level 2, Grade D*].
    b. Strong opioid use is discouraged, and patients who continue to use opioids should show improved pain and function. Healthcare professionals must monitor for continued efficacy, side effects or evidence of aberrant drug behaviours [*Level 5, Grade D*].
3) **Lee 2014**, British Pain Society treatment guidelines for chronic widespread pain, including fibromyalgia
    a. The use of opioids other than tramadol is not generally advocated in this pathway, although a trial of weak opioids is suggested in primary care. Generally, evidence for benefit is lacking19 and using opioids liberally has led to problems at a national level for large numbers of people.
    b. Commencing opioids in CWP and fibromyalgia, especially those without a clear prescribing ceiling, needs a great deal of experience and justification. Drugs that fall into this cautionary category include buprenorphine, fentanyl, methadone, morphine, oxycodone, hydrocodone, and meperidine. Starting long-term opioids is not recommended in this pathway and should be reserved for use by pain specialists to prevent the risk of inappropriate escalation.

Additional literature identified by Aggregate Analytics, Inc

1) **Turner 2016**, prospective cohort study of opioid use for fibromyalgia vs other chronic pain conditions
    a. N=1,218 patients
        i. 429 (35%) met our definition of fibromyalgia.
    b. Lower pain intensity scores and lower activity interference found at all time periods for patients with and without fibromyalgia without opioid use compared to opioid use
    c. Among patients who discontinued opioids by 12 months, those with fibromyalgia were more likely to report bothersome side effects and less likely to report pain improvement as important reasons for discontinuation (P-values < 0.05).
    d. Conclusions: Among patients continuing COT, pain and activity interference outcomes were worse than those of patients with minimal/no opioid use and did not differ for those with fibromyalgia versus those with diverse other chronic pain conditions

Appendix B
Detailed summary of previously reviewed literature

HERC staff have summarized the overall level of evidence for the various treatment modalities proposed for the new line. This evidence has been previously reviewed by the CPTF and VbBS; however, two of the reviewed articles [AHRQ 2018, Cochrane 2017] have subsequently been updated and are included in the abstracts below.

Evidence for Non-Pharmacologic Therapies

1) **Exercise (including Tai Chi)**
    a. AHRQ 2018
    https://effectivehealthcare.ahrq.gov/sites/default/files/pdf/nonpharma-chronic-pain-cer-209.pdf
        i. Tai Chi and quigong
            1. Over the short-term, two trials of mind-body practices reported slight improvement in function for qigong compared with waitlist (MD −7.5, 95% CI −13.3 to −1.68) and for tai chi compared with attention control (MD −23.5, 95% CI −30 to −17) based on 0 to 100 scale total FIQ score; Significantly more participants in the tai chi group also showed clinically meaningful improvement on total FIQ (RR 1.6, 95% CI 1.1 to 2.3) consistent with a slight effect (SOE: low).
                a. Note: minimum clinically important difference (MCID) in the 100 point FIQ scale is 14% change
            2. Qigong and tai chi were associated with moderately greater improvement in pain (0-10 scale) compared with waitlist and attention control in the short term (2 trials, pooled MD −1.54, 95% CI −2.67, −0.41, I2=75%). Significantly more participants in the tai chi group also showed clinically meaningful improvement on VAS pain (RR 2.0, 95% CI 1.1 to 3.8) consistent with a slight effect (SOE: low).
                a. Note: MCID for VAS pain scale is 1.0-1.4
            3. No evidence in the intermediate or long term.
            4. Data for harms were insufficient.
        ii. Exercise
            1. Exercise improved function short term (7 trials, pooled MD −7.61 on a 0 to 100 scale, 95% CI −12.78 to −2.43, I2= 59.9%) (SOE: low) and intermediate term (8 trials, pooled MD −6.04, 95% CI −9.05 to −3.03, I2=0%) (SOE: moderate). There were no clear effects in the long term (3 trials, pooled MD −4.33, 95% CI −10.18 to 1.52, I2=0%) (SOE: low).
                a. Note: minimum clinically important difference (MCID) in the 100 point FIQ scale is 14% change
            2. Exercise had a slightly greater effect on VAS pain (0 to 10 scale) compared with usual care, attention control, or no treatment short term (6 trials, pooled MD −0.89, 95% CI −1.32 to −0.46, I2=0%), but there were no clear effects at intermediate term (7 trials, pooled MD −0.41, 95% CI −0.87 to 0.05, I2=9.5%) or long term (4 trials, pooled

MD −0.18, 95% CI −0.77 to 0.42, I2=0%) (SOE: moderate for all time frames).
    a. Note: MCID for VAS pain scale is 1.0-1.4
3. Data on harms were insufficient.

b. Cochrane review 2017 (Geneen)
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5461882/
    i. Conclusions: The evidence in this overview suggests that the broad spectrum of physical activity and exercise interventions assessed here (aerobic, strength, flexibility, range of motion, and core or balance training programmes, as well as yoga, Pilates, and tai chi) are potentially beneficial, though the evidence for benefit is low quality and inconsistent.

c. Cochrane review 2018 (Geneen 2017b)
https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD011279.pub3/full
    i. N=264 studies (19,642 participants)
    ii. Pain conditions included rheumatoid arthritis, osteoarthritis, fibromyalgia, low back pain, intermittent claudication, dysmenorrhoea, mechanical neck disorder, spinal cord injury, postpolio syndrome, and patellofemoral pain.
    iii. Interventions included aerobic, strength, flexibility, range of motion, and core or balance training programmes, as well as yoga, Pilates, and tai chi.
    iv. The quality of evidence was low due to participant numbers (most included studies had fewer than 50 participants in total), length of intervention and follow-up (rarely assessed beyond three to six months).
    v. Pain severity: several reviews noted favourable results from exercise but results were inconsistent across interventions and followup
    vi. Physical function: significantly improved as a result of the intervention in 14 reviews, though even these statistically significant results had only small-to-moderate effect sizes
    vii. Psychological function and quality of life**:** had variable results, results were either favourable to exercise (generally small and moderate effect size, with two reviews reporting significant, large effect sizes for quality of life), or showed no difference between groups.
    viii. **Authors' conclusions** The quality of the evidence examining physical activity and exercise for chronic pain is low. There were some favourable effects in reduction in pain severity and improved physical function, though these were mostly of small to-moderate effect, and were not consistent across the reviews.

2) Acupuncture

a. AHRQ 2018
https://effectivehealthcare.ahrq.gov/sites/default/files/pdf/nonpharma-chronic-pain-cer-209.pdf
    i. Acupuncture was associated with slightly greater improvements in function based on 0 to 100 FIQ Total Score compared with sham acupuncture in the short term (2 trials, pooled MD −8.63, 95% CI −12.12 to −5.13, I2=0%) and intermediate term (2 trials, pooled MD −9.41, 95% CI −13.96 to −4.85, I2=27.4%) (SOE: moderate).
        1. Note: minimum clinically important difference (MCID) in the 100 point FIQ scale is 14% change

ii. There was no clear effect of acupuncture on pain (0 to 10 scale) versus sham acupuncture in the short term (3 trials, pooled MD −0.13, 95% CI −1.06 to 0.79, I2=72%) or intermediate term (3 trials, pooled MD −0.53, 95% CI −1.15 to 0.09, I2=45.5%) (SOE: low).
iii. No data on long-term effects were reported.
iv. Discomfort & bruising were the most common adverse events. (SOE: moderate).

Mindfulness therapy

a. AHRQ 2018 https://effectivehealthcare.ahrq.gov/sites/default/files/pdf/nonpharma-chronic-pain-cer-209.pdf
   i. No clear short-term effects of mindfulness-based stress reduction (MBSR) were seen on function compared with waitlist or attention control (MD 0 to 0.06 on a 0-10 scale) in two trials (one fair and one poor quality) (SOE: moderate).
   ii. No clear short-term effects of MBSR on pain (MD 0.1 on a 0-100 VAS pain scale in one poor quality trial; MD −1.38 to −1.59 on the affective and −0.28 to −0.71 on the sensory dimension [scales not reported] of the Pain Perception Scale in one fair-quality trial) compared with waitlist or attention control in two trials (SOE: moderate). Intermediate-term and long-term outcomes were not reported.
b. Cochrane review 2017 (Eccleston) https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD010323.pub3/full
   i. N=3 studies. Two studies found a significant difference between groups at post-treatment and follow-up in opioid consumption. The remaining study found reduction in opioid consumption in both treatment and control groups, and between-group differences were not significant. We also found mixed findings for pain intensity and physical functioning.
   ii. Authors' conclusions No conclusions can be drawn from this small amount of information.

3) Multidisciplinary rehabilitation programs

a. AHRQ 2018 https://effectivehealthcare.ahrq.gov/sites/default/files/pdf/nonpharma-chronic-pain-cer-209.pdf
   i. More multidisciplinary treatment participants experienced a clinically meaningful improvement in FIQ total score (≥14% change) compared with usual care at short (odds ratio [OR] 3.1, 95% CI 1.6 to 6.2), intermediate (OR 3.1, 95% CI 1.5 to 6.4) and long term (OR 8.8, 95% CI 2.5 to 30.9) in one poor-quality trial. Multidisciplinary treatment was associated with a slight improvement in function (based on a 0-100 FIQ total score) versus usual care or waitlist in the short-term (3 trials, pooled MD −6.52, 95% CI −12.84 to −0.21, I2=67.3%), and versus usual care at intermediate term (3 trials, pooled MD −7.84, 95% CI −11.43 to −4.25, I2=18.2%) and long term (2 trials, pooled MD −8.42, 95% CI −13.76 to −3.08, I2=24.9%) (SOE: low for short, intermediate and long term).
   ii. Multidisciplinary treatment was associated with a slight improvement in pain compared with usual care or waitlist at intermediate term (3 trials,

pooled MD −0.68, 95% CI −1.07 to −0.30, I2 = 0%); there were no clear differences compared with usual care or waitlist in the short term (2 trials [excluding an outlier trial], pooled MD on a 0-10 scale −0.24, 95% CI −0.63 to 0.15, I2 = 0%) or with usual care in the long term (2 trials, pooled MD −0.25, 95% CI −0.68 to 0.17, I2 = 0%) (SOE: low for short, intermediate and long-term).
        1. Note: MCID for VAS pain scale is 1.0-1.4
    iii. Data were insufficient for harms.
b. MED 2014
    i. Multidisciplinary chronic pain programs are likely to be more effective than usual care at reducing pain intensity, disability, and number of sick days, and increasing quality of life and return-to-work likelihood compared to usual care. The majority of studies evaluating multidisciplinary chronic pain programs focus on, or include a high proportion of, individuals with low back pain.
    ii. A limited body of evidence suggests that multidisciplinary pain programs may be cost-effective at reducing sick absences and increasing return-to-work status for individuals with chronic non-cancer pain. There is insufficient evidence to determine the cost-effectiveness of multidisciplinary pain programs for other outcomes.

4) Massage

a. See AHRQ 2018 under Physical Therapy below
b. 2016 meta-analysis (Crawford 2016) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4925170/pdf/pnw099.pdf
    i. For pain
        1. N=5 studies of massage vs sham for musculoskeletal pain
            a. overall standardized mean difference (SMD) of -0.44 (95% CI, -0.84 to -0.05).
            b. Note: MCID for VAS pain scale is 1.0-1.4
        2. N=4 studies (245 patients) of massage vs no treatment
            a. The overall SMD across these studies (219 participants) was -1.14 (95% CI, -1.94 to -0.35)
        3. N=24 studies (1349 patients) of massage vs active therapy
            a. Overall SMD of -0.26 (95% CI, -0.53 to 0.003)
    ii. For activity
        1. N=3 studies (211 patients) of massage vs sham
            a. overall SMD of 0.36 (95% CI, -0.53 to 1.25);
            b. Note: unclear what scale was utilized
        2. N=7 studies (450 patients) of massage vs active therapy
            a. The overall SMD of -0.23 (95% CI, -0.50 to 0.05
    iii. Overall, low confidence in evidence that showed a small but statistically significant improvement in pain with massage for pain, activity and mood [note: not clinically meaningful]

5) Cognitive behavioral therapy

a. AHRQ 2018 https://effectivehealthcare.ahrq.gov/sites/default/files/pdf/nonpharma-chronic-pain-cer-209.pdf

i. CBT was associated with a slightly greater effect on function (FIQ Total Score) compared with usual care or waitlist in the short term (2 trials, pooled MD −10.67, 95% CI −17 to −4.30, I2=0%, 0-100 scale). The pooled estimate at intermediate term was not statistically significant (SOE: low for short term and intermediate term, insufficient for long term).
   1. Note: MCID for FIQ is a 14% change

ii. CBT was associated with a slight improvement in pain (on a 0-10 scale) compared with usual care or waitlist in the short term (3 trials, pooled MD −0.78, 95% CI −1.30 to −0.17), but not in the intermediate term (2 trials, pooled MD −0.44, 95% CI −1.30 to 0.01); evidence from one poor-quality trial was insufficient to determine effects on long-term pain (SOE: low for short term and intermediate term, insufficient for long term
   1. Note: MCID for VAS pain scale is 1.0-1.4

iii. Data on harms were insufficient.

b. Cochrane review 2017 (35 studies, 4788 patients) (Williams) https://www.ncbi.nlm.nih.gov/pubmed/23152245
   i. CBT vs active control (N=13 studies, 1258 patients)
      1. The overall effect of CBT on pain was not significant immediately post treatment (Z = 1.43, P > 0.05) or at follow up (Z = 1.12, P > 0.05)
      2. The effects of CBT on disability immediately after treatment was significant (Z = 2.66, P < 0.01) with a small effect size: standardised mean difference (SMD) -0.19 (95%confidence interval (CI) -0.33 to -0.05). The effect of CBT at follow-up was significant (Z = 2.28, P < 0.05) with a small effect size of SMD -0.15 (95% CI -0.28 to -0.02)
      3. The effect of CBT on mood; the overall effect was not significant (Z = 0.72, P > 0.05) immediately after treatment or at follow up (Z = 1.15, P > 0.05)
   ii. CBT vs usual care (N=16 studies with 1148 patient)
      1. The effect on pain was significant (Z = 2.59, P < 0.05) with an effect size of SMD -0.21 (95% CI -0.37 to -0.05) immediately after treatment; however, on follow up, the effect was non-significant (Z = 0.99, P > 0.05)
      2. The effect on disability was significant (Z = 2.35, P < 0.05) with an effect size of SMD - 0.26 (95% CI -0.47 to -0.04) immediately after treatment; however, on follow up, the effect was non-significant (Z = 0.66, P > 0.05)
   iii. The effect on mood was significant (Z = 3.84, P < 0.01) with an effect size of SMD -0.38 (95% CI -0.57 to -0.18) immediately after treatment; follow up showed with an overall effect of CBT was just significant (Z = 1.99, P = 0.05) with a small effect size of SMD -0.26 (95%CI -0.51 to 0.00)

6) Pain education

a. 2015 systematic review and meta-analysis (9 studies) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4591560/pdf/13643_2015_Article_120.pdf
   i. Pooled data from five studies, where the comparator group was usual care, showed no improvement in pain or disability.

ii. Conclusions: The evidence base is limited by the small numbers of studies, their relatively small sample sizes, and the diversity in types of education studied.

7) Physical therapy (specifically myofascial release)

a. AHRQ 2018 https://effectivehealthcare.ahrq.gov/sites/default/files/pdf/nonpharma-chronic-pain-cer-209.pdf

i. Myofascial release therapy was associated with a slightly greater effect on intermediate-term function as measured by the FIQ (mean 58.6 ± 16.3 vs. 64.1 ± 18.1 on a 100 point scale, P=0.048 for group by repeated measures ANOVA), but not long-term function (mean 62.8 ± 20.1 vs. 65.0 ± 19.8 on the FIQ, 0-100 scale, P=0.329), compared with sham in one fair-quality trial (SOE: low). Short-term function was not reported.

1. Note: MCID for FIQ is a 14% change

ii. There was insufficient evidence to determine the effects of myofascial release therapy on short-term pain (1 poor-quality trial) and intermediate-term pain (1 fair-quality and 1 poor-quality trial) compared with sham; there were inconsistencies in effect estimates between the intermediate-term trials (SOE: insufficient).

iii. Data were insufficient for harms

Appendix C
Update of Evidence for Opioid Therapy

1) **Busse 2018,** JAMA systematic review and meta-analysis of opioids for chronic non-cancer pain
    a. N=96 RCTs (26, 169 patients) http://www.partnershiphp.org/Providers/Quality/Documents/MPS%202019/jama_busse_2018_01_09_19.pdf
        i. 25 trials of neuropathic pain, 32 trials of nociceptive pain, 33 trials of central sensitization (pain present in the absence of tissue damage), and 6 trials of mixed types of pain.
        ii. Studies were a minimum of 4 weeks long
        iii. It was not stated what the maximum length of studies were
    b. The primary outcomes were pain intensity (score range, 0-10 cm on a visual analog scale for pain; lower is better and the minimally important difference [MID] is 1 cm), physical functioning (score range, 0-100 points on the 36-item Short Form physical component score [SF-36 PCS]; higher is better and the MID is 5 points)
    c. Compared with placebo, opioid use was associated with reduced pain (weighted mean difference [WMD], −0.69 cm [95%CI, −0.82 to −0.56 cm] on a 10-cm visual analog scale for pain, although the difference did not reach the minimally important difference of 1 cm; modeled risk difference for achieving the MID, 11.9% [95%CI, 9.7%to 14.1%]). Studies with longer follow-up reported less pain relief.
    d. High-quality evidence from 51RCTs (15,754 patients) showed opioids were associated with a small improvement in physical functioning compared with placebo, but did not meet the criterion for the minimally important difference (weighted mean difference, 2.04 points [95% CI, 1.41-2.68 points] on the 100-point SF-36 physical component score, *P* < .001; minimally important difference, 5 points; modeled risk difference for achieving the minimally important difference, 8.5% [95% CI, 5.9%-11.2%]
    e. Opioids were not significantly associated with emotional functioning compared with placebo (weighted mean difference, 0.14 points [95% CI, −0.58 to 0.86 points] on the 100-point SF-36 mental component score, *P* = .70)
    f. Opioids were associated with increased vomiting (5.9% with opioids vs 2.3% with placebo for trials that excluded patients with adverse events during a run-in period).
    g. Low- to moderate-quality evidence suggested similar associations of opioids with improvements in pain and physical functioning compared with nonsteroidal anti-inflammatory drugs (pain: WMD, −0.60 cm [95%CI, −1.54 to 0.34 cm]; physical functioning: WMD, −0.90 points [95%CI, −2.69 to 0.89 points]), tricyclic antidepressants (pain: WMD, −0.13 cm [95%CI, −0.99 to 0.74 cm]; physical functioning: WMD, −5.31 points [95%CI, −13.77 to 3.14 points]), and anticonvulsants (pain: WMD, −0.90 cm[95%CI, −1.65 to −0.14 cm]; physical functioning: WMD, 0.45 points [95%CI, −5.77 to 6.66 points]).
    h. CONCLUSIONS Compared with placebo, opioids were associated with small improvements in pain, physical functioning, and sleep quality; unimportant improvements in social functioning; and no improvements in emotional functioning or role functioning. Compared with placebo, opioids were associated with increased vomiting, drowsiness, constipation, dizziness, nausea, dry mouth, and pruritus.

2) **Els 2018**, Cochrane review on intermediate and long-term harms of opioid therapy for chronic non-cancer pain
https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD012509.pub2/epdf/full
    a. N=16 reviews
        i. The longest study was 13 months in duration, with most in the 6- to 16-week range.
        ii. The quality of the included reviews was high using AMSTAR criteria
        iii. The quality of the evidence for the generic adverse event outcomes according to GRADE ranged from very low to moderate. A GRADE assessment of the quality of the evidence for specific adverse events led to a downgrading to very low- to moderate-quality evidence due to risk of bias, indirectness, and imprecision.
    b. Based on the 14 selected Cochrane Reviews, there was a significantly increased risk of experiencing any adverse event with opioids compared to placebo (risk ratio (RR) 1.42, 95% confidence interval (CI) 1.22 to 1.66) as well as with opioids compared to a non-opioid active pharmacological comparator, with a similar risk ratio (RR 1.21, 95% CI 1.10 to 1.33).
    c. There was also a significantly increased risk of experiencing a serious adverse event with opioids compared to placebo (RR 2.75, 95% CI 2.06 to 3.67).
    d. Furthermore, we found significantly increased risk ratios with opioids compared to placebo for a number of specific adverse events: constipation, dizziness, drowsiness, fatigue, hot flushes, increased sweating, nausea, pruritus, and vomiting.
    e. There was no data on any of the following prespecified adverse events of interest in any of the included reviews in this overview of Cochrane Reviews: addiction, cognitive dysfunction, depressive symptoms or mood disturbances, hypogonadism or other endocrine dysfunction, respiratory depression, sexual dysfunction, and sleep apnea or sleep-disordered breathing.
    f. **Authors' conclusions** A number of adverse events, including serious adverse events, are associated with the medium- and long-term use of opioids for CNCP. The absolute event rate for any adverse event with opioids in trials using a placebo as comparison was 78%, with an absolute event rate of 7.5% for any serious adverse event. Based on the adverse events identified, clinically relevant benefit would need to be clearly demonstrated before long-term use could be considered in people with CNCP in clinical practice.
3) **CDC, information on prescription opioid deaths**
    a. Available at https://www.cdc.gov/drugoverdose/data/prescribing.html
    b. In 2017, prescription opioids continue to contribute to the epidemic in the U.S. – they were involved in more than 35% of all opioid overdose deaths.
4) **Seth 2018**, overview of opioid overdose deaths
    a. Examined deaths from opioid overdoses, using a more conservative method than the CDC, including only natural and semisynthetic opioids and methadone (illicit fentanyl is explicitly excluded)
    b. With the more conservative method, 17 087 prescription opioid–involved deaths occurred in 2016 [in the US]

Evidence on Opioid Tapering

The following is a summary of the MED 2018 Evidence Review for opioid tapering as completed by Oregon Health & Science University's Center for Evidence-based Policy:

1) Overall quality of the evidence is very low
2) Findings suggested that pain, function, and quality of life might improve during and after opioid discontinuation or dose reduction
3) Scant evidence on harms associated with tapering strategies
    a. Adverse events—mortality, suicide or overdose
        i. 5 studies in the Frank review included adverse events
            1. 1 opioid-related overdose death in a patient in a buprenorphine treatment program (after discontinuation of buprenorphine) out of a total of 5 studies (no N given)
        ii. A retrospective cohort study conducted in a VA population whose opioid therapy was discontinued by their clinician (primarily for aberrant behaviors) reported that 12% of the cohort had documented suicidal ideation and nonfatal suicidal self-directed violence (SSV) in the 12 months after opioid discontinuation
            1. This study identified Hispanic ethnicity (adjusted odds ratio [OR] 7.25 (95% CI 1.96–27.18), PTSD diagnosis: 2.56 (1.23–5.32), and psychotic-spectrum disorder diagnoses (OR 3.19; 95% CI 1.14 to 8.89) were correlated with suicidal ideation and SSV in the 12 months following clinician-initiated opioid discontinuation.
        iii. Other new studies did not report information on serious adverse events such as mortality, suicide, or overdose events.
    b. Adverse events—opioid withdrawal symptoms
        i. In the systematic review by Frank et al., 18 studies (3 fair and 15 poor methodological quality) reported opioid withdrawal symptoms. Rates of withdrawal symptoms ranged widely across the studies (0% to 100%).
4) Taper length
    a. Not able to draw any conclusions regarding rapid versus slow tapering.
5) Patient-initiated vs nonpatient-initiated tapering
    a. Very little information found on this issue. In almost all of the studies included in the previous MED report and in this update, patients had some autonomy in the decision to taper their opioids.

HERC Proposed Chronic Pain Policy Evidence Appraisal – Final Report

Provided by:

Aggregate Analytics, Inc.

Prepared by:

Andrea C. Skelly, PhD, MPH
Erika D. Brodt, BS
Shelby Kantner, BA

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Executive Summary

Chronic pain (i.e., pain lasting longer than 3 to 6 months or past normal time for tissue healing)[1] is a tremendous public health burden, impacting the physical, mental and social functioning, productivity and quality of life of millions adults in the United States and is a leading cause of disability.[1] Due to its complex nature, diagnosis and management of chronic pain is challenging. It is best understood from a biopsychosocial perspective, and effective therapies should address biological factors as well as the psychosocial contributors to pain.[1,2]

The Oregon Health Evidence Review Commission (HERC) has started to explore expanding coverage to five chronic pain conditions that are currently in the "unfunded region" of the HERC's Prioritized List of Services. The five conditions are: fibromyalgia, chronic pain syndrome, chronic pain due to trauma, other chronic post-procedural pain and other chronic pain. The Oregon Health Authority (OHA) has recently asked the HERC to pause their deliberation and decision-making on this coverage topic so that an external review of the proposal under consideration could be completed.

Purpose and methods:

The primary purpose of this report is to provide a rapid turnaround, independent external review of the evidence base cited in HERC's proposal and how it aligns with proposed changes for coverage of specific treatments for the five conditions specified. This report also captures additional evidence sources for consideration as identified through a review of public and expert comment submitted to the HERC. Primary components for assessing the evidence base cited in the March 2019 "Reprioritization of Certain Chronic Pain Conditions" and scope of work included use of validated critical appraisal instruments (or appropriate modifications) based on the study design to be appraised, general listing of the Patients, Interventions, Outcomes, Timing and Settings (PICOTS) of included studies for comparison with the populations (the five conditions) and interventions in the proposed policy, and notation of the overall strength of evidence represented to identify potential gaps. (See full report.)

Summary of findings, observations and suggestions:

- The literature on evaluation and management of chronic pain is vast and complex. With the exception of fibromyalgia, the conditions considered for benefit expansion are very broad and poorly defined. These factors, combined with the large number of interventions considered in the proposed policy, make it a challenge to systematically search for and identify high quality syntheses of methodologically sound scientific studies. The search strategies and inclusion/exclusion criteria used to obtain the evidence specific to the proposal were not delineated. This report identifies some areas for which an expanded search for high quality systemic reviews and evidence-based clinical guidelines may be of benefit.

- HERC staff summarized a vast amount of literature across the 12 reviews/reports[3-14] and a single randomized controlled trial (RCT).[15] The overall quality of the included systematic reviews and reports was good based on accepted critical appraisal methods. (This is not to say that the overall quality of the evidence contained in the reviews was good.) Overall, the evidence summary provided in the March 2019 document was well done; extensive evaluation of its accuracy was not done by the authors of this report. Explicit links to specific policy components and populations being considered for expanded benefits were less clear. Similarly, based on public and expert comments, there may be a lack of clarity regarding the intent and expected implementation of proposed policies particularly related to opioid use and tapering.
- Included studies were focused on adult populations. The proposed policy does not appear to specify a restriction to adults or describe whether children or adolescents would be included.
- For a number of interventions, cited evidence across studies included patients with pain conditions other than those considered for policy expansion. In many instances, the overall strength of evidence was low (low confidence that the effect is consistent with the true effect) or very low (insufficient); in other instances no evidence specific to an intervention was cited for one or more of the proposed conditions. The HERC will need to carefully consider the extent to which findings for some treatments for conditions studied, particularly those with sparse or no evidence, can be logically extrapolated to the broad range of conditions (and pain characteristics) in the proposed policy, together with the relative costs and harms of the various interventions.
- Treatments were most frequently compared with placebo, usual care, wait list or similar non-active comparators. Very limited high quality evidence for opioids versus non-opioids or versus non-pharmacologic treatment was available, thus comparisons of these interventions to each other are indirect, precluding firm conclusions.
- The proposed policy includes non-pharmacologic treatments considered as part of a multimodal approach to chronic pain management as suggested in the 2016 CDC guideline; the bulk of the cited evidence is specific to fibromyalgia and for most treatments is sparse. Limited or no evidence for these treatments is cited for the other proposed conditions.
- The included evidence base doesn't appear to explicitly address exclusion of fibromyalgia for the use of opioids either in the short or long term.
- The 2016 CDC guideline[16] forms the basis of some proposal recommendations, particularly with regard to long-term opioid use and tapering. These have been controversial and there has been confusion regarding their interpretation and implementation; concern about potential misapplication of them and unintended consequences has been raised. These concerns have been reflected in both public and expert comments received on the proposed policy. Some appear to have been addressed in proposal revisions. Evaluation of the CDC guideline or its evidence base was not

within the scope of this report. Consideration of points made in two recent publications[17,18] by clinical experts and guideline authors on the intent and implementation of the CDC guidelines may, however, help HERC evaluate the extent to which the proposed policy is or is not in alignment with the intent of the guidelines and determine if changes or clarifications are needed.

- The quality of evidence for the tapering portion of the proposed policy is very low (insufficient) with no clear evidence-based strategies for tapering identified in the sources cited. Similarly the potential benefits and harms of tapering are not well described in the available research evidence, particularly where opioid doses are high. The proposed policy does not seem to link well with the evidence sources cited. Context and clarification regarding the relationship between the cited evidence and proposed policy would be beneficial. Included studies did not evaluate different tapering strategies such as how quickly to taper or change dose or for what duration. Studies did not assess the impact of tapering completely versus to another target dose (e.g., <50 MMED or <90 MMED) or tapering to a specific hard dose versus other strategies (e.g., tapering decisions based on weighing benefits and harms, shared decision making, etc.). Most trials evaluated adjunctive treatment. While it appears that the proposed policy covers and supports tapering on an individual basis, the intent and implementation of this is not clear. Consideration should be given to linking HERC support for tapering and use of adjunctive therapies more directly in the proposed policy. Forced tapering and/or to hard dosing targets do not appear to be consistent with the intent of the CDC guidelines. The intent of the proposed policy is unclear regarding these points. It may be beneficial for the HERC to consider the extent to which the proposed policy is consistent with the intent and nuances of the CDC guidelines and to clarify the proposed policy's intent and support if tapering is considered.
- Justifications for specific levels of improvement (15% and 30% for non-opioid and opioid therapies respectively) for continuation of medications >90 days are not provided. Estimates of clinical importance based on a magnitude of benefit for a given population are subjective and may vary depending on the risk and benefits for a specific patient.

Background

Chronic pain (i.e., pain lasting longer than 3 to 6 months or past normal time for tissue healing)[1] is a tremendous public health burden, impacting the physical, mental and social functioning, productivity and quality of life of millions of adults in the United States and costing an estimated $560-635 billion per year.[1] It is the leading cause of disability and is often refractory to treatment.[19,20] As research in this area has evolved so have perceptions of chronic pain. It is now understood to be a multifaceted condition influenced by a variety of factors (e.g., genetic, central nervous system, psychological, and environmental factors), with complex interactions; therefore, assessment and management of chronic pain can be a challenge. Chronic pain is best understood from a biopsychosocial perspective, and effective therapies should address biological factors as well as the psychosocial contributors to pain.[1,2] Research on the management of chronic pain also continues to evolve.

The Oregon Health Evidence Review Commission (HERC) has started to explore expanding coverage to five chronic pain conditions that are currently in the "unfunded region" of the HERC's Prioritized List of Services.[a] The five conditions are: fibromyalgia, chronic pain syndrome, chronic pain due to trauma, other chronic post-procedural pain and other chronic pain. Treatments for these conditions are currently not intended to be covered by the Oregon Health Plan. Specific treatments being considered for expanded coverage include the following (from March 2019 "Reprioritization of Certain Chronic Pain Conditions" document):

- Non-pharmacologic treatments: Tai Chi, Yoga, exercise, acupuncture, interdisciplinary rehabilitation, mindfulness, massage/physical therapy, cognitive behavioral therapy, and pain education
- Non-opioid pharmacologic therapies: milnacipran, duloxetine, and pregabalin if all of the following apply: 1) Patient is also being treated with active therapy (e.g., PT, CBT) or is continuing maintenance of self-management strategies learned from such therapy. 2) Benefits of non-opioid medication is re-evaluated every 90 days and are only continued if there is documented evidence of initial improvement of function of at least fifteen percent as compared to baseline based on a validated tool and function is maintained thereafter. Less frequent monitoring may be appropriate for certain medications after safety and efficacy are established.
- Short term (<90 days) opioid therapy for all considered conditions except for fibromyalgia only when prescribed in alignment with the Oregon Opioid Prescribing Guidelines (2017–2018)
- Long-term opioid therapy (>90 days) for all considered conditions except FM when the all of the following conditions are met:

[a] Lines 1-469 of January 1, 2019 Prioritized List of Health Services represent funded services under the Oregon Health Plan. These five conditions are included on line 528. See https://www.oregon.gov/oha/HPA/DSI-HERC/PrioritizedList/1-1-2019 Prioritized List of Health Services.pdf.

- In alignment with Oregon Opioid Prescribing Guidelines (2017–2018)
- Prescribing criteria:
    - Initial functional improvement has been documented of at least 30% and function is maintained throughout the prescribing period
    - When prescribed with non-pharmacologic treatment options for managing pain
    - Careful reassessment of the evidence of individual benefits and risks should be undertaken for dosages >50 MED. Dosages >90 MED should be avoided or carefully justified. When dosages >50 MED are prescribed, naloxone should also be prescribed to the patient.
    - Patient and provider have assessed the relative risks and benefits of therapy and agree benefits outweigh risks, and have completed a material risk notice https://www.oregon.gov/omb/OMBForms1/material-risk-notice.pdf
    - No additional opioids are prescribed for flares of the chronic pain condition, although opioids may be prescribed separately for other acute injuries or surgeries as clinically appropriate
    - Comorbid mental health disorders are appropriately addressed

Opioid use is not included when prescribed for fibromyalgia or for patients who fail to meet the guideline requirements regarding opioids above who have chronic pain syndrome, chronic pain due to trauma, other chronic post-procedural pain, and other chronic pain conditions included on this line.

If a patient is already receiving long-term opioid therapy for these conditions/situations, then tapering is indicated. Opioid tapering should be done on an individualized basis which includes a taper goal of zero. Tapering should be unidirectional with a shared goal set by the patient and provider, generally with a 5–10% decrease monthly, and can be paused or slowed if the prescriber believes this is medically appropriate based on the patient's overall status. Taper plans should include non-pharmacological treatment strategies for managing the patient's pain. During the taper, behavioral health conditions need to be regularly assessed and appropriately managed. In some situations (e.g., in the setting of active substance use disorder, history of opioid overdose, aberrant behavior), more rapid tapering or transition to medication assisted treatment may be appropriate and should be directed by the prescribing provider. If a patient has developed opioid use disorder, treatment is included on Line 4 SUBSTANCE USE DISORDER.

The above policy proposal was developed by HERC with the Chronic Pain Task Force (CPTF) based on evidence gathered from sources identified by the HERC staff and experts on the CPTF. The policy has been revised in response to comments from the public and clinical experts. HERC's general process for finding and considering evidence to inform guideline development is outlined on their website: https://www.oregon.gov/oha/HPA/DSI-HERC/Pages/Policy-

QOE.aspx. Overall, the HERC seeks to base their decisions on the highest quality evidence and evidence-based guidelines using an approach most consistent with rapid review methodology. The approach focuses on inclusion of evidence sources that follow accepted standards for high quality medical research synthesis as described on the website. This approach is consisted with general principles of evidence-based practice

The Oregon Health Authority (OHA) has recently asked the HERC to pause their deliberation and decision-making on this coverage topic so that an external review of the proposal under consideration could be completed. This pause is due to potential conflicts of interest that have recently been disclosed among participants who helped to develop the proposal. The external review being undertaken here is to assess whether the proposal aligns with existing evidence.

Purpose

The primary purpose is to provide a rapid turnaround, independent external review of whether the evidence base cited in HERC's proposal on expansion of coverage aligns with proposed changes for coverage of specific treatments for fibromyalgia, chronic pain syndrome, chronic pain due to trauma, other chronic post-procedural pain and other chronic pain and to review public and expert comment to capture evidence sources cited.

Exclusions to the scope of this review

- Additional literature search for relevant evidence
- Review of Oregon's opioid prescribing guidelines
- Formal evaluation of the potential impact of proposed changes, logistics or costs
- Recommendation for or against implementation of a new line on the Prioritized List
- Formal critical appraisal or assessment of evidence suggested by commenters or formal evaluation of applicability to the proposal of evidence described by commenters
- Recommendations regarding back and neck pain
- Evaluation of 2016 CDC Guideline

Methods

For purposes of this report, evidence was defined as that from formal clinical research studies or syntheses of such studies published in the peer-reviewed medical literature, consistent with the evidence considerations outlined on the HERC website. Primary components for assessing the evidence base cited in the March 2019 "Reprioritization of Certain Chronic Pain Conditions" and scope of work included use of validated critical appraisal instruments (or appropriate modifications of them) based on the study design to be appraised, general listing of the Patients, Interventions, Outcomes, Timing and Settings (PICOTS) of included studies to compare with the proposed guideline populations (the five conditions) and interventions and notation of the overall strength of evidence represented in the evidence base (Appendix Tables 1 and 2).

For systematic reviews the AMSTAR-2 critical appraisal tool was used.[21] For randomized controlled trials, a modification of the Cochrane Risk of Bias tool was used.[22,23] Some of the included evidence reports followed a rapid review methodology. These were assessed based on methodological concepts outlined by AHRQ[24] and consideration of applicable AMSTAR-2 criteria (Appendix Tables 3 and 5). Individual studies contained within systematic reviews or rapid reviews were not critically appraised for this report; risk of bias assessments of these individual studies reflect what was reported in the original review.

Limited abstraction of PICOTS components from included evidence sources/reviews was done in addition to a summary of primary results and conclusions (Appendix B); this served as a basis for the creation of summary tables to compare the PICOTS from the evidence base with the intended populations and interventions in the proposal.

In addition, public and expert comments were reviewed to gain a general sense of the concerns raised and to capture citations of formal clinical research studies or syntheses of such studies published in the peer-reviewed medical literature. Retrieved citations are listed in Appendix Table 8; it may not be a complete listing of all citations provided by commenters. Appraisal and evaluation of these citations for inclusion into the proposal is the purview of the HERC (and for pharmaceuticals, the Pharmacy and Therapeutics Committee). Minutes from the CPTF and VbBS meetings related to the proposal from September 2017 through March 2019 were briefly reviewed to get a sense of proposal development only. No formal assessment of the public comments, meeting minutes or proposal development process was made in this report.

The CPTF were also asked to identify relevant sources of evidence, based on review of meeting minutes. We understand that HERC reviewed citations described in expert and public comment. Additional citations of research we are aware of are included in Appendix Table 9 (these are not based on any formal systematic search of the literature and HERC may wish to evaluate them against their inclusion/exclusion criteria).

A draft of this report was submitted for limited, informal peer-review to two individuals with substantial expertise in systematic review methodology in general and particularly that related to management of chronic pain.

Results

A total of 12 reviews/reports were identified in the March 2019 document titled “Reprioritization of Certain Chronic Pain Conditions” that made up the evidence base for the HERC policy proposal; nine were systematic reviews (SRs) or compilations of SRs,[3,5-10,12,14] some of which included meta-analyses (MAs), and three[4,11,13] appeared to use approaches most consistent with rapid review methodology[25,26] (these will be referred to as rapid reviews). Additionally, one randomized controlled trial (RCT) was specifically cited.[15] Non-pharmacologic therapies were assessed by six reviews (5 SRs, 1 rapid review), opioid therapy by five reviews (4 SRs, 1 rapid review) and the RCT, and one rapid review assessed non-opioid pharmacologic therapies. The

tables below (Tables 1-3) briefly summarize the evidence by treatment category as outlined in the proposed guideline based on the PICOTS framework. Critical appraisal of the evidence sources cited and brief summary of general findings related to the treatments is provided as are general descriptions of potential evidence gaps and suggestions for consideration. This summary is of the evidence sources identified in the March 2019 document.

Overall, the quality of evidence synthesis in the included reviews was very good, with reliance on Cochrane reviews, AHRQ reviews and reviews that follow similar accepted methodologies for rigorous objective systematic reviews and comparative effectiveness reviews including evaluation of the overall strength of evidence for primary outcomes. (This is not to say that the overall quality of the evidence contained in the reviews was good.) With the exception of the two MED rapid reviews, all reviews were considered to be high quality (i.e., low risk of bias) with AMSTAR-2 scores ranging from 75 to 100 (See Appendix Tables 5–7). The MED reports (2014 on multidisciplinary programs for chronic pain and 2018 on opioids) were considered fair quality (i.e., moderate risk of bias) using the AMSTAR-2 tool, however, as these were more akin to rapid reviews and not full systematic reviews (which may take a year or more to develop) it would be expected that some criteria would not be met.

Non-opioid pharmacologic therapy

One high quality systematic review (SR)[3] and one fair quality rapid review[11] were used to inform proposed policy for non-opioid pharmacologic treatments for chronic pain (Table 1). The SR included 22 randomized controlled trials (RCTs) encompassing a range of non-cancer chronic pain conditions (i.e., central sensitization, nociceptive pain, neuropathic pain, and mixed types of pain) and compared various non-opioid pharmacologic agents versus opioid therapy; the rapid review focused specifically on fibromyalgia and included 24 SRs and 10 RCTs (representing over 14,000 people) which compared non-opioid therapies with placebo and with active non-pharmacologic treatments (of note, there may be some overlap between reviews in the included studies; we did not evaluate the extent to which this occurred). The risk of bias of individual studies cited in the SR appeared to be primarily low to moderate risk of bias while those in the rapid review were primarily moderate to high risk of bias as reported by the review authors.

Table 1. Summary: Evidence related to proposed policy on non-opioid medications

Policy Component	Evidence Base	Public comment	Observations regarding link of evidence to proposal, considerations and potential gaps
Coverage of non-opioid pharmacologic treatment (Milnacipran, duloxetine, pregabalin) Patient also engaged in active therapy (e.g., PT, CBT) or is continuing maintenance of self-management strategies learned from such therapy Benefit re-evaluation at least every 90 days; medication continued if documented evidence of at least 15% improvement in function from baseline based on a validated tool	**P&T Committee/OSU Drug Use Research and Management Program 2019[11] (AMSTAR-2 75, Low RoB):** 24 SRs, 10 RCTs represented over 14,000 people and evaluated harms and benefits of non-opioid pharmacologic treatment. Evidence synthesized in this report is specific to FM. (Non-analgesics for chronic non-cancer pain or neuropathic pain and tramadol were previously reviewed.) Strength of evidence was low for the interventions that showed most benefit for improving function and/or pain. The report also describes recommendations from clinical guidelines (assessment of guideline quality not reported) which recommend non-pharmacologic treatments including active therapies (e.g., exercise, CBT, multicomponent therapy); the strength of recommendations and recommendations for use/use as primary, second-line therapies with non-opioid pharmacologic management varied. **Busse 2018[3] (AMSTAR-2 100, Low RoB):** Of 14 RCTs reporting single comparisons, 5 were in patients with OA and 3 were in those with LBP, 1 in fibromyalgia and others included neuropathic and non-neuropathic pain. Opioids were generally associated with similar improvements in pain and physical functioning vs. NSAIDS (9 RCTs, 1431 patients, mostly tramadol	Specific study citations by a commenter regarding tramadol were forwarded to OHA for evaluation and were assessed by the OSU program for inclusion in their review; one of the RCTs met inclusion criteria and was included in the final report.	**P&T Committee:** Evidence synthesis across 24 high quality systematic reviews and 10 RCTs of non-opioid pharmacologic treatments for FM appears to be substantial. SOE was low for pain improvement vs. placebo for milnacipran, duloxetine and pregabalin; effect sizes for some may be below various thresholds for what is clinically meaningful. Adverse effects were more common with pharmacologic treatment vs. placebo. Evidence was considered insufficient for tricyclic antidepressants, gabapentin, and tramadol and for comparisons of pharmacologic vs. non-pharmacologic therapies. Data were sparse for long-term benefits (and persistence of benefits long term) and harms; most trials were <3 months, with few studies reporting outcomes beyond 6 months. Evidence was considered insufficient to determine long-term benefit in FM and also to determine relative efficacy of pharmacologic treatment compared to non-pharmacologic therapies. Cited guidelines (P&T Report) may provide some support for the requirement that FM patients be concurrently engaged in active therapy or continuing maintenance of self-management from such therapies. While the P & T committee/OSU report describes commonly used thresholds for improvement for specific scales for FM and chronic pain, the authors also caution that estimates of clinical importance based on a magnitude of benefit for a given population are subjective and may vary depending on the risk and benefits for a specific patient. **Busse 2018** compared opioid with non-opioid therapies across a range of chronic non-cancer pain conditions (neuropathic pain, nociceptive pain, central sensitization and mixed conditions). These findings may provide some evidence for use of non-opioid treatments for a broader range of chronic pain patients; however, some important limitations to the evidence are noted. First, evidence comparing opioids vs. specific non-opioids is limited overall and small sample sizes for many comparisons are noted; meta-analyses were thus limited. Five of the 11 RCTS used tramadol (3 in combination with acetaminophen, 1 in combination with amitriptyline) to compare with NSAIDs. Tramadol is weak opioid so results may not apply to different/stronger opioids.

Policy Component	Evidence Base	Public comment	Observations regarding link of evidence to proposal, considerations and potential gaps
	vs. NSAID), tricyclic antidepressants (3 RCTs, 246 patients), anticonvulsants (3 RCTs, 303 patients) and synthetic cannabinoids (1 RCT, 73 patients) SOE was low for no difference in pain or function outcomes for opioid vs. tricyclic antidepressants, moderate for small improvement in pain but low for no difference in function for opioids vs. anticonvulsants, and low for no difference in pain or function vs. synthetic cannabinoids. High quality evidence showed a >4 fold increase in vomiting with opioid vs. NSAIDS across 5 RCTs (2632 patients). Five additional RCTs made multiple comparisons of various opioids alone, or in combination with nortriptyline or gabapentin vs. nortriptyline (3 RCTs), gabapentin (1 RCT). Different tramadol doses vs. celecoxib were evaluated in 1 RCT. **Williams 2017[14] (AMSTAR-2 81.3, Low RoB):** Evaluated CBT and behavioral therapy but not explicitly as an adjunct to pharmacologic treatment (see below under non-pharmacologic treatments).		Opioids were combined with other agents in many of the trials of opioid vs. non-opioid medications, complicating interpretation of results. Approximately one half of the included trials were in populations with conditions such as LBP, OA and neuropathic pain vs. the conditions specified in the proposal for expanded coverage, thus applicability of these results to the populations proposed for expanded benefits needs to be carefully considered. As noted by the P&T Committee report, chronic pain is a very broad topic. Evidence (and guidelines) cited in the P&T report for FM may or may not apply to the other new line chronic pain conditions. The conditions proposed for expanded benefits include a very broad, heterogeneous set of patient conditions and circumstances. The report indicates that previous reviews for chronic non-cancer or neuropathic pain and tramadol had been done. It may be helpful to review these previous reports and consider the extent to which they may be relevant to the proposed expansion or not if they haven't been considered for this proposal. An AHRQ review of non-opioid management of various chronic pain conditions currently in process will provide additional evidence for some conditions. Search for and inclusion of information from recent, updated and high quality evidence-based clinical guidelines supporting engagement of patients with various active treatments together with non-pharmacologic therapy for the new line conditions other than FM could be considered. Again, given the broad scope of included conditions, finding such guidelines may be a challenge. Overall, while there is some evidence for the use of specific non-opioid medications vs. placebo for FM, the evidence cited doesn't address use of non-opioid medications of the other conditions listed in the proposal. Patient responses to treatment may be influenced by the type of pain, i.e., nociceptive, neuropathic or nociplastic (central sensitization). The conditions considered for policy expansion are vague and broad and search for evidence specific to them is likely challenging; however there may be benefit to doing additional

Policy Component	Evidence Base	Public comment	Observations regarding link of evidence to proposal, considerations and potential gaps
			searches specific to use of non-opioid pharmacologic treatments (NSAIDS, gabapentin, etc.) for chronic pain in general. We are aware of a few systematic reviews that evaluate opioid and non-opioid agents in neuropathic pain which could be assessed by HERC, again with the caveat that results may not directly apply the populations under consideration.

AHRQ = Agency for Healthcare Research and Quality; AMSTAR-2: A MeaSurement Tool to Assess systematic Reviews version 2; CBT = cognitive behavioral therapy; FM = fibromyalgia; LBP = low back pain; NSAIDS = non-steroidal anti-inflammatory drugs; OA = osteoarthritis; OHA = Oregon Health Authority; OSU = Oregon State University; PT = physical therapy; RCT = randomized controlled trial; RoB = risk of bias; SOE = strength of evidence; SR = systematic review.

Opioid therapy

A total of six reports – four high quality SRs,[3,6-8] one fair quality rapid review,[4] and one fair quality (i.e., moderately low risk of bias) RCT[15] – were used to inform the proposed policy for opioid treatment and opioid tapering for chronic pain (Table 2). Two SRs provided evidence for short-term opioid use; one SR and the RCT provided evidence for long-term opioid use; and two SRs and the rapid review provided evidence for tapering in patients receiving long-term opioid therapy (LTOT). In addition, one SR evaluated whether or not there was evidence of differential effectiveness for opioids (versus placebo) based on pain type. The studies encompassed a wide range of non-cancer chronic pain conditions, including nociceptive pain (primarily osteoarthritis and low back pain), central sensitization (e.g., fibromyalgia), neuropathic pain, and combinations thereof; opioid therapy was compared with placebo and with active non-opioid pharmacologic agents. Across all reviews, over 225 studies (primarily RCTs) were included evaluating over 57,000 patients (of note, there may be some overlap between reviews in the included studies; we did not evaluate the extent to which this occurred). Regarding the risk of bias of individual studies included in the reviews (as determined by the review authors), the majority of studies were considered low risk of bias in two SRs[3,7]; high risk of bias in two reviews (one SR and the rapid review, likely due to the fact that these reviews included a large number of observational studies)[4,8]; and unclear in the fifth review (authors state that overall the risk of bias was mixed across studies).[6]

Table 2. Summary: Evidence related to proposed policy on opioid therapy

Policy Component	Evidence Base	Public comment	Observations regarding link of evidence to proposal, considerations and potential gaps
Short-term (< 90 days) opioid therapy (all considered conditions except FM)	**Busse 2018[3] (AMSTAR-2 100, Low RoB):** 96 RCTs across 26,169 patients; compared opioid with non-opioid pharmacologic agents and usual care. The majority of trials were in patients with OA (24 trials) and LBP (24 trials). Authors categorized pain as neuropathic (e.g., diabetic neuropathy, 25 trials), nociceptive (e.g., OA, 32 trials) and central sensitization (e.g., fibromyalgia, 33 trials); 6 trials were of mixed CP conditions. Outcomes included pain, function (physical and social), sleep quality and harms. Subgroup analyses of opioids vs. placebo for <3 months vs. ≥3 months from 80 RCTs (42 RCT followed patients for ≥3 months, N=16,617 patients) and based on pain type and other factors were performed. Only 21 of 96 trials addressed mean or median MED of ≥90 mg. For comparison with NSAIDs, tramadol was commonly used. **Els 2017 (Cochrane)[7] (AMSTAR-2 81.3, Low RoB, all included reviews scored 9 or 10 out of 10 points):** 16 Cochrane reviews (14 different opioids), 14 included in meta-analysis (61 studies; 18,679 patients) across various chronic pain conditions including neuropathic pain, LBP, OA, RA and phantoms limb pain, evaluated medium and long-term adverse events associated with opioid use; information on some serious side	Most commenters expressed concern about limiting access to opioids in general. Comparative research studies from peer-reviewed journals suggested by commenters regarding short-term opioid were identified and listed in the Appendix table 8. . If not yet evaluated by OHA staff, it may be beneficial to do so.	High quality recent systematic reviews of large number of RCTs form the primary evidence base and evaluated potential benefits as well as some harms overall and provide a substantial evidence base relevant to use of opioids short-term. A wide range of pain conditions was included in RCTs across the systematic reviews and some conditions are not included in the new line conditions (e.g., OA, CLBP, CNP); applicability to the new line conditions needs to be considered. **Busse 2018:** Across time frames for the 96 trials, compared with placebo, opioids were statistically associated with pain relief, improved physical functioning, social functioning and sleep quality but the mean differences generally did not reach the minimally important differences stated in the review (SOE high);[Modeled risk differences for achieving minimally important differences tended to favor opioids over placebo and could be clinically important; verification of this based on patient report (versus modeling) in future studies would be important]. Specific to the short term, across 38 trials with <3 months follow-up mean differences in pain relief marginally met the 1.0 cm threshold (-0.97, 95% CI -1.16 to -0.78). Across 16 trials with <3 months follow-up, sleep quality was statistically better in those receiving opioid vs. placebo; however the threshold for minimally important difference was not reached. Data for other outcomes at shorter term were not described. **Els 2017**: A small but statistically significant increase in risk of any adverse event for opioids vs. placebo or an active non-opioid pharmacologic comparator (SOE moderate) was reported. The absolute risk of any AE with opioids was 78% compared with placebo and 58% compared with an active non-opioid comparator; for any serious AE the absolute risks were 7.5% and 9.3%, respectively. Opioids were associated with over a 2-fold increase in risk of serious AEs vs. placebo (SOE moderate) but no statistical difference between opioids vs. active non-opioids was seen (SOE very low). Serious AEs were not defined. There was moderate quality evidence of an association between opioid

Policy Component	Evidence Base	Public comment	Observations regarding link of evidence to proposal, considerations and potential gaps
	effects (e.g., addiction, depression, sleep problems) was not reported in the included reviews. Not all reviews reported on common adverse events. The authors defined medium term use as 2 weeks to 2 months and ≥2 months as long term use, but don't provide separate effect estimates by time frame or formally compare them. As most trials were 6 to 16 weeks duration, results are included here with short term.		use and constipation, dizziness, drowsiness, increased sweating, and nausea versus placebo but low evidence for vomiting and very low quality evidence for fatigue, hot flushes, and pruritus; for the comparison of opioids with active non-opioid pharmacologic agents, no data were reported for specific adverse events (any severity). An AHRQ review of opioid management of various chronic pain conditions which will include consideration of both short and longer term benefits and harms of opioid use currently in process will provide additional evidence for some conditions.
Long-term opioid therapy, >90 days (all considered conditions except FM) when following are met: • Alignment with Oregon Opioid Prescribing Guidelines (2017-2018) • 30% functional improvement • When prescribed with non-pharmacologic treatment for managing pain. • Careful reassessment of benefits/risks for dosages >50MED; Dosages >90MED avoided or carefully justified; with dosages >50 MED, naloxone should also be prescribed. • Completion of risk assessment • No additional opioids	**Busse 2018[3] (AMSTAR-2 100, Low RoB) (see general results and description above):** 42 RCTs followed patients for ≥3 months, and included 16,617 patients; Only 21/96 trials addressed mean or median MMED of ≥90 mg. **Krebs 2018[15] (RCT, N=240, Moderately Low RoB):** Conditions evaluated were moderate to severe CLBP and knee OA; patients on long-term opioid therapy were excluded. Opioids were titrated to a maximum daily dose of 100 ME mg; if no response at 60 ME mg/day, another opioid was considered before dose in escalation.	Most commenters expressed concern about opioids in general not being available. Comparative research studies from peer-reviewed journals suggested by commenters are listed in Appendix Table 8. If not yet evaluated by OHA staff, it may be beneficial to do so. Based on a very limited look at the citations it appears that many: • May have already been included in the evidence bases or systematic reviews considered. • May reflect older publications (e.g., systematic review by Noble) that had been	One high quality systematic review was cited as the primary evidence base. Studies have used variable definitions of medium and long-term opioid therapy making comparisons across studies challenging; Els 2018 (above) defined medium term use as 2 weeks to 2 months and ≥2 months as long term use. Busse used a cut-off of <30 vs. ≥30 days follow-up. Only about a quarter of the included RCTs reported use of a median or mean MMED ≥90 mg. A 2017 Cochrane report (Els, et al.)[27] failed to find any Cochrane reviews that evaluated high-dose opioids for non-cancer pain. Thus, there appears to be limited evidence regarding the benefits and harms of high opioid doses particularly for conditions in the proposed policy. **Busse 2018:** Authors performed subanalyses to compare pain relief and sleep quality between trials with <30 days follow-up vs. ≥30 days follow-up. Opioids were associated with slightly less pain relief during longer trials (42 RCTs) and the difference did not meet the criterion for minimally important difference; similarly a smaller impact of opioids on sleep quality was seen in studies with longer follow-up (15 RCTs) and the difference did not meet the criterion for minimally important difference. **Krebs 2018**: Focuses on moderate to severe CLBP and OA; Pain-related function was not significantly different between opioid and non-opioid groups at 12 months; pain intensity was statistically lower in the non-opioid group, however the

Policy Component	Evidence Base	Public comment	Observations regarding link of evidence to proposal, considerations and potential gaps
for flare-ups of chronic condition (may be prescribed for acute injuries, surgery as clinically appropriate • Comorbid mental health disorders appropriately addressed		updated with new evidence and/or subsequently included in the evidence reviewed. Commenters also expressed concern regarding use of CDC guidelines for dosages in the proposed policy.	difference may not be clinically meaningful. Adverse medication-related symptoms were significantly more common in the opioid group over 12 months. Results may or may not be applicable to the chronic pain conditions in the proposed lines. In the absence of described inclusion/exclusion criteria or search strategy for the proposal evidence, it is unclear why this single trial was included for review and whether or not other contemporary trials would have logically been included for consideration. If the intent was to identify new RCTs that are not included in the systematic reviews, and/or to identify trials with longer-term follow-up a structured search with defined criteria should be considered. Evaluation of the evidence bases related to the Oregon Opioid Prescribing Guidelines was not within the scope of this present report. Recommendations for doses and co-prescription of naloxone for those >50 MED come from the 2016 CDC guidelines as do recommendations for combining opioid therapy with non-pharmacologic and non-opioid pharmacologic therapies. Evaluation of these guidelines or their evidence base was not within the scope of this present report. The extent to which the proposed policy is in line with the intent and nuances of the CDC guideline should be considered (See report text). As previously discussed, estimates of clinical importance base on a magnitude of benefit for a given population are subjective and may vary depending on the risk and benefits for a specific patient.
Exclusion of FM from opioid therapy	**Busse 2018[3] (AMSTAR-2 100, Low RoB; See previous descriptions)** Authors categorized pain as neuropathic (e.g., diabetic neuropathy, 25 trials), nociceptive (e.g., OA, 32 trials) and central sensitization (e.g., fibromyalgia, 33 trials); Performed stratified analyses on these	Commenters expressed concern regarding exclusion of FM patients for opioid therapy, particularly tramadol, as well as for tapering opioids in FM patients currently taking	**Busse 2018**: Although pain relief varied a little based on type of pain, there was no evidence of differential effectiveness for pain relief based on pain type (NS p-value for interaction). However, results suggest that pain type may differentially impact social functioning in favor of opioids, though improvement did not meet thresholds for minimally important differences The included evidence base doesn't appear to explicitly address

Policy Component	Evidence Base	Public comment	Observations regarding link of evidence to proposal, considerations and potential gaps
	pain types comparing opioids versus placebo.	them.	exclusion of FM for the use of opioids either in the short or long term. If prior reviews described in the P&T report provide relevant evidence, they should be considered for inclusion. Clinical practice guidelines generally recommend against the use of long-term opioids. Data on the efficacy and safety of opioids in FM are sparse and primarily from observational studies. (See report text.) Review of the evidence base and brief description of relevant studies and evidence-based clinical guidelines is suggested. The two AHRQ reports (on opioid and the other on non-opioid pharmacologic treatments) that are in process will include patients with fibromyalgia and may provide additional evidence regarding pharmacologic treatment of it.
Tapering in patients receiving long-term opioid therapy (individualized with taper goal of zero; shared goal set by patient and provider generally with 5-10% decrease/month, can be paused or slowed based as medically appropriate based on patient's overall status. Taper plans should include non-pharmacologic interventions. During the taper, behavioral health conditions need to be regularly assessed and appropriately managed. In some situations (e.g., in the setting of active substance use disorder, history of opioid	**MED 2018 Report[4] (AMSTAR-2 64.3, Moderate RoB):** Frank SR (below), plus 9 additional poor quality observational studies. Across studies, opioid doses varied and appear to have ranged from ~25 MME to >400 mg. **Frank 2017[8] (AMSTAR-2 93.8, Low RoB):** 67 studies (11 RCTS, 56 observational) (N=12,546 patients on LTOT); included a variety of interventions, methods and settings for reducing or discontinuing long-term opioid use resulting in substantial heterogeneity across studies. Similarly there was substantial heterogeneity with regard to the pain conditions encompassed in included studies. This review largely informed the evidence base for the MED 2018 report. **Eccleston 2017 (Cochrane)[6] (AMSTAR-2 100, Low RoB):** 5 small RCTs (278 patients with non-	Most commenters expressed concern opioids in general would not be available to patients and the requirement to taper to zero. There were concerns regarding unintended consequences related to depression, suicidality and ineffective pain relief. In response to patient and expert comment, the CPTF composition was changed, the updated (March 2019) proposal reflects language changes that removed a previously considered 12 month time frame, and new language appears to provide for	The evidence base consists of two good quality systematic reviews and one fair quality rapid review which included more recently published observation studies. Both reports are heterogeneous and complex. There was overlap in included studies across the reviews. The majority of studies were poor quality observational studies, leading to an overall SOE of very low/insufficient for various outcomes (i.e., no confidence that effects reflect the true effect and new research will likely change effect estimates). The quality of evidence for this portion of the proposed policy is very low (insufficient) with no clear evidence-based strategies for tapering. The proposed policy does not seem to be based on the evidence sources cited. The included RCTs and observational studies did not assess tapering strategies with regard to how quickly to taper or change doses or describe duration of tapering. The majority of trials looked at use of adjunctive treatments and strategies (e.g., tapering support, use of various medications, acupuncture, etc.) which the proposed policy doesn't seem to explicitly address. In addition, none of the trials evaluated tapering off completely vs. tapering to another target (e.g., <50 MED or <90 MED), tapering to strictly defined dose targets versus strategies such as shared decision making to taper based on assessments of benefits versus harms. Little is known about the benefits and harms of reducing

Policy Component	Evidence Base	Public comment	Observations regarding link of evidence to proposal, considerations and potential gaps
overdose, aberrant behavior), more rapid tapering or transition to medication assisted treatment may be appropriate and should be directed by the prescribing provider.	cancer chronic pain, including headache, back and muscle pain, in patients on opioid management for ≥ 3 months): Sought to include any intervention aimed at facilitating voluntary or compulsory opioid dose reduction or cessation as either a primary or secondary outcome. Primary outcomes were prescribed opioid use and adverse events related to opioid reduction; secondary outcomes included evaluation of pain, function and psychological functioning. Acupuncture, CBT and mindfulness were among the reported strategies for reducing the amounts of opioids taken. Pooled analyses were not possible given the heterogeneity of studies.	shared decision making between patients and providers regarding goals as well as support during the process. We note that some of comparative clinical research published in peer-reviewed journals suggested by commenters (e.g., Darnall, Thakral 2018) has already been included in the evidence bases presented for this review. If not already done, OHA may wish to evaluate the list of comparative research published in peer-reviewed journals to verify inclusion of additional cited studies in the syntheses included in the proposal or if not included evaluate the extent to which they should be considered as part of the evidence base for the proposal.	high opioid doses. Additional context and clarification regarding the relationship between the cited evidence and proposed policy should be considered. If forced tapering and/or hard dosing targets are being considered, this may not be in alignment with evidence or the intent of the CDC's guideline; again clarification of the proposed policy's intent would be helpful. Adverse events were variably reported in the included literature. The MED review did report on a study within the VA that identified suicide risk in patients with clinician-initiated discontinuation of opioid therapy, but the methodological quality was considered poor leading to an overall SOE of very low (insufficient). **Frank 2017:** While authors conclude that several types of interventions may be effective to reduce or discontinue LTOT and that pain, function and quality of life may improve with opioid dose reduction, the majority of evidence came from poor quality observational studies and evidence was considered insufficient. Authors provide their perspective on clinical implications and next steps for research, given the insufficient evidence. **Eccleston2017:** Given the small number of RCTs and included patients, authors indicate that best methods for reducing opioid use are not clear; results across trials were mixed and adverse events were variably reported across trials, precluding definitive conclusions regarding the efficacy or safety of method for reducing opioid consumption. **The MED 2018 report:** Incorporated findings from 9 additional, poor quality observational studies in addition to the Frank 2017 review and conclude that tapering or discontinuation of opioid therapy is not associated with increased pain, and may be associated with reduced pain and improved functional outcome but the overall strength of evidence is very low. The conclusions are consistent with the quality of studies identified and include the following: Most of the included studies examined voluntary

Policy Component	Evidence Base	Public comment	Observations regarding link of evidence to proposal, considerations and potential gaps
			participation in a clinical program or research intervention. The findings may therefore not be generalizable to patients for whom LTOT is reduced or discontinued involuntarily and given the heterogeneity across interventions and the overall poor quality of studies; data do not currently support assessment of comparative effectiveness of the different models of care or opioid tapering protocols used in included studies. There is not high quality evidence to suggest a specific approach to reduction of opioid use. We are aware of addition recently published observational studies which could be considered (Appendix Table 9). These may or may not impact the above conclusions. An AHRQ review of opioid management of various chronic pain conditions is currently in process. It will include consideration of dosing strategies and unintended consequences of implementing the 2016 CDC opioid guidelines and consideration of patient values and preferences.

AHRQ = Agency for Healthcare Research and Quality; AMSTAR-2: A MeaSurement Tool to Assess systematic Reviews version 2; CDC = Centers for Disease Control and Prevention; CLBP = chronic low back pain; CMS = Centers for Medicare and Medicaid Services; CNP = chronic neck pain; FM = fibromyalgia; LTOT = long-term opioid therapy; MMED = morphine milligram equivalent dose; OA = osteoarthritis; RCT = randomized controlled trial; RoB = risk of bias; SOE = strength of evidence; SR = systematic review; UC = usual care

Non-pharmacologic therapy

A total of seven reports – five high quality SRs[5,9,10,12,14] and two rapid reviews (one high[11] and one fair[13] quality) – were used to inform policy decisions regarding the expansion of non-pharmacologic interventions for the treatment of chronic pain (Table 3). The studies encompassed a wide range of non-cancer chronic pain conditions, many of which were musculoskeletal-related pain; one SR provided information on the treatment of fibromyalgia. One of the included SRs (of massage therapy) did not focus specifically on chronic pain but included patients presenting with pain in the general population. Interventions were compared with usual care, waitlist or attention control, with very limited evidence for such interventions versus either active comparators or pharmacologic therapy. Across all reviews, over 400 studies (primarily RCTs) were included evaluating over 25,000 patients (of note, there may be some, likely minimal, overlap between reviews in the included studies; we did not evaluate the extent to which this occurred). Regarding the risk of bias of individual studies included in the reviews (as determined by the review authors), the majority of studies were considered low risk of bias in one SR[10]; low to moderate risk of bias in two reviews (one SR and one rapid review)[5,13]; moderate to high risk of bias in two reviews (one SR and one rapid review)[11,12]; and in the remaining two reviews, the overall quality of the studies was unclear (authors state that risk of bias for the specific criteria assessed was mixed across studies with some having low risk of bias and some having high/uncertain risk of bias).[9,14]

Table 3. Summary: Evidence related to proposed policy on non-pharmacologic treatments

Policy Component	Evidence Base	Public comment	Observations regarding link of evidence to proposal, Considerations and potential gaps
Non-pharmacologic interventions (overall)	See below	Commenters appear to support the use of non-pharmacologic interventions as part of a multimodal approach to chronic pain management; some expressed concern that such interventions would not be effective as replacements for pharmacologic interventions	Interventions were most frequently compared with usual care, no/minimal intervention, attention control or waitlist. Comparisons with active or pharmacologic agents were sparse. Comparisons of non-pharmacologic treatments with opioids and other pharmacologic treatments are therefore indirect. There is evidence in the AHRQ 2018 report of persistent improvement (≥1 month) post intervention for some treatments in persons with FM. In general, few studies evaluated impact beyond 1 year. Across studies included in all reviews, it is likely that patients continued pharmacologic and other therapies during the course of the trial. Overall, data for the use of many interventions is sparse for FM and evidence specific to the other conditions not presented. The extent to which it is reasonable to extrapolate these findings across the proposed pain conditions needs to be considered. For the included interventions, there was no evidence suggesting serious harms from any of the interventions studied; data on harms were limited, however.

Policy Component	Evidence Base	Public comment	Observations regarding link of evidence to proposal, Considerations and potential gaps
Education **Office evaluation, consultation, education**	**Geneen 2015[9] (AMSTAR-2 93.8, Low RoB)**: 9 RCTs; 8 included in meta- analysis on pain education: Education vs. usual care and comparison of different educational interventions as stand-alone management. Trials included a diverse set of educational approaches. Pooled analysis was limited due to heterogeneity and reported generally for 3 months follow-up. As a stand-alone intervention educational approaches were not associated with improved pain; one study noted a decrease in disability with pain neurophysiology education (PNE). Post-hoc analysis of psychosocial outcomes reported in the studies showed evidence of a reduction in catastrophizing and an increase of knowledge about pain following PNE.	See general comments above	The type and content of education suggested by the proposed policy is not specified. **Geneen 2015:** The small number of studies, most of which had small sample sizes and heterogeneity of educational interventions, led authors to conclude that evidence that education as a sole intervention was insufficient alone is effective in reducing pain intensity or related disability in chronic pain in adults and that it should logically be used *in conjunction* with other pain management approaches. There may or may not be new high quality evidence that could be considered. If not already considered, search for high quality evidence synthesis of educational and self-management interventions that are part of a multi-modal approach to management could be considered. As noted previously, given the vast and complex literature on the range of chronic pain conditions, this may be a challenge.
Cognitive behavioral therapy	**AHRQ 2018 (Fibromyalgia)[12] (AMSTAR-2 100, Low RoB)**: Included RCTs reporting follow-up of at least 1 month. 4 RCTs compared psychological therapies (primarily CBT) with usual care, attention control or waitlist. 1 RCT compared CBT with pregabalin; duloxetine.	See general comments above	**AHRQ 2018 (Fibromyalgia):** Psychological therapies (primarily CBT) were associated with slight improvements in pain and function short and intermediate term (SOE low) vs. usual care, waitlist, attention control; evidence was insufficient at long term. Limited evidence from 1 RCT showed

Policy Component	Evidence Base	Public comment	Observations regarding link of evidence to proposal, Considerations and potential gaps
	Williams 2017 (Cochrane)[14] (AMSTAR-2 81.3, Low RoB): 42 RCTs; 35 (4788 patients) provided data for chronic pain (excluding headache) treatment with CBT vs. usual care, waitlist or active control and behavioral therapy vs. active control. **P&T Committee/OSU Drug Use Research and Management Program 2019 – Evidence Synthesis on FM treatment[11] (AMSTAR-2 75, Low RoB):** describes recommendations from clinical guidelines (assessment of guideline quality not reported) which recommend non-pharmacologic treatments including CBT, exercise; specific data or quality appraisal of guidelines was not reported.		improvement in function but not in pain at intermediate term for CBT vs. pregabalin, duloxetine (SOE low). No evidence was available at other time frames. [This report is being updated.] **Williams 2017 (Cochrane):** CBT has small positive effects on disability and catastrophizing, but not on pain or mood, when compared with active controls. CBT has small to moderate effects on pain, disability, mood and catastrophizing immediately post-treatment when compared with treatment as usual/waiting list, but all except a small effect on mood had disappeared at follow-up. An absence of evidence for behavior therapy, except a small improvement in mood immediately following treatment when compared with an active control was reported. Authors note that average effect sizes collapsed across studies were relatively small as they are across pharmacologic and physical treatments for chronic pain.
Yoga, Tai Chi, mindfulness training	**AHRQ 2018 (Fibromyalgia)[12] (AMSTAR-2 100, Low RoB):** Included RCTs reporting follow-up of at least 1 month. Mind-body practices (N=2) and Mindfulness-based stress reduction therapy (N=2) vs. waitlist or attention control **Geneen 2017[10] (See below) (AMSTAR-2 93.8, Low RoB):** Analysis included Yoga, Pilates and Tai Chi as exercise for patients with a range of chronic pain conditions but results were not synthesized separately for	See general comments above	**AHRQ 2018** (fibromyalgia)**:** Evidence was available only for short-term. Yoga and Tai Chi were associated with slight functional and moderate pain improvement versus controls (SOE low); no clear effects of mindfulness training were seen on function or pain compared with controls (SOE moderate) **Geneen 2017:** (See below for summary of results across exercise interventions) The applicability of these findings across

Policy Component	Evidence Base	Public comment	Observations regarding link of evidence to proposal, Considerations and potential gaps
	these interventions.		the broad range of new line conditions may need to be considered. Overall, data for the use of these interventions is sparse for FM and evidence specific to the other conditions not presented. The extent to which it is reasonable to extrapolate these findings across the proposed a pain conditions needs to be considered.
Massage	**AHRQ 2018 (Fibromyalgia)[12] (AMSTAR-2 100, Low RoB):** Included RCTs reporting follow-up of at least 1 month. 1 RCT of myofascial release vs. usual care. **Crawford 2016[5] (AMSTAR-2 100, Low RoB):** (N=67 RCTs; 32 included in meta-analysis) comparing massage with sham, no treatment and active comparators. Patients presenting with pain the general population (those that would seek help from a GP) including musculoskeletal pain, headache, visceral pain, chronic pain (FM, spinal cord pain, venous insufficiency). Chronic pain was not the focus of this review.	See general comments above	**AHRQ 2018** (fibromyalgia)**:** Myofascial release was associated with slight functional improvement intermediate term that did not persist to long term and slight pain improvement long-term (SOE low); evidence at all other times was insufficient. **Crawford 2016:** Massage therapy was associated with small to moderate improvement in pain compared to sham, no treatment, and active comparators. Compared to active comparators, massage therapy was also beneficial for reducing anxiety, and improving health-related quality of life. Adverse events were rarely reported; those reported as serious included nausea, shortness of breath, chest pain, and prolapsed intervertebral disc and were considered unrelated to the treatment in the report. Reported strength of recommendations were: efficacy of massage therapy compared to no treatment (strongly recommended) and sham and active comparators (weakly recommended vs. both). Compared to active comparators,

Policy Component	Evidence Base	Public comment	Observations regarding link of evidence to proposal, Considerations and potential gaps
			massage therapy was also beneficial for treating anxiety and health-related quality of life (weakly recommended) Given the limited data available for patients with FM and lack of specificity for other conditions in the Crawford review, the applicability of these findings to the broad range of conditions for the new line needs to be carefully considered.
Supervised exercise therapy	**AHRQ 2018 (Fibromyalgia)[12] (AMSTAR-2 100, Low RoB):** Included RCTs reporting follow-up of at least 1 month. Exercise vs. usual care, etc. (N=21 RCTs) and vs. pharmacologic therapy (N=1 RCT); Exercise included aerobic, strengthening, and other forms of exercise. Yoga, Tai Chi were evaluated separately as mind-body practices. **Geneen 2017[10] (AMSTAR-2 93.8, Low RoB):** 21 SRs, 264 studies across 19,642 patients with a range of chronic pain conditions, some of which may be included in the pain categories proposed for benefit expansion. None of the reviews assessed 'chronic pain' or 'chronic widespread pain' as a general term or specific condition. A diverse set of exercise interventions was compared with no exercise/minimal intervention. Interventions included aerobic, strength, flexibility, range of motion, and core or balance training programs. Analysis also included Yoga, Pilates and Tai Chi.	See general comments above	Compared with usual care and other non-active controls, exercise is generally associated with improved function and pain across a large number of RCTs. Evidence comparing exercise with pharmacologic agents is insufficient. **AHRQ 2018:** Exercise was associated with slight improvement in function at short term (SOE low) and intermediate term (SOE moderate), but not at longer term (SOE low). Pain was slightly improved in the short term (SOE moderate). [This report is currently being updated]. **Geneen 2017:** The overall strength of evidence for reported outcomes was low. Exercise was associated with small to moderate improvement in physical function but did not consistently improve self-reported pain across reviews or time frames or for psychological function or quality of life. While this review includes a large evidence base of RCTs, effects specific

Policy Component	Evidence Base	Public comment	Observations regarding link of evidence to proposal, Considerations and potential gaps
			to a given exercise or relevant to a specific condition are not explicitly reported in detail. None-the-less this review provides a general sense of the effect of exercise across a large number of studies. Additional search for reviews that compare exercise and other non-pharmacologic therapies could be considered.
Intensive interdisciplinary rehabilitation	**AHRQ 2018 (Fibromyalgia)[12] (AMSTAR-2 100, Low RoB):** Included RCTs reporting follow-up of at least 1 month. 6 RCTs versus usual care or wait list in addition one trial compared it with exercise. **MED 2014 Report[13] (AMSTAR-2 64.3, Moderate RoB):** included 5 SRs specific to pain management in patients with chronic or sub-acute LBP, neck/shoulder pain, fibromyalgia and chronic pain not otherwise specified with interdisciplinary rehabilitation	Commenters expressed concern regarding the availability of such programs.	**The AHRQ 2018** report as cited only provides evidence related to FM. Multidisciplinary rehabilitation was associated with slight improvement in function short, intermediate and long term (SOE low) but pain was improved slightly only at intermediate term (SOE low) vs. UC, waitlist or attention control. Evidence comparing multidisciplinary rehab with exercise was only identified for long term; no differences in function or pain were seen (SOE low). **Findings in the MED 2014** report may or may not be applicable to the broad range of conditions proposed for the new line. It is possible that additional evidence has been published subsequent to the MED 2014 report for conditions other than FM. There may be benefit to searching for new evidence if such a search was not performed or documentation of lack of new evidence meeting pre-defined inclusion criteria.

Policy Component	Evidence Base	Public comment	Observations regarding link of evidence to proposal, Considerations and potential gaps
			Applicability of these finding to the broader range of conditions in the proposed policy needs to be considered.
Acupuncture	**AHRQ 2018 (Fibromyalgia)[12] (AMSTAR-2 100, Low RoB):** Included RCTs reporting follow-up of at least 1 month. 3 RCTs (2 traditional needle and 1 electrical stimulation acupuncture) versus sham.	No citations specific to acupuncture were evident	**The AHRQ 2018** report as cited only provides evidence related to FM. Acupuncture was associated with slightly greater improvements in function, but not pain, in the short and intermediate term compared with sham (SOE moderate for function, low for pain). No data on long-term effects were reported. Data on the persist effect (≥1 month post-intervention) of acupuncture in patients with FM are limited; no evidence was included for the other proposed conditions. The applicability of these finding to the broader range of conditions in the proposed policy needs to be considered. Additional search for evidence that may be applicable to a broader range of conditions should be considered.

AHRQ = Agency for Healthcare Research and Quality; AMSTAR-2: A MeaSurement Tool to Assess systematic Reviews version 2; FM = fibromyalgia; RCT = randomized controlled trial; RoB = risk of bias; SOE = strength of evidence; SR = systematic review; UC = usual care.

Discussion

Chronic pain and its management are complex and there are a large number of chronic pain conditions to consider. There is a large complex research literature base devoted to better understanding aspects of chronic pain and chronic pain management including the benefits and harms of pharmacologic and non-pharmacologic treatments that continues to evolve. No single study or systematic review will likely provide definitive answers. Given the vast literature, use of recent methodologically rigorous systematic reviews to evaluate the overall benefits and harms of the treatments considered is logical. Formulation of such systematic reviews that encompass the broad range of conditions and interventions under consideration presents a challenge and the strengths and limitations of individual reviews as well as the quality of literature they contain need to be considered. A vast amount of literature was summarized by HERC staff across the 12 reviews/reports which encapsulated a broad range of chronic pain conditions and interventions; hundreds of individually critically appraised clinical studies, many of which were RCTs were included. The search process (e.g., whether or not Medline or other databases were searched), search criteria, and inclusion/exclusion criteria specific to the proposed policy were not clear in the minutes or proposal itself. It is therefore not possible to assess what may or may not have met specific inclusion criteria or the extent to which potentially eligible high quality evidence may have not been captured. Suggestions have been made to consider additional search for high quality SRs for specific areas (see Summary Tables). It should be acknowledged that is it is not possible or necessary to capture all SRs. Data for a SR that may be missed is likely to be captured in another SR; if the evidence base is robust, the addition of one or two new studies in a different SR is unlikely to change the overall conclusions. Overall the evidence summary done by HERC and provided in the March 2019 document was well done; an extensive evaluation of its accuracy was not within the scope of this report. Explicit links to specific policy components and populations being considered for expanded benefits were less clear.

A large number of the cited reviews included patients with conditions (e.g., chronic low back pain) other than conditions under consideration (e.g., chronic pain secondary to trauma). Included studies were focused on adult populations. The proposed policy does not appear to specify a restriction to adults or describe whether children or adolescents would be included. Reviews/reports included generally described benefits and harms across various included patient conditions. Extrapolation of the benefits and harms of a given intervention for one condition to other conditions may or may not be appropriate. It is possible that persons with different conditions may respond differently to any given treatment based on the type of pain and/or underlying etiology and comorbid conditions. For some of the non-pharmacologic interventions evidence on fibromyalgia was limited and for the other conditions not available and/or difficult to assess given the vague definition of the pain condition (e.g., “other chronic pain”). For conditions such as chronic post-procedural pain, patient response to various treatments may depend on whether the persistent pain presents more like fibromyalgia or osteoarthritis or another condition. HERC will need to carefully consider the extent to which findings from some

of the cited reviews are applicable to the patient populations under consideration for expanded benefits, together with the relative costs and harms of the various interventions.

The proposed treatments were most frequently compared with placebo, usual care, wait list or similar non-active comparators. Very limited high quality evidence for opioids versus non-opioids or versus non-pharmacologic treatment is available, thus comparisons of these interventions to each other are indirect, precluding firm conclusions.

The use of opioids in FM, particularly long-term, is controversial given the lack of high quality trials. Data on the efficacy and safety of opioids in FM is likely sparse and primarily from observational studies.[28] There is some evidence to support the theory that patients with nociplastic (central sensitization) pain such as FM may respond differently than those with other types of pain; this may in part explain observed lack of effectiveness and poorer outcomes among those using opioids long term versus those not receiving opioids in some studies. Search for and description of relevant studies and evidence-based clinical guidelines is suggested for the proposed exclusion.

A cornerstone of evidence-based practice is the critical appraisal of clinical research to facilitate informed interpretation of the literature and integration of this interpretation with clinical expertise to facilitate decision making. The overall strength of evidence was low or very low (insufficient) strength of evidence for some of the proposed therapies and guideline suggestions, particularly those related to potential benefits and harms of reduction of opioid reduction and tapering and for some of the nonpharmacologic treatments. In these situations, clarification of the strengths and limitations of the literature should be combined with consideration of expert perspectives on how to best apply the evidence to clinical decision making.

The 2016 CDC guidelines[16] form the basis of some of the proposed recommendations, particularly related to long term opioid use and tapering. Its development was based on the GRADE process and included consideration of evidence from high quality systematic reviews, assessment of the balance of benefits and harms, values and preferences and resource allocation as well as input from subject matter experts and perspectives across a wide range of stakeholders. Evaluation of it, the related evidence base, implications and consequences related to its implementation are not within the scope of this report. The CDC guidelines have been controversial and there has been confusion regarding their interpretation and implementation and concern regarding potential misapplication of them and unintended consequences. Some of these concerns have been reflected in both public and expert comments received on the proposed HERC policy. A recent consensus panel report[18] and a perspective on the CDC guidelines' intent by its authors[17] provide some examples of implementation policies and practices that are not consistent with intent of the guidelines. A cited example relates to the recommendation that "clinicians should ….avoid *increasing* dosage to ≥90 MME (morphine milligram equivalents/day or carefully justifying a decision to titrate dosage to ≥90 MME/day)." Use of this statement to justify abruptly stopping opioid prescriptions or coverage is cited as a mis-

implementation and not consistent with the CDC's intent; the CDC statement does not address or suggest discontinuation of opioids already prescribed at higher doses.[17,18] Similarly, the CDC guideline does not advocate forced tapering or tapering to a given hard target during a specific time frame but does include guidance on when tapering may be appropriate and that it should be a collaborative effort with patients done in conjunction with maximizing non-opioid and non-pharmacologic treatments. In light of these examples and other points made in these articles, the HERC may wish to evaluate the extent to which the proposed policy follows the intent of the CDC guidelines.

Other observations

Public and expert comment primarily focused on concerns regarding limiting access to opioids, unintended effects of opioid tapering and cessation and application of the 2016 CDC guidelines on opioid use. Based on cursory review of CPTF and VbBS minutes; it appears that revisions to the proposed policy (e.g., removal of a 12 month requirement for tapering) were made and that the composition of and input to the CPFT were changed to include additional expertise in pain management. General review of comments suggest that there has been some confusion regarding the intent, scope and limitations of the proposed guidelines/policy and conditions to be included for expanded benefits. The proposed policies were not clearly written; context, including context regarding implementation, and re-organization may be needed to facilitate understanding of the proposal. Again, the HERC may benefit from evaluation of the extent to which the proposed policy and any plans for implementation align with the intent and nuances of the CDC guidelines and provide clarification regarding implementation and limitations of the proposed policy consistent with the CDC's intent.

The guidelines stipulate that treatment delivery by "licensed provider". For some of the interventions, e.g., teachers of Yoga, Tai Chi, and Qigong, providers are not licensed and it is unlikely that most licensed healthcare providers are certified/trained in these practices.

Limitations of this report

This report focused on rapid evaluation of the evidence base cited in the March 2019 document to identify areas where evidence may not align with proposed expansion of benefits for the five conditions under consideration. This report does not formally evaluate the proposed guidelines/policy changes or their potential cost, impact or challenges to implementation. This report doesn't constitute an evaluation of the HERC process or development of the proposed guidelines. No formal literature searching was done.

Forth-coming evidence

Three concurrent AHRQ-funded comparative effectiveness reviews are currently in process. All have or will include consideration of input from technical/clinical experts and will be posted for public comment. Links to the protocols for these reviews are listed below.

Nonopioid Pharmacologic Treatments for Chronic Pain
https://effectivehealthcare.ahrq.gov/topics/nonopioid-chronic-pain/protocol
The purpose of this report is to evaluate the effectiveness and comparative effectiveness as well as harms of oral or topical non-opioid pharmacologic agents used for chronic pain management at short, intermediate and long-term.

Opioid Treatments for Chronic Pain
https://effectivehealthcare.ahrq.gov/topics/opioids-chronic-pain/protocol
The rationale for this evidence review update is in part related to concerns regarding possible unintended consequences of implementing the 2016 CDC guideline on chronic pain management (e.g., worsened mood and increased suicidality, worsening quality of life or function and increased use of illicit opioids) in addition to the need to evaluate new evidence. The scope includes evaluation of short and long-term benefits and harms of opioid use as well as dosing strategies, discontinuation and tapering of opioid therapy from randomized and observational studies. The review will also provide context with regard to clinician and patient values and preferences.

Systematic Review Update: Noninvasive Nonpharmacologic Treatments for Chronic Pain
https://effectivehealthcare.ahrq.gov/topics/noninvasive-nonpharm-pain-update/protocol
This update will incorporate research published subsequent to the 2018 AHRQ report cited in the OHA proposal.

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HERC Proposed Chronic Pain Policy Evidence Appraisal – Final Report Appendix

Aggregate Analytics, Inc.

Final Report APPENDIX

April 29, 2019

Contents

Appendix Table 1. Overview of included evidence reports used to inform the proposed policy under consideration by OHA.

Evidence base Conditions Treatments	Overview of Results	Authors' Conclusion
Opioid vs. Nonopioid Therapies		
Busse 2018 High quality SR N = 96 RCTs 61% female, mean age 58 years 76 (79%) trials reported receiving industry funding Only 21/96 trials addressed mean or median MMED of ≥90 mg 6 mixed CP conditions 25 neuropathic pain 32 nociceptive pain 33 central sensitization (e.g., fibromyalgia) **Opioids vs. placebo (76 RCTs)** • OA (24) • LBP, NOS (24) • Painful diabetic neuropathy (8) • Mixed neuropathic/non-neuropathic conditions (4) • RA (2) • Postherpetic neuralgia (2) • Postherpetic neuralgia and painful diabetic neuropathy (2) • Painful polyneuropathy (2) • Fibromyalgia (2) • Chronic neck pain, NOS (1) • Chronic posttraumatic pain, NOS (1) • Phantom limb pain (1) • Post-traumatic neuralgia (1) • Mixed neuropathic conditions (1) • Parkinson's disease (1) **Opioids vs. NSAIDs (11 RCTs)** • OA (5)	Compared with placebo, opioids were associated with (1) small improvements in pain, physical functioning, and sleep quality; (2) unimportant improvements in social functioning; and (3) no improvements in emotional functioning or role functioning. Compared with placebo, opioids were associated with increased vomiting, drowsiness, constipation, dizziness, nausea, dry mouth, and pruritus. – The use of opioids compared with placebo was associated with significantly less pain (−0.69 cm on a 10-cm scale) and significantly improved physical functioning (2.04 of 100 points), but the magnitude of the association was small. Opioid use was significantly associated with increased risk of vomiting. Moderate- to low-quality evidence suggested that opioids were associated with similar improvements in pain and physical functioning compared with NSAIDs, tricyclic antidepressants, and synthetic cannabinoids and were associated with small improvements in pain but not physical functioning compared with anticonvulsants. *Additional Analyses*: Most eligible trials allowed for postrandomization titration of opioid dose, which precluded between-trial subgroup analyses of higher vs lower doses of opioids. In 6 RCTs that compared different doses of opioids, meta-regression of moderate-quality evidence showed no dose response for pain relief (P = .39), functional recovery (P = .22), or gastrointestinal adverse events (P = .12)	High quality evidence suggested that opioids (vs. placebo) may provide benefit (pain and physical function) for chronic noncancer pain, but the magnitude is likely to be small. Opioid use was significantly associated with increased risk of vomiting. Moderate- to low-quality evidence suggested that opioids were associated with similar improvements in pain and physical functioning compared with NSAIDs, tricyclic antidepressants, and synthetic cannabinoids and were associated with small improvements in pain but not physical functioning compared with anticonvulsants. Opioids were associated with less pain relief during longer trials perhaps as a result of opioid tolerance or opioid induced hyperalgesia (a condition in which opioid use results in hypersensitivity to painful stimuli). A reduced association with benefit over time might lead to prescription of higher opioid doses and consequent harms. Moreover, long-term opioid therapy causes physical dependence, and symptoms of opioid withdrawal (including pain) resolve when opioids are resumed. Therefore, patients may continue to use opioids after analgesic benefits have waned to avoid withdrawal. Although clinical practice guidelines discourage long term opioid therapy for headache, fibromyalgia, or axial low back pain, we found no evidence for differential condition-specific associations with neuropathic, nociceptive, or

• LBP, NOS (3) • Fibromyalgia (1) • Mixed neuropathic/non-neuropathic conditions (1) • Postherpetic neuralgia (1) **Multiple comparisons (5 RCTs)** • Postherpetic neuralgia (1) and pain diabetic neuropathy (1) • Lumbar radiculopathy (1) • Mixed neuropathic pain conditions (1) • OA (1) **Opioids vs. Tricyclic Antidepressants (3 RCTs)** • Chronic noncancer pain, NOS (3) **Opioids vs. Anticonvulsants (2 RCTs)** • Painful diabetic neuropathy (1) • Mixed neuropathic/non-neuropathic conditions (1) **Opioids vs. Synthetic Cannabinoids (1 RCT)** • Chronic neuropathic pain, NOS **Opioids vs. Usual Care (1 RCT)** • OA Referenced AHRQ SR (Chou et al.) on opioids for chronic pain.	No additional subgroup analyses or meta-regressions proved credible. Associations were independent of whether trials administered pure opioids or opioids combined with acetaminophen; subgroup analysis found 1 significant test of interaction (P = .002 for interaction), suggesting an association with improved role functioning with combination products, but with low credibility.	central sensitization conditions. Prior inferences may have been driven by systematic reviews focusing on average effects alone.*
Els 2017 (Cochrane) High quality SR N = 16 SRs, 14 included in meta-analysis (N=61 studies, 18,679 patients) 6 neuropathic pain 3 chronic LBP 2 hip or knee OA 2 unspecified chronic non-cancer pain 1 hip or knee OA or chronic LBP 1 phantom limb 1 rheumatoid arthritis Opioids vs. placebo Opioids vs. non-opioid active pharma comparator	There was a small but significantly increased risk of experiencing any adverse event with opioids compared to placebo (risk ratio (RR) 1.42, 95% confidence interval (CI) 1.22 to 1.66) as well as with opioids compared to a non-opioid active pharmacological comparator, with a similar risk ratio (RR 1.21, 95% CI 1.10 to 1.33). There was also a significantly increased risk of experiencing a serious adverse event with opioids compared to placebo (RR 2.75, 95% CI 2.06 to 3.67). Furthermore, the authors found significantly increased risk ratios with opioids compared to placebo for a number of specific adverse events: constipation, dizziness, drowsiness, fatigue, hot	There is good-quality evidence showing that side effects can occur in people with chronic non-cancer pain who use opioid medicines for longer than two weeks • Quality of included reviews: very good (9 or 10 out of 10) • Quality of evidence from studies: very low to moderate No mention of MMEDs A number of adverse events, including serious adverse events, are associated with the medium- and long-term use of opioids for chronic noncancer pain. The absolute event rate for any

	flushes, increased sweating, nausea, pruritus, and vomiting.	adverse event with opioids in trials using a placebo as comparison was 78%, with an absolute event rate of 7.5% for any serious adverse event. Based on the adverse events identified, clinically relevant benefit would need to be clearly demonstrated before long-term use could be considered in people with CNCP in clinical practice. The absence of data for many adverse events represents a serious limitation of the evidence on opioids.
Krebs 2018 RCT (N=240), SPACE trial Moderately low risk of bias Chronic Back Pain (65%) or Hip or Knee OA (35%); patients on long-term opioid therapy were excluded Opioids (immediate-release morphine, oxycodone, or hydrocodone/acetaminophen) vs. Nonopioids (acetaminophen (paracetamol) or a NSAID). Opioids were titrated to a maximum daily dosage of 100 morphine-equivalent (ME) mg. If dosages were titrated to 60 ME mg/d without a response, rotation to another opioid was considered before dosage escalation.	Groups did not significantly differ on pain-related function over 12 months (overall p=0.58), mean 12-month Brief Pain Inventory Interference was 3.4 for the opioid group and 3.3 for the nonopioid group (difference 0.1, 95% CI −0.5 to 0.7). Pain intensity was significantly better in the nonopioid group over 12 months (overall p=0.03), mean 12-month Brief Pain Inventory Severity was 4.0 for the opioid group and 3.5 for the nonopioid group (difference 0.5, 95% CI 0.0 to 1.0). Adverse medication-related symptoms were significantly more common in the opioid group over 12 months (overall p=0.03); mean medication-related symptoms at 12 months were 1.8 in the opioid group and 0.9 in the nonopioid group (difference 0.9, 95% CI 0.3 to 1.5).	Treatment with opioids was not superior to treatment with nonopioid medications for improving pain-related function over 12 months. Results do not support initiation of opioid therapy for moderate to severe chronic back pain or hip or knee osteoarthritis pain.
Opioid Tapering/Therapies to Promote Reduction		
MED 2018 Fair quality "rapid review" (previous MED report based on Frank et al. SR) NEW: 9 observational studies (all poor quality, N=32 to 1588) (2 pro cohort, 3 retro cohort, 4 case series) Adult patients (18 years and older) using opioids for chronic (6 months or longer) noncancer pain; specific conditions not specified [with the exception of one study of primarily LBP (59%), neck pain (14%) and polyarthralgia (10%)]; see	The previous MED report found very low-quality evidence that several types of interventions could be effective to reduce or discontinue long-term opioid therapy and that pain, function, and quality of life might improve with opioid dose reduction. Although many studies reported positive dose-reduction outcomes, the systematic review by Frank et al. rated the overall quality of the evidence as very low for the effectiveness of all interventions to reduce or discontinue long-term opioid therapy because of methodological	Based on Frank et al. SR below, same conclusions. Addition of 9 new, poor-quality studies does not change the rating of the overall quality of evidence (very low) and findings for most outcomes were consistent with previous evidence.

Appendix Table 2 below for more details regarding these studies; Also see SR by Frank et al. 2017 below 4 individualized tapering developed by health care providers in partnership with patients; 2 multidisciplinary pain programs; 2 in patients with and without substance use disorders (SUD) whose clinicians had discontinued their opioid therapy; 1 health plan-initiated dose reduction and risk mitigation program	limitations across studies and an absence of adequately powered randomized trials. 9 new studies published since the last reported were identified; these studies' findings for most outcomes were consistent with previous evidence. Because of their poor methodological quality, the new evidence did not change the rating of the overall quality of the evidence. Importantly, the preponderance of evidence from both the systematic review by Frank et al. and more recent studies indicates that tapering or discontinuation of opioid therapy is not associated with increased pain, and may be associated with reduced pain and improved functional outcomes. One study conducted within the VA did identify suicide risk among a group of patients with clinician-initiated discontinuation of opioid therapy. However, this study was also of poor methodological quality and the overall strength of evidence for this finding is very low.	
Frank 2017 High quality SR N = 67 studies (11 RCTS, 56 observational; N=12,546 patients) To synthesize studies of the effectiveness of strategies to reduce or discontinue long-term opioid treatment (LTOT) and patient outcomes after dose reduction among adults prescribed LTOT for chronic pain. **Chronic Pain NOS – patient on opioids** (24 total studies; 6 RCT, 7 pro cohort, 11 retro cohort) **Chronic Pain NOS** (16 total studies; 2 RCT, 2 pro cohort, 12 retro cohort) **Condition NOS** (5 total studies; 1 pro cohort, 4 retro cohort) **Chronic LBP** (4 total studies; 1 RCT, 1 pro cohort, 2 retro cohort)	Study quality was good for 3 studies, fair for 13 studies, and poor for 51 studies. Many studies reported dose reduction, but rates of opioid discontinuation ranged widely across interventions and the overall quality of evidence was very low. Among 40 studies examining patient outcomes after dose reduction (very low overall quality of evidence), improvement was reported in pain severity (8 of 8 fair-quality studies), function (5 of 5 fair-quality studies), and quality of life (3 of 3 fair-quality studies).	Very low quality evidence (overall poor quality suggests that several types of interventions may be effective to reduce or discontinue LTOT and that pain, function, and quality of life may improve with opioid dose reduction. Given the heterogeneity across interventions and the overall poor quality of studies, data do not currently support assessment of comparative effectiveness of the different models of care or opioid tapering protocols used in included studies. Furthermore, most of the included studies examined voluntary participation in a clinical program or research intervention. The findings may therefore not be generalizable to patients for whom LTOT is reduced or discontinued involuntarily.

Fibromyalgia (4 total studies; 1 RCT, 1 pro cohort, 2 retro cohort) **Chronic Pain on Narcotics** (2 total studies; 1 RCT, 1 retro cohort) Headache (2 retro cohorts) **Occupational Musculoskeletal/Spinal Disorder** (2 retro cohorts) **Work Injury** (1 retro cohort) **Brain Injury** (1 retro cohort) **Abdominal Pain** (1 retro cohort) **Inflammatory bowel disease** (1 retro cohort) **Other** (4 total studies, 1 pro cohort [detoxification from LTOT] and 3 retro cohorts [PCP-referred opioid discontinuation; on opioids; implantable drug delivery system] Interdisciplinary pain programs (31 studies, n=9915) Buprenorphine-assisted dose reduction (10 studies, n=470) Behavioral interventions (6 studies, n=238) Other outpatient programs (5 studies, n=1169) Detoxification (4 studies, n=200) Other interventional programs (4 studies, n=308) Ketamine-assisted dose reduction (4 studies, n=168) Acupuncture (3 studies, n=78)		Common themes across intervention types can provide insight into the program components that may provide effective support for opioid tapering. In the 3 good-quality trials of behavioral interventions and the 11 fair-quality studies of interdisciplinary pain programs, patients received multimodal care that emphasized nonpharmacologic and self-management strategies. Such care is consistent with expert guidelines for management of LTOT and chronic pain. In addition to the content of these interventions, the quantity of care provided is likely an important factor. Multidisciplinary care and close follow-up (at least weekly) were common attributes of evaluated programs in good- and fair-quality studies. Such team-based, intensive support would require additional resources to implement in primary care settings, where most opioid medications are prescribed.
Eccleston 2017 (Cochrane) High quality SR N = 5 RCTs (278 patients) 66% female; mean age 49.6 years Opioid users receiving an intervention vs. control (treatment as usual, active control, or placebo). The aim of the study had to include a treatment goal of dose reduction or cessation of opioid medicine. 3 mixed chronic pain conditions 1 chronic back or neck pain	**Bottom line** Based on the available evidence, we do not know the best method of reducing opioids in adults with chronic pain conditions. We found mixed results from a small number of studies included in this review. **Key results** No conclusions can be drawn from this small amount of information. Therefore, it is not clear whether these treatments decrease the amount of opioids in adults with chronic pain (primary outcome) or reduce pain intensity, physical ability	There is no evidence (i.e., insufficient evidence) for the efficacy or safety of methods for reducing prescribed opioid use in chronic pain. There is a small number of randomized controlled trials investigating opioid reduction, which means conclusions are limited regarding the benefit of psychological, pharmacological, or other types of interventions for people with chronic pain trying to reduce their opioid consumption. The findings to date are mixed: there were reductions in opioid consumption after intervention, and often in control groups too.

1 chronic musculoskeletal pain 2 CBT vs. treatment as usual 1 MORE vs. support group 1 Opioid taper support vs. treatment as usual 1 Electroacupuncture vs. sham	or mood (secondary outcomes). Three studies did include negative effects of their treatment, and two reported that the participants did not have anything negative happen to them because of the trial they were in. Non-randomized studies, not included in this review, do indicate that for many people intensive rehabilitation packages may bring about major reduction in opioid use. Reducing prescribed opioid use in chronic non-cancer pain is an important topic in need of more systematic research.	
Nonopioid Pharmacologic Therapy		
P&T Review Committee Jan 2019 (24 SRs, 10 RCTs) High quality "rapid review" **Fibromyalgia** **<u>SRs</u>** Pregabalin vs. placebo (2016 Cochrane SR, 8 RCT, N=3283; Cochrane) SNRIs vs. placebo (2018 Cochrane SR, 18 RCT, N=7903; 7 duloxetine, 9 milnacipran, 1 desvenlafaxine) Milnacipran vs. placebo (2015 Cochrane SR, included many of the same milnacipran studies (N=6, N=4238) as above 2018 Cochrane on SNRIs) Mirtazapine vs. placebo (2018 Cochrane SR, 3 RCTs, N=606) Various pharmacologic and nonpharmacological treatments in adult subgroups (2015 AHRQ SR, 34 RCTs and observational) Amitryptyline vs. cyclobenzaprine, fluoxetine, nortriptyline, and immediate release paroxetine (4	There is no moderate or high strength evidence for any pharmacological treatment compared to placebo or other therapy. Like many other conditions for chronic pain, evidence supporting benefit of long-term pharmacological treatment for fibromyalgia is limited, efficacy of pharmacotherapy is relatively modest, and clinical trials often document a large placebo response upon evaluation of symptom improvement. Pharmacological interventions with the most evidence of benefit include duloxetine, milnacipran, and pregabalin, but applicability to a broader population is limited. In many trials, patients with comorbid medical conditions, particularly mental health conditions, were excluded. Similarly, many patients with a placebo response during run-in periods were excluded from trials. The strongest available evidence for efficacy outcomes for fibromyalgia drugs was of low strength meaning there is limited confidence that the estimated effects in the studies reflect the true effect, and further research is likely to change the estimated effect.	There is low strength evidence that, compared to placebo, milnacipran, duloxetine or pregabalin may improve pain symptoms; evidence of benefit or harms for other pharmacological treatments (including tricyclic antidepressants, gabapentin, and tramadol) was insufficient. Adverse effects more common with pharmacologic treatment vs. placebo There is insufficient evidence on long-term use of pharmacological therapy for treatment of fibromyalgia, and it is unclear if modest improvements in pain outcomes would be sustained over time. The average duration of most trials was less than 3 months and few trials assessed outcomes beyond 6 months. There is insufficient evidence to determine relative efficacy of pharmacological treatment compared to non-pharmacological therapies. Guidelines for fibromyalgia recommend patient education and focus primarily on nonpharmacological treatments such as exercise to improve symptoms of fibromyalgia. Pharmacotherapy and other non-pharmacotherapy options (e.g., cognitive behavioral therapy,

RCTS), paroxetine vs. placebo (1 RCT) (2011 DERP report) Various others (mostly Cochrane reviews, 18 SRs; one SR each: MAOIs, SSRIs, cannabinoids, oral NSAIDs, antipsychotics, gabapentin, topiramate, lamotrigine, oxycodone, phenytoin, clonazepam, carbamazepine, lacosamide, valproic acid or valproate, antiepileptic drugs in children and adolescents, combination treatments [tramadol/acetaminophen, pregabalin/duloxetine, NSAIDs/benzodiazepines, amitriptyline/fluoxetine, amitriptyline/naproxen, amitriptyline/lidocaine, melatonin/antidepressant, carisoprodol/acetaminophen/caffeine, malic acid/magnesium, and MAOI/5-hydroxytryptophan]; 2 SRs: amitriptyline) **<u>10 RCTs</u>** Desvenlafaxine vs. placebo Desvenlafaxine vs. pregabalin vs. placebo Milnacipran vs. placebo Pregabalin vs. placebo Pramipexole vs. placebo ACT vs. pregabalin vs. waitlist CBT vs. amitriptyline/acetaminophen/ tramadol Pregabalin vs. pregabalin + milnacipran Cyclobenzaprine vs. placebo Memantine vs. placebo Amitriptyline vs. venlafaxine, paroxetine Tramadol vs. placebo No guidelines The primary focus of the evidence is on high quality systematic reviews and evidence-based guidelines. RCTs will be emphasized if evidence is lacking or insufficient from those preferred sources.		multicomponent therapy, acupuncture, hydrotherapy, meditative movement, and mindfulness-based stress reduction) are recommended as second-line treatment options. Guidelines note that benefits of pharmacological treatments are relatively modest and, as magnitude of benefits are approximately equivalent to incidence of adverse effects from treatment, risks of therapy should be weighed against potential benefits.
Nonpharmacologic Interventions		

MED 2014 Fair quality "rapid review" (Prior reported based on Bunker et. al 2013, primarily based on 2003 Cochrane review and CADTH 2011) <u>2 SRs for this update</u>: 1 fair-quality SR (total 14 SRs and MAs); only 6 SRs on pain summarized here†: Chronic pain NOS (1 SR) Chronic LBP (2 SRs) Subacute LBP (1 SR) Neck/shoulder pain (1 SR) Fibromyalgia (1 SR) 1 good-quality Cochrane SR (41 RCTs) Chronic LBP Multidisciplinary pain programs (MPPs) vs. standard care	**Prior report:** There is low strength of evidence that there are no significant differences in terms of pain relief between MPPs and standard care. There is low strength of evidence that MPPs are associated with greater functional improvements than standard care. Overall, the evidence described improvements in function among those receiving multidisciplinary care, but the magnitude of benefit over standard care was inconsistently described. Similarly, the components of a 'standard care' treatment plan were not often specified within the literature, which may partially account for the heterogeneity of findings **Update:** The conclusion from the two new SRs support the findings from the previous reports discussed in the 2013 MED report. The findings suggest that MPPs are effective at reducing pain intensity, disability, and sick absences, while increasing functionality and ability to return to work for individuals with chronic pain, low back pain, and/or fibromyalgia. Based on two low-quality trials, it is not possible to determine the effectiveness of MPPs for individuals with shoulder or chronic pain. These conclusions differ slightly from the 2013 MED report. The 2013 report relied on the 2003 Cochrane review as the studies were more thoroughly described than in the CADTH review (2011). However, the consistent findings from the recent fair- to good-quality systematic reviews by Momsen (2012) and Kamper (2014), coupled with the findings from the CADTH (2011) review, create a strong evidence base to support the effectiveness of MPPs for individuals with chronic pain.	Low strength of evidence of no significant differences in pain and greater functional improvements with MPPS vs. standard care; however, the magnitude of benefit over standard care for function was inconsistently described. New evidence from two SRs (fair- to good-quality) support previous findings (though they differ slightly) and suggest that MPPs are effective at reducing pain intensity, disability, and sick absences, while increasing functionality and ability to return to work for individuals with chronic pain, low back pain, and/or fibromyalgia.
AHRQ 2018 High quality SR **Fibromyalgia** (N=47 RCTs across 54 publications)	<u>In the short term</u>: Acupuncture (SOE moderate), CBT, Tai Chi, Qigong, and exercise (SOE low) were associated with slight improvements in function compared	Interventions that improved function and/or pain for at least 1 month (SOE low to moderate): • Exercise, CBT, myofascial release massage, Tai Chi, Qigong, acupuncture, MDR.

Exercise vs. usual care, etc. (N=21) and vs. pharma (N=1) **Psychological therapies** vs. usual care, etc. (N=10) and vs. pharma (N=3) and vs. exercise (N=5) **Physical Modalities** vs. usual care, etc. (N=2) **Manual Therapies** vs. usual care, etc. (N=2) **Mindfulness Practices** vs. usual care, etc. (N=2) **Mind-body Practices** vs. usual care, etc. (N=2) **Acupuncture** vs. usual care, etc. (N=3) **Multidisciplinary rehabilitation (MDR)** vs. usual care, etc. (N=6) and vs. exercise (N=1) (Data on chronic low back pain, chronic neck pain, osteoarthritis, and chronic tension headache are not included here)	with an attention control, sham, no treatment, or usual care. Exercise (SOE moderate) and CBT improved pain slightly, and tai chi and qigong (SOE low) improved pain moderately in the short term. <u>At intermediate term</u>: For exercise (SOE moderate), acupuncture, and CBT (SOE low), the slight functional improvements persisted; they were also seen for myofascial release massage and multidisciplinary rehabilitation (SOE low); pain was improved slightly with multidisciplinary rehabilitation in the intermediate term (SOE low). <u>In the long term</u>: Small improvements in function continued for multidisciplinary rehabilitation but not for exercise or massage (SOE low for all); massage (SOE low) improved long-term pain slightly, but no clear impact on pain for exercise (SOE moderate) or multidisciplinary rehabilitation (SOE low) was seen. Short-term CBT was associated with a slight improvement in function but not pain compared with pregabalin.	Most effects were small. Long-term evidence was sparse. There was no evidence suggesting serious harms from any of the interventions studied; data on harms were limited.
Geneen 2017 (Cochrane) High quality SR [21 SRs, 264 studies (N=19,642) included in qualitative analysis] RA, OA, fibromyalgia, LBP, intermittent claudication, dysmenorrhea, mechanical neck disorder, spinal cord injury, post-polio syndrome, and patellofemoral pain; none of the reviews assessed “chronic pain” or “chronic widespread pain” as a general term or specific condition. Exercise versus no exercise/minimal intervention	The quality of the evidence examining physical activity and exercise for chronic pain is low. This is largely due to small sample sizes (<50) and potentially underpowered studies. A number of studies had adequately long interventions, but planned follow-up was limited to less than one year in all but six reviews. There were some favorable effects in reduction in pain severity and improved physical function, though these were mostly of small to-moderate effect, and were not consistent across the reviews. There were variable effects for psychological function and quality of life.	The available low quality evidence suggests physical activity and exercise is an intervention with few adverse events that may improve pain severity and physical function, and consequent quality of life. However, further research is required and should focus on increasing participant numbers, including participants with a broader spectrum of pain severity, and lengthening both the intervention itself, and the follow-up period.

Interventions: aerobic, strength, flexibility, range of motion, core or balance training programs, Yoga, Pilates, and Tai hi.		
Crawford 2016 High quality SR (N=67 RCTs; 32 included in meta-analysis) Pain the general population (those that would seek help from a general practitioner) including musculoskeletal pain, headache, visceral pain, chronic pain (fibromyalgia, spinal cord pain, venous insufficiency) Massage (alone or in combination) vs. sham, no treatment or active comparator	Sixty high quality and seven low quality studies were included in the review. Results demonstrate massage therapy effectively treats pain compared to sham (SMD, – 0.44], no treatment (SMD, – 1.14), and active (SMD, – 0.26) comparators. Compared to active comparators, massage therapy was also beneficial for treating anxiety (SMD, – 0.57) and health-related quality of life (SMD, 0.14).	Massage therapy may be beneficial, with minimal safety concerns, for treating various pain and function-related outcomes in pain populations. Specifically, results demonstrate the efficacy of massage therapy compared to no treatment (strongly recommended) and sham and active comparators (weakly recommended vs. both). Compared to active comparators, massage therapy was also beneficial for treating anxiety and health-related quality of life (weakly recommended).
Geneen 2015 (9 RCTs; 8 included in meta-analyses) 2 Chronic (generalized) pain 4 Chronic back pain 1 Fibromyalgia 5 Education vs. usual care 4 comparison of difference Educational interventions	Pooled data from five studies, where the comparator group was usual care, showed no improvement in pain or disability. In the other four studies, comparing different types of education, there was no evidence for an improvement in pain; although, there was evidence (from one study) of a decrease in disability with a particular form of education—pain neurophysiology education (PNE). Post-hoc analysis of psychosocial outcomes reported in the studies showed evidence of a reduction in catastrophizing and an increase of knowledge about pain following PNE.	The evidence base is limited by the small numbers of studies, their relatively small sample sizes, and the diversity in types of education studied (i.e., insufficient evidence) It therefore remains sensible to recommend that education be delivered *in conjunction* with other pain management approaches as we cannot confidently conclude that education alone is effective in reducing pain intensity or related disability in chronic pain in adults.
Williams 2017 (42 RCTs, 35 provided data (N=4788)) Chronic pain (excluding headache) CBT vs. usual care/waitlist or vs. active controls Behavioral therapy vs active controls	Overall there is an absence of evidence for behavior therapy, except a small improvement in mood immediately following treatment when compared with an active control. CBT has small positive effects on disability and catastrophizing, but not on pain or mood, when compared with active controls. CBT has small to moderate effects on pain, disability, mood and catastrophizing immediately	CBT is a useful approach to the management of chronic pain. Benefits of CBT emerged almost entirely from comparisons with treatment as usual/waiting list, not with active controls. CBT, but not behavior therapy, has weak effects on pain improvement (immediately post-treatment only) and has small effects on disability (with some maintenance at six months) when compared with treatment as usual/waiting list.

	post-treatment when compared with treatment as usual/waiting list, but all except a small effect on mood had disappeared at follow-up. At present there are insufficient data on the quality or content of treatment to investigate their influence on outcome. The quality of the trial design has improved over time but the quality of treatments has not.	CBT is effective in altering mood and catastrophizing outcomes, when compared with treatment as usual/waiting list, with some evidence that this is maintained at six months; behavior therapy has no effects on mood, but showed an effect on catastrophizing immediately post-treatment.

ACT = acceptance and commitment therapy; AHRQ = Agency for Healthcare Research and Quality; CBT = cognitive behavioral therapy; CI = confidence interval; LBP = low back pain; LTOT = long-term opioid therapy; MA = meta-analysis; MAOI = monoamine oxidase inhibitor; MDR = multidisciplinary rehabilitation; MMED = morphine milligram equivalent dosage; MORE = Mindfulness-oriented recovery enhancement; MPPs: Multidisciplinary pain programs; NOS = not otherwise specified; NSAIDS = non-steroidal anti-inflammatory drugs; OA = osteoarthritis; OHA = Oregon Health Authority; PCP = primary care provider; PNE = pain neurophysiology education; pro = prospective study design; RA = rheumatoid arthritis; RCT = randomized controlled trial; retro = retrospective study design; SMD = standardized mean difference; SOE = strength of evidence; SNRIs = serotonin-norepinephrine reuptake inhibitors; SR = systematic review; SSRIs = selective serotonin reuptake inhibitors; TIVR: Therapeutic Interactive Voice Response

*According to the authors: "the limitations of calculating the average benefit associated with opioids are (1) the assumption that all patients experience comparable analgesia and (2) lack of consideration for the distribution around the mean and the proportion of patients who achieve the minimally important difference. Therefore, we converted the average effects to the proportion of responders. Based on a prior study, some patients may find the modeled proportion of 12% for achieving the minimally important difference for pain relief warrants a trial of treatment with opioids."

†The following is stated in the report: "The other included reviews assessed functionality, hospitalization, and self-efficacy in patients with brain injury, hip fracture, hip and joint replacement, mental illness, motor neuron disease, and stroke, and are not summarized in this report."

Appendix Table 2. Overview of newly identified observational studies cited in the MED 2018 update report

Study	Design	Setting (Country)	Population	Intervention	Opioid length of use	Baseline opioid dose
Nine new observational studies in MED 2018 report (all poor quality)						
Gilliam et al., 2018	Prospective cohort	Pain clinic (US)	N=285 Specific pain conditions NR	Intensive, outpatient interdisciplinary rehabilitation program focusing on functional restoration in patients using (n=142) and not using (n=143) opioids at baseline	mean 5.8 years	mean MME 66.2 mg, median MME 40 mg
Thakral et al., 2018	Prospective cohort	Group Health clinics (WA, US)	N=1588 Specific pain conditions NR	opioid risk reduction initiatives for chronic opioid therapy patients in 2 phases (n=935) vs. non-GH clinics (n=653)	NR	mean daily MME 58 mg
McCann et al., 2018	Retrospective cohort	1 rural PCP practice (US)	N=32 • LBP 59% • neck 14% • polyarthralgia 10% • upper back 7% • shoulder, knee, peripheral neuropathy 3% each	Structured monitoring plan; options to continue opioids or wean off opioids	NR	Mean MME 24.98 mg (overall); 30.61 mg (those who remained on opioids); 17.01 mg (those who weaned off)
McPherson et al., 2018	Retrospective cohort	VA Health Systems (US)	N=600 Specific pain conditions NR	Discontinuation of opioid therapy by a clinician (15% patient-initiated) in patients with (n=300) vs. without (n=300) substance abuse disorder	NR	Average daily dose 75.8 mg MME
Oldfield et al., 2018	Retrospective cohort	VA Health Systems (US)	N=105 Specific pain conditions NR	Opioid Reassessment Clinic (ORC): referred and successfully received (n=66) vs. did not receive (n=39) a tapering appointment	NR	MME median 85 mg (intervention) vs. 60 mg (control)
Darnall et al., 2018	Case series	Community pain clinics (US)	N=110 Specific pain conditions NR	Physicians partnered with patients to initiate slow, individually designed taper.	Median 6 years	median 288 mg

Demidenko et al., 2017	Case series	VA Health Systems (US)	N=509 Specific pain conditions NR	Discontinuation of opioid therapy by a clinician (due to aberrant behavior 75%, safety concerns 7%).	NR	Mean MME 75.7 mg
Guildford et al., 2018	Case series	Specialty pain service (UK)	N=452 Specific pain conditions NR	4-week, residential, interdisciplinary, group-based pain management program	Median *pain* duration 8.7 years	Mean MME 64.6 mg; Median MME 25 mg; 16% taking MME ≥120 mg/24 hours
Rivich et al., 2018	Case series	Single center (US)	N=147 Specific pain conditions NR	Opioid Safety Initiative (education, monitoring, safe prescribing)	NR	median 315 mg; all taking ≥200 mg MME,

GH = Group Health; LBP = low back pain; NR = not reported; MME = morphine milligram equivalent; PCP = primary care provider; UK = United Kingdom; US = United States; VA = Veterans' Affairs.

Risk of Bias Assessment/Study Quality

Each study was rated against pre-set criteria that resulted in a Risk of Bias (RoB) assessment; details of those assessments are presented Appendix Tables 4, 6 and 7. The criteria for assessing risk of bias for studies on therapy (Appendix Table 3) (note: for this report, this applies only to the randomized controlled trial by Krebs, et al. 2018) and for systematic reviews and meta-analyses (Appendix Table 5) are described below.

Appendix Table 3. Risk of bias criteria for studies on therapy*

Risk of Bias	Studies of Therapy*	
	Study design	**Criteria***
Low risk: Study adheres to commonly held tenets of high quality design, execution and avoidance of bias	Good quality RCT	Random sequence generation Statement of allocation concealment Intent-to-treat analysis Blind or independent assessment for primary outcome(s) Co-interventions applied equally F/U rate of 80%+ and <10% difference in F/U between groups Controlling for possible confounding‡
Moderately low risk: Study has potential for some bias; study does not meet all criteria for class I, but deficiencies not likely to invalidate results or introduce significant bias	Moderate quality RCT	Violation of one or two of the criteria for good quality RCT
	Good quality cohort	Blind or independent assessment for primary outcome(s) Co-interventions applied equally F/U rate of 80%+ and <10% difference in F/U between groups Controlling for possible confounding‡
Moderately High risk: Study has significant flaws in design and/or execution that increase potential for bias that may invalidate study results	Poor quality RCT	Violation of three or more of the criteria for good quality RCT
	Moderate or poor quality cohort	Violation of any of the criteria for good quality cohort
	Case-control	Any case-control design
High risk: Study has significant potential for bias; lack of comparison group precludes direct assessment of important outcomes	Case series	Any case series design

* Additional domains evaluated in studies performing a formal test of interaction for subgroup modification (i.e., HTE) based on recommendations from Oxman and Guyatt[3]:
† Outcome assessment is independent of healthcare personnel judgment. Reliable data are data such as mortality or re-operation.
‡ Authors must provide a description of robust baseline characteristics, and control for those that are unequally distributed between treatment groups.

Appendix Table 4. Risk of Bias assessment: Krebs et al. 2018 RCT on opioid vs. nonopioid therapy for fibromyalgia

Methodological Principle	Krebs et al. 2018
Study design	
Randomized controlled trial	■
Prospective Cohort Study	
Retrospective Cohort Study	
Prospective Case Series	
Retrospective Case Series	
Random sequence generation*	Yes
Concealed allocation*	No‡
Intention-to-treat*	Yes
Independent/blind assessment	Yes
Co-interventions applied equally	Yes (see below)§
Complete follow-up of ≥80%	Yes (all timepoints)
<10% difference in follow-up between groups	Yes (all timepoints)
Controlling for possible confounding†	Yes**
Risk of Bias	**Moderately Low**

*Applies only to randomized controlled trials

†Groups must be comparable on baseline characteristics or evidence of control for confounding present.

‡Approximately 1 week after the enrollment visit, patients met with the study clinical pharmacist, who initiated random group assignment using a programmed study application that automatically assigned the next unused position in the randomization table. This process simultaneously informed the pharmacist and patient of group assignment. EHR documentation informed patients' primary care clinicians of study participation and group assignment. Study medications were visible in the EHR.

§To maximize applicability to primary care, the trial was designed to be pragmatic. Eligibility criteria facilitated enrollment of diverse patients from primary care. Interventions were delivered with flexibility in medication selection and dosage. Patients were allowed to participate in nonpharmacological pain therapies outside of the study and were encouraged to complete outcome assessments regardless of their participation in the active interventions. Patients were instructed to receive medications for back, hip, or knee pain only from the study.

**They controlled for smoking which was unbalanced at baseline (21% vs. 11% for opioid vs. non-opioid groups, respectively). Employment was different between groups also (opioid vs. nonopioid): employed for wages, 42% vs. 26%; retried, 36% vs. 47%; however it is unclear how important a factor this might be.

Appendix Table 5. AMSTAR Checklist (modified) for quality assessment of systematic reviews and meta-analyses.

1.	**Was there duplicate study selection and data extraction?** *There should be at least two independent data extractors and a consensus procedure for disagreements should be in place.*
2.	**Was a comprehensive literature search performed?** *At least two electronic sources should be searched. The report must include years and databases used (e.g. PUBMED, EMBASE, etc.). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided.*
3.	**Were any restrictions applied regarding inclusion of publications (i.e. publication status, language, etc.)?*** *The authors should state that they searched for reports regardless of their publication type. The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status, language etc*
4.	**Was the scientific quality of the included studies assessed and documented?** *Study quality should be assessed utilizing standard assessment tools for randomized trials (e.g. Cochrane Risk of Bias Tool).*
5.	**Was the scientific quality of the included studies used appropriately in formulating conclusions?** *The results of the methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations.*
6.	**If meta-analysis was conducted, were the methods used to combine the findings of studies appropriate (i.e. was it sensible to combine)?** *For pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e. Chi-squared test for homogeneity, I^2). If heterogeneity exists, a random effects model should be used.*
7.	**Was the likelihood of publication bias assessed?** *An assessment of publication bias should be included through graphical aids (e.g., funnel plot) and/or statistical tests (e.g., Egger regression test).*
8.	**Was the conflict of interest explicitly stated?** *Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.*

*Authors were given credit if they clearly described and gave a rationale for the exclusion criteria for publications; given the vast scope of these reviews it is logical that restrictions will be required.

Appendix Table 6. AMSTAR ratings for systematic review and meta-analyses of pharmacological therapies

	Opioids					Non-opioids
	Busse 2018	**Eccleston 2017 (Cochrane)**	**Els 2017 (Cochrane)**	**Frank 2017**	**MED 2018**	**P&T Review Committee 2019**
1. Was there duplicate study selection and data extraction?	Yes (1)	Yes (1)	Yes (1)	Yes (1)	No (0)*	No (0)*
2. Was a comprehensive literature search performed?	Yes (1)	Yes (1)	Partly (0.5)†	Yes (1)	Partly (0.5)‡	Yes (1)
3. Were any restrictions applied regarding inclusion of publications (i.e. publication status, language, etc.)?	No (1)	No (1)	No (1)	No (1)	No (1)	No (1)
4. Was the scientific quality of the included studies assessed and documented?	Yes (1)	Yes (1)	Yes (1)	Yes (1)	Yes (1)	Yes (1)
5. Was the scientific quality of the included studies used appropriately in formulating conclusions?	Yes (1)	Yes (1)	Yes (1)	Yes (1)	Yes (1)	Yes (1)
6. If meta-analysis was conducted, were the methods used to combine the findings of studies appropriate (i.e. was it sensible to combine)?	Yes (1)	N/A	Yes (1)	Yes (1)	N/A	Yes (1)
7. Was the likelihood of publication bias assessed?	Yes (1)	Yes (1)	No (0)	Partly (0.5)§	No (0)	No (0)
8. Was the conflict of interest explicitly stated?	Yes (1)	Yes (1)	Yes (1)	Yes (1)	Yes (1)	Yes (1)
TOTAL SCORE (%) (RoB)	100 (Low)	100 (Low)	81.3 (Low)	93.8 (Low)	64.3 (Moderate)	75 (Low)

RoB = risk of bias; "Low" = >70% points; "Moderate" = 50-70% points; "High" = <50% points; percentage points were calculated by dividing the total points by the number of questions; responses with N/A were no included in the final percentage calculation.
N/A = not applicable.
*No statements about either the study selection or data extraction process were included in the report.
†Only Cochrane systematic reviews were sought. However, the purpose of the review was to summarize other Cochrane reviews.
‡Only searched Ovid MEDLINE
§Authors state that publication bias may have limited the evidence that was available for the review, but did not formally evaluate/assess it.

Appendix Table 7. AMSTAR ratings for systematic review and meta-analyses of nonpharmacological therapies

	AHRQ 2018	Crawford 2016	Geneen 2017 (Cochrane)	Geneen 2015	MED 2014	Williams 2017
1. Was there duplicate study selection and data extraction?	Yes (1)	Yes (1)	Yes (1)	Partly (0.5)*	No (0)†	Partly (0.5)‡
2. Was a comprehensive literature search performed?	Yes (1)	Yes (1)	Partly (0.5)§	Yes (1)	Yes (1)	Yes (1)
3. Were any restrictions applied regarding inclusion of publications (i.e. publication status, language, etc.)?	No (1)	No (1)	No (1)	No (1)	No (1)	No (1)
4. Was the scientific quality of the included studies assessed and documented?	Yes (1)	Yes (1)	Yes (1)	Yes (1)	Partly (0.5)**	Yes (1)
5. Was the scientific quality of the included studies used appropriately in formulating conclusions?	Yes (1)	Yes (1)	Yes (1)	Yes (1)	Yes (1)	Yes (1)
6. If meta-analysis was conducted, were the methods used to combine the findings of studies appropriate (i.e. was it sensible to combine)?	Yes (1)	Yes (1)	Yes (1)	Yes (1)	N/A	Yes (1)
7. Was the likelihood of publication bias assessed?	Yes (1)††	Yes (1)	Yes (1)	Yes (1)††	No (0)	No (0)
8. Was the conflict of interest explicitly stated?	Yes (1)	Yes (1)	Yes (1)	Yes (1)	Yes (1)	Yes (1)
TOTAL SCORE (%) (RoB)	100 (Low)	100 (Low)	93.8 (Low)	93.8 (Low)	64.3 (Moderate)	81.3 (Low)

RoB = risk of bias; "Low" = >70% points; "Moderate" = 50-70% points; "High" = <50% points; percentage points were calculated by dividing the total points by the number of questions; responses with N/A were no included in the final percentage calculation.
N/A = not applicable.
*Only dual review at Full Text not at Title/Abstract.
†Unclear; only state that "staff" identified several reviews but do not indicate the number of reviewers involved at any step.
‡Study selection was dual reviewed but data abstraction process was unclear.
§Only Cochrane systematic reviews were sought. However, the purpose of the review was to summarize other Cochrane reviews.
**The quality of the reviews is mentioned but no methods reported or documentation showing how the quality ratings were reached.
††Author's indicate that assessment of publication bias was not possible but was considered.

Appendix Table 8. Literature cited by public commenters to be reviewed by OHA

1. Affairs DoV. VA/DoD clinical practice guideline for opioid therapy for chronic pain. Tapering and Discontinuation of Opioid Therapy. Washington, DC: Dept of …; 2017.
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8. Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain--United States, 2016. Jama. 2016 Apr 19;315(15):1624-45. doi: 10.1001/jama.2016.1464. PMID: 26977696.
9. Edlund MJ, Martin BC, Russo JE, et al. The role of opioid prescription in incident opioid abuse and dependence among individuals with chronic noncancer pain: the role of opioid prescription. Clin J Pain. 2014 Jul;30(7):557-64. doi: 10.1097/ajp.0000000000000021. PMID: 24281273.
10. Kim J, Lee KS, Kong SW, et al. Correlations Between Electrically Quantified Pain Degree, Subjectively Assessed Visual Analogue Scale, and the McGill Pain Questionnaire: A Pilot Study. Ann Rehabil Med. 2014 Oct;38(5):665-72. doi: 10.5535/arm.2014.38.5.665. PMID: 25379496.
11. Macfarlane GJ, Kronisch C, Dean LE, et al. EULAR revised recommendations for the management of fibromyalgia. Ann Rheum Dis. 2017 Feb;76(2):318-28. doi: 10.1136/annrheumdis-2016-209724. PMID: 27377815.
12. Manhapra A, Arias AJ, Ballantyne JC. The conundrum of opioid tapering in long-term opioid therapy for chronic pain: A commentary. Subst Abus. 2017 Sep 20:1-10. doi: 10.1080/08897077.2017.1381663. PMID: 28929914.
13. Sullivan MD, Turner JA, DiLodovico C, et al. Prescription Opioid Taper Support for Outpatients With Chronic Pain: A Randomized Controlled Trial. J Pain. 2017 Mar;18(3):308-18. doi: 10.1016/j.jpain.2016.11.003. PMID: 27908840.
14. Thakral M, Walker RL, Saunders K, et al. Comparing Pain and Depressive Symptoms of Chronic Opioid Therapy Patients Receiving Dose Reduction and Risk Mitigation Initiatives With Usual Care. J Pain. 2018 Jan;19(1):111-20. doi: 10.1016/j.jpain.2017.09.006. PMID: 29038060.
15. Wang PP, Huang E, Feng X, et al. Opioid-associated iatrogenic withdrawal in critically ill adult patients: a multicenter prospective observational study. Ann Intensive Care. 2017 Sep 2;7(1):88. doi: 10.1186/s13613-017-0310-5. PMID: 28866754.

In the absence of clear search methodology and inclusion/exclusion criteria in the HERC proposal, the extent to which the studies listed in Appendix Table 9 below are relevant will need to be evaluated by the HERC. Some of these may have already been captured. A number of the reviews cited in the table below include chronic pain conditions other than the proposed conditions (e.g., neuropathic pain), however, given that many of the reviews included as evidence in the proposed policy had similar populations as part of their evidence base it might be worthwhile to consider the applicability of these studies.

Appendix Table 9. Additional citations of research we are aware of

1. Axon DR, Patel MJ, Martin JR, et al. Use of multidomain management strategies by community dwelling adults with chronic pain: evidence from a systematic review. Scand J Pain. 2019 Jan 28;19(1):9-23. doi: 10.1515/sjpain-2018-0306. PMID: 30375350.
2. Ball EF, Nur Shafina Muhammad Sharizan E, Franklin G, et al. Does mindfulness meditation improve chronic pain? A systematic review. Curr Opin Obstet Gynecol. 2017 Dec;29(6):359-66. PMID: 28961631.
3. Denneny D, Frawley HC, Petersen K, et al. Trigger Point Manual Therapy for the Treatment of Chronic Noncancer Pain in Adults: A Systematic Review and Meta-analysis. Arch Phys Med Rehabil. 2019 Mar;100(3):562-77. doi: 10.1016/j.apmr.2018.06.019. PMID: 30025997.
4. Derry S, Bell RF, Straube S, et al. Pregabalin for neuropathic pain in adults. Cochrane Database Syst Rev. 2019 Jan 23;1:Cd007076. doi: 10.1002/14651858.CD007076.pub3. PMID: 30673120.
5. Fishbain DA, Pulikal A. Does Opioid Tapering in Chronic Pain Patients Result in Improved Pain or Same Pain vs Increased Pain at Taper Completion? A Structured Evidence-Based Systematic Review. Pain Med. 2018 Dec 28doi: 10.1093/pm/pny231. PMID: 30597076. [Epub ahead of print]
6. Hall A, Copsey B, Richmond H, et al. Effectiveness of Tai Chi for Chronic Musculoskeletal Pain Conditions: Updated Systematic Review and Meta-Analysis. Phys Ther. 2017 Feb 1;97(2):227-38. PMID: 27634919.
7. Huffman KL, Rush TE, Fan Y, et al. Sustained improvements in pain, mood, function and opioid use post interdisciplinary pain rehabilitation in patients weaned from high and low dose chronic opioid therapy. Pain. 2017 Jul;158(7):1380-94. PMID: 28328578.
8. Hughes LS, Clark J, Colclough JA, et al. Acceptance and Commitment Therapy (ACT) for Chronic Pain: A Systematic Review and Meta-Analyses. Clin J Pain. 2017 Jun;33(6):552-68. PMID: 27479642.
9. Ju ZY, Wang K, Cui HS, et al. Acupuncture for neuropathic pain in adults. Cochrane Database Syst Rev. 2017 Dec 2;12:Cd012057. doi: 10.1002/14651858.CD012057.pub2. PMID: 29197180.
10. Khoo EL, Small R, Cheng W, et al. Comparative evaluation of group-based mindfulness-based stress reduction and cognitive behavioural therapy for the treatment and management of chronic pain: A systematic review and network meta-analysis. Evid Based Ment Health. 2019 Feb;22(1):26-35. doi: 10.1136/ebmental-2018-300062. PMID: 30705039.
11. Macfarlane GJ, Kronisch C, Dean LE, et al. EULAR revised recommendations for the management of fibromyalgia. Ann Rheum Dis. 2017 Feb;76(2):318-28. PMID: 27377815.
12. Ottman AA, Warner CB, Brown JN. The role of mirtazapine in patients with fibromyalgia: a systematic review. Rheumatol Int. 2018 Dec;38(12):2217-24. PMID: 29860538.
13. Riediger C, Schuster T, Barlinn K, et al. Adverse Effects of Antidepressants for Chronic Pain: A Systematic Review and Meta-analysis. Front Neurol. 2017;8:307. doi: 10.3389/fneur.2017.00307. PMID: 28769859.
14. Sullivan MD, Turner JA, DiLodovico C, et al. Prescription Opioid Taper Support for Outpatients With Chronic Pain: A Randomized Controlled Trial. J Pain. 2017 Mar;18(3):308-18. PMID: 27908840.

15. Thakral M, Walker RL, Saunders K, et al. Impact of Opioid Dose Reduction and Risk Mitigation Initiatives on Chronic Opioid Therapy Patients at Higher Risk for Opioid-Related Adverse Outcomes. Pain Med. 2018 Dec 1;19(12):2450-8. PMID: 29220525.
16. Thornton JD, Goyat R, Dwibedi N, et al. Health-related quality of life in patients receiving long-term opioid therapy: a systematic review with meta-analysis. Qual Life Res. 2017 Aug;26(8):1955-67. doi: 10.1007/s11136-017-1538-0. PMID: 28255745.
17. Turner JA, Shortreed SM, Saunders KW, et al. Does association of opioid use with pain and function differ by fibromyalgia or widespread pain status? Pain. 2016 Oct;157(10):2208-16. PMID: 27643834.
18. Watson JA, Ryan CG, Cooper L, et al. Pain Neuroscience Education for Adults With Chronic Musculoskeletal Pain: A Mixed-Methods Systematic Review and Meta-Analysis. J Pain. 2019 Mar 1. pii: S1526-5900(18)30747-8. PMID: 30831273. [Epub ahead of print]
19. Wiffen PJ, Derry S, Bell RF, et al. Gabapentin for chronic neuropathic pain in adults. Cochrane Database Syst Rev. 2017 Jun 9;6:CD007938. doi: 10.1002/14651858.CD007938.pub4. PMID: 28597471.
20. Wylde V, Dennis J, Beswick AD, et al. Systematic review of management of chronic pain after surgery. Br J Surg. 2017 Sep;104(10):1293-306. PMID: 28681962.

Links to Protocols for AHRQ reviews currently in process that address chronic pain management strategies of relevance to OHA policy:

Systematic Review Update: Noninvasive Nonpharmacologic Treatments for Chronic Pain:
https://effectivehealthcare.ahrq.gov/topics/noninvasive-nonpharm-pain-update/protocol

Nonopioid Pharmacologic Treatments for Chronic Pain:
https://effectivehealthcare.ahrq.gov/topics/nonopioid-chronic-pain/protocol

Opioid Treatments for Chronic Pain:
https://effectivehealthcare.ahrq.gov/topics/opioids-chronic-pain/protocol

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Note: P&T review focused on drug effectiveness for treatment of fibromyalgia
Note: HERC review focused on guidelines and evidence for treatments of fibromyalgia and chronic pain syndromes

Study	Included/Excluded	Rational for Inclusion/Exclusion
1. Affairs DoV. VA/DoD clinical practice guideline for opioid therapy for chronic pain. Tapering and Discontinuation of Opioid Therapy. Washington, DC: Dept of …; 2017.	Included in HERC review	HERC staff: included in original CEBP opioid tapering report given to CPTF
2. Bennett RM, Kamin M, Karim R, et al. Tramadol and acetaminophen combination tablets in the treatment of fibromyalgia pain: a double-blind, randomized, placebo-controlled study. Am J Med. 2003 May;114(7):537-45. PMID: 12753877.	P&T review: Included; only briefly discussed due to significant risk of bias and limitations in the evidence	P&T review: This study was included in a Cochrane systematic review of combination pharmacotherapy for the treatment of fibromyalgia in adults (Thorpe et al. 2018). Evidence was graded as "very low" for all outcomes and comparisons due to high risk of bias.
3. Bennett RM, Schein J, Kosinski MR, et al. Impact of fibromyalgia pain on health-related quality of life before and after treatment with tramadol/acetaminophen. Arthritis Rheum. 2005 Aug 15;53(4):519-27. doi: 10.1002/art.21319. PMID: 16082646.	Excluded from P&T review	P&T review: This study was a secondary, post-hoc analysis of the same population studied in Bennett, et al. 2003. Due to significant risk of publication and reporting bias associated with post-hoc analyses, this study was excluded from the review.
4. Busse JW, Craigie S, Juurlink DN, et al. Guideline for opioid therapy and chronic noncancer pain. Cmaj. 2017 May 8;189(18):E659-e66. doi: 10.1503/cmaj.170363. PMID: 28483845.	Included in HERC review	HERC staff: included in original CEBP opioid tapering report given to CPTF
5. Chou R. 2009 Clinical Guidelines from the American Pain Society and the American Academy of Pain Medicine on the use of chronic opioid therapy in chronic noncancer pain: what are the key messages for clinical practice? Pol Arch Med Wewn. 2009 Jul-Aug;119(7-8):469-77. PMID: 19776687.	Excluded from P&T review	P&T review: Not identified in literature search; focus of literature search was on treatment of fibromyalgia. Previous P&T reviews have evaluated other, more recent guidelines for the treatment of chronic noncancer pain.
6. Cording M, Derry S, Phillips T, et al. Milnacipran for pain in fibromyalgia in adults. Cochrane Database Syst Rev. 2015 Oct 20(10):Cd008244. doi: 10.1002/14651858.CD008244.pub3. PMID: 26482422.	P&T review: Included	P&T review: Met quality inclusion criteria for a systematic review.

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7. Derry S, Phillips T, Moore RA, et al. Milnacipran for neuropathic pain in adults. Cochrane Database Syst Rev. 2015 Jul 6(7):Cd011789. doi: 10.1002/14651858.cd011789. PMID: 26148202.	Excluded from P&T review	P&T review: This review focused on evidence for fibromyalgia; literature of treatment for other conditions were excluded.
8. Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain--United States, 2016. Jama. 2016 Apr 19;315(15):1624-45. doi: 10.1001/jama.2016.1464. PMID: 26977696.	Included in HERC review	HERC staff: included in original CEBP opioid tapering report given to CPTF; guidelines discussed extensively at VbBS and HERC meetings; comprise basis for OR opioid guidelines referred to in proposed new guideline
9. Edlund MJ, Martin BC, Russo JE, et al. The role of opioid prescription in incident opioid abuse and dependence among individuals with chronic noncancer pain: the role of opioid prescription. Clin J Pain. 2014 Jul;30(7):557-64. doi: 10.1097/ajp.0000000000000021. PMID: 24281273.	HERC staff: not included, but appropriate for inclusion	HERC staff: evidence of harms of opioid use for chronic noncancer pain. Similar evidence already reviewed
10. Kim J, Lee KS, Kong SW, et al. Correlations Between Electrically Quantified Pain Degree, Subjectively Assessed Visual Analogue Scale, and the McGill Pain Questionnaire: A Pilot Study. Ann Rehabil Med. 2014 Oct;38(5):665-72. doi: 10.5535/arm.2014.38.5.665. PMID: 25379496.	HERC staff: excluded	HERC staff: pilot study. Higher levels of evidence available
11. Macfarlane GJ, Kronisch C, Dean LE, et al. EULAR revised recommendations for the management of fibromyalgia. Ann Rheum Dis. 2017 Feb;76(2):318-28. doi: 10.1136/annrheumdis-2016-209724. PMID: 27377815.	P&T review: Excluded	P&T review: Six of the 19 authors of this guideline (including the primary author) had significant conflicts of interest with the pharamceutical industry. Excluded according to current methods for quality assessment.
12. Manhapra A, Arias AJ, Ballantyne JC. The conundrum of opioid tapering in long-term opioid therapy for chronic pain: A commentary. Subst Abus. 2017 Sep 20:1-10. doi: 10.1080/08897077.2017.1381663. PMID: 28929914.	HERC staff: excluded	HERC staff: opinion piece not meeting inclusion criteria for HERC review
13. Sullivan MD, Turner JA, DiLodovico C, et al. Prescription Opioid Taper Support for Outpatients With Chronic Pain: A Randomized Controlled Trial. J Pain. 2017 Mar;18(3):308-18. doi: 10.1016/j.jpain.2016.11.003. PMID: 27908840.	HERC staff: not included, but appropriate for inclusion	HERC staff: supports reduction in pain with opioid tapering. Similar evidence already reviewed. Does not result in change in current proposal

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14. Thakral M, Walker RL, Saunders K, et al. Comparing Pain and Depressive Symptoms of Chronic Opioid Therapy Patients Receiving Dose Reduction and Risk Mitigation Initiatives With Usual Care. J Pain. 2018 Jan;19(1):111-20. doi: 10.1016/j.jpain.2017.09.006. PMID: 29038060.	P&T review: Not included	P&T review: Not identified in literature search; focus of literature search was on treatment of fibromyalgia
15. Wang PP, Huang E, Feng X, et al. Opioid-associated iatrogenic withdrawal in critically ill adult patients: a multicenter prospective observational study. Ann Intensive Care. 2017 Sep 2;7(1):88. doi: 10.1186/s13613-017-0310-5. PMID: 28866754.	HERC staff: excluded	HERC staff: not a relevant patient population

Disposition of Literature Identified by Aggregate Analytics, Inc.

Response to Appendix Table 9

Study	Included/Excluded	Rational for Inclusion/Exclusion & Comments
1. Axon DR, Patel MJ, Martin JR, et al. Use of multidomain management strategies by community dwelling adults with chronic pain: evidence from a systematic review. Scand J Pain. 2019 Jan 28;19(1):9-23. doi: 10.1515/sjpain-2018-0306. PMID: 30375350.	HERC staff: Not in Ovid Medline, unable to obtain full copy for review	Based on abstract: Multiple modalities reported for treatment of chronic pain in various studies. Unable to determine outcomes of modalities from abstract
2. Ball EF, Nur Shafina Muhammad Sharizan E, Franklin G, et al. Does mindfulness meditation improve chronic pain? A systematic review. Curr Opin Obstet Gynecol. 2017 Dec;29(6):359-66. PMID: 28961631.	HERC staff: appropriate for inclusion	Mindfulness meditation significantly reduced depression symptoms and improved quality of life in chronic pain patients. Unable to determine if statistically significant improvements noted above were clinically significant based on article Would not change current staff summary or proposal
3. Denneny D, Frawley HC, Petersen K, et al. Trigger Point Manual Therapy for the Treatment of Chronic Noncancer Pain in Adults: A Systematic Review and Meta-analysis. Arch Phys Med Rehabil. 2019 Mar;100(3):562-77. doi: 10.1016/j.apmr.2018.06.019. PMID: 30025997.	HERC staff: Not in Ovid Medline, unable to obtain full copy for review	Based on abstract: trigger point manual therapy not helpful for the treatment of chronic pain
4. Derry S, Bell RF, Straube S, et al. Pregabalin for neuropathic pain in adults. Cochrane Database Syst Rev. 2019 Jan 23;1:Cd007076. doi: 10.1002/14651858.CD007076.pub3. PMID: 30673120.	P&T excluded	P&T: addresses neuropathic pain rather than fibromyalgia.
5. Fishbain DA, Pulikal A. Does Opioid Tapering in Chronic Pain Patients Result in Improved Pain or Same Pain vs Increased Pain at Taper Completion? A Structured Evidence-Based Systematic Review. Pain Med. 2018 Dec 28doi: 10.1093/pm/pny231. PMID: 30597076. [Epub ahead of print]	HERC staff: Not in Ovid Medline, unable to obtain full copy for review	From abstract: “There is consistent type 3 and 4 study evidence that opioid tapering in [chronic pain patients] reduces pain or maintains the same level of pain”
6. Hall A, Copsey B, Richmond H, et al. Effectiveness of Tai Chi for Chronic Musculoskeletal Pain Conditions: Updated Systematic Review and Meta-Analysis. Phys Ther. 2017 Feb 1;97(2):227-38. PMID: 27634919.	HERC staff: excluded	Did not include relevant patient populations

Disposition of Literature Identified by Aggregate Analytics, Inc.

7. Huffman KL, Rush TE, Fan Y, et al. Sustained improvements in pain, mood, function and opioid use post interdisciplinary pain rehabilitation in patients weaned from high and low dose chronic opioid therapy. Pain. 2017 Jul;158(7):1380-94. PMID: 28328578.	HERC staff: appropriate for inclusion	Does not change current recommendations. Retrospective cohort study found reductions in pain and improvements in function and mood with opioid reduction
8. Hughes LS, Clark J, Colclough JA, et al. Acceptance and Commitment Therapy (ACT) for Chronic Pain: A Systematic Review and Meta-Analyses. Clin J Pain. 2017 Jun;33(6):552-68. PMID: 27479642.	HERC staff: appropriate for inclusion	Statistically significant improvement in pain and functioning with ACT. Unable to determine if effect sizes were clinically meaningful based on data presented Would not change current staff summary or proposal
9. Ju ZY, Wang K, Cui HS, et al. Acupuncture for neuropathic pain in adults. Cochrane Database Syst Rev. 2017 Dec 2;12:Cd012057. doi: 10.1002/14651858.CD012057.pub2. PMID: 29197180.	HERC staff: excluded	Did not include relevant patient populations—neuropathic pain is already on a covered line. No evidence in article to suggest adding acupuncture to current lines containing neuropathic pain
10. Khoo EL, Small R, Cheng W, et al. Comparative evaluation of group-based mindfulness-based stress reduction and cognitive behavioural therapy for the treatment and management of chronic pain: A systematic review and network meta-analysis. Evid Based Ment Health. 2019 Feb;22(1):26-35. doi: 10.1136/ebmental-2018-300062. PMID: 30705039.	HERC staff: appropriate for inclusion	Cognitive behavioral therapy and mindfulness based stress reduction had statistically significant reduction on pain and functioning, but did not appear to have clinically significant impacts. Would not change staff ratings of effectiveness of these therapies in the evidence summary or the current proposal
11. Macfarlane GJ, Kronisch C, Dean LE, et al. EULAR revised recommendations for the management of fibromyalgia. Ann Rheum Dis. 2017 Feb;76(2):318-28. PMID: 27377815.	HERC staff: appropriate for inclusion	Authors note no significant changes from 2007 guidelines, which were included in the HERC review. Only exercise is recommended with a strong strength of recommendation. Opioids other than tramadol are strongly not recommended; tramadol is recommended with a weak strength of recommendation

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		Would not change current proposal, unless HERC wishes to consider the addition of tramadol as a treatment modality for fibromyalgia
12. Ottman AA, Warner CB, Brown JN. The role of mirtazapine in patients with fibromyalgia: a systematic review. Rheumatol Int. 2018 Dec;38(12):2217-24. PMID: 29860538.	P&T staff: excluded	did not include an assessment of scientific quality of the included studies, risk of bias, or internal validity of included studies. Similarly, because there was no adequate quality assessment the scientific quality of the studies was not included in formulating conclusions in the article.
13. Riediger C, Schuster T, Barlinn K, et al. Adverse Effects of Antidepressants for Chronic Pain: A Systematic Review and Meta-analysis. Front Neurol. 2017;8:307. doi: 10.3389/fneur.2017.00307. PMID: 28769859.	HERC staff: not included	HERC staff: adverse effects reviewed; effectiveness not reviewed
14. Sullivan MD, Turner JA, DiLodovico C, et al. Prescription Opioid Taper Support for Outpatients With Chronic Pain: A Randomized Controlled Trial. J Pain. 2017 Mar;18(3):308-18. PMID: 27908840.	Included in table 8 above	
15. Thakral M, Walker RL, Saunders K, et al. Impact of Opioid Dose Reduction and Risk Mitigation Initiatives on Chronic Opioid Therapy Patients at Higher Risk for Opioid-Related Adverse Outcomes. Pain Med. 2018 Dec 1;19(12):2450-8. PMID: 29220525.	HERC staff: appropriate for inclusion	Does not change current recommendations. Supports ability of patients on long term opioid therapy to successfully taper down on dose
16. Thornton JD, Goyat R, Dwibedi N, et al. Health-related quality of life in patients receiving long-term opioid therapy: a systematic review with meta-analysis. Qual Life Res. 2017 Aug;26(8):1955-67. doi: 10.1007/s11136-017-1538-0. PMID: 28255745.	HERC staff: appropriate for inclusion	Unclear based on article if the statistically significant improvement in physical health component scores reflected a clinically meaningful difference
17. Turner JA, Shortreed SM, Saunders KW, et al. Does association of opioid use with pain and function differ by fibromyalgia or widespread pain status? Pain. 2016 Oct;157(10):2208-16. PMID: 27643834.	HERC staff: appropriate for inclusion	Does not change current recommendations. Fibromyalgia patients had similar pain response to opioids as other chronic pain patients and all had worse outcomes for pain and function with chronic opioid use compared to patients not treated with opioids

Disposition of Literature Identified by Aggregate Analytics, Inc.

18. Watson JA, Ryan CG, Cooper L, et al. Pain Neuroscience Education for Adults With Chronic Musculoskeletal Pain: A Mixed-Methods Systematic Review and Meta-Analysis. J Pain. 2019 Mar 1. pii: S1526-5900(18)30747-8. PMID: 30831273. [Epub ahead of print]	HERC staff: Not in Ovid Medline, unable to obtain full copy for review	Based on abstract: pain education had no effect on pain and disability in the short or medium term. There was a statistically significant effect on catastrophizing in the medium term
19. Wiffen PJ, Derry S, Bell RF, et al. Gabapentin for chronic neuropathic pain in adults. Cochrane Database Syst Rev. 2017 Jun 9;6:CD007938. doi: 10.1002/14651858.CD007938.pub4. PMID: 28597471.	HERC staff: excluded	Neuropathic pain is not part of the current review.
20. Wylde V, Dennis J, Beswick AD, et al. Systematic review of management of chronic pain after surgery. Br J Surg. 2017 Sep;104(10):1293-306. PMID: 28681962.	HERC staff: appropriate for inclusion	No evidence of effectiveness of any therapy found. Opioids had no difference in pain control vs other therapies.

March 15, 2019

Dr. Hargunani,

As requested, here is a formal letter stating my involvement in two research studies evaluating the impact of the HERC back pain policy changes that were implemented July 1, 2016.

I have listed the funders, key involved institutions, and my role.

- Funder: Patient-Centered Outcomes Research Institute (PCORI)
    - Collaboration between Kaiser Permanente Washington Health Research Institute, OCHIN, and Harvard University
    - I am a consultant for Kaiser Permanente Washington Health Research Institute on this PCORI grant

- Funder: National Institute for Drug Abuse (NIDA)
    - Study Institution: OHSU
    - Study Partners: HealthInsight Oregon and Oregon State University
    - I am an OHSU co-investigator

Cat Livingston, MD, MPH

13 March 2019

Dana Hargunani, MD, MPH
Chief Medical Officer
Oregon Health Authority
500 Summer Street, NE, E-20
Salem, OR 97301-1097

Dear Dr. Hargunani:

It has been my pleasure to serve as a volunteer member of the Chronic Pain Task Force convened by the Health Evidence Review Commission in 2017-2018 (and potentially ongoing upon request by the HERC). This letter serves as a formal written declaration of a potential conflict of interest.

During the time that the Chronic Pain Task Force has been active, I have been participating as an advisor to a 3-year PCORI-funded study project charged with studying the impacts of the Oregon Medicaid change in approach to spinal conditions that was implemented in 2016. As such, I serve as an independent contractor with Kaiser Permanente Washington Health Research Institute, and work on this project less than 50 hours per year.

My apologies for not making this disclosure sooner. It had not occurred to me that involvement in the PCORI study could be seen as a conflict of interest.

Sincerely,

Laura E. Ocker, LAc, MAcOM

3/16/2019
Darren Coffman
Director, Health Evidence Review Commission (HERC)

RE: Possible Conflict of Interest, Disclosure

Dear Mr. Coffman,

This correspondence is to inform you of a possible conflict of interest I may have as a member of the HERC, Value-Based Benefits Subcommittee. I have been working as a paid consultant for the Kaiser Permanente Washington Health Research Institute for the last 16 months relative to a 3-year study that involves opioid prescribing.

Our study is studying a new State of Oregon healthcare policy that involves Oregon Health Plan (OHP-Medicaid) patients in short, how this new state policy effects opioid prescribing. This new state policy initiated July 1, 2016, now allows OHP patients with back and spinal pain, limited access to the non-pharmacological interventions of chiropractic spinal manipulation, acupuncture, physical therapy, and massage therapy. The principle outcomes being studied are how this new policy effects first start opioid prescribing in OHP patients with acute low back pain as well as how the policy impacts OHA patients with chronic low back pain who are already on prescribed opioids. As a chiropractic physician in active practice my role is to simply provide an understanding of a chiropractor's scope of practice, practical insights as per chiropractic treatment of OHP patients with low back pain, as well as answer questions regarding chiropractic practice.

Sincerely,

Vern Saboe, DC, FACO
Member, HERC Value-Based Benefits Subcommittee

Quantifying the Epidemic of Prescription Opioid Overdose Deaths

In 2016, 63 632 persons died of a drug overdose in the United States; 66.4% (42 249) involved an opioid.[1] Opioid-involved deaths include prescription opioid analgesics (e.g., morphine, oxycodone), illicit opioids (e.g., heroin, illicitly manufactured fentanyl [IMF]), or both. Although prescription and illicit opioid overdoses are closely entwined,[2] it is important to differentiate the deaths to craft appropriate prevention and response efforts. Unfortunately, disentangling these deaths is challenging because multiple drugs are often involved. Additionally, death certificate data do not specify whether the drugs were pharmaceutically manufactured and prescribed by a health care provider, pharmaceutically manufactured but not prescribed to the person (i.e., diverted prescriptions), or illicitly manufactured.

THE CHANGING OPIOID OVERDOSE EPIDEMIC

The United States has seen rapid changes in the illicit opioid supply. Availability of illicitly manufactured synthetic opioids (e.g., fentanyl) that traditionally were prescription medications has increased. This has blurred the lines between prescription and illicit opioid-involved deaths. In one study in 27 states, Gladden et al.[3] examined data on drug products obtained by law enforcement that tested positive for fentanyl (fentanyl submissions) and deaths involving synthetic opioids other than methadone (referred to as synthetic opioids). From 2013 to 2014, fentanyl submissions increased by 426%. The increases were strongly correlated with increases in synthetic opioid deaths but not with pharmaceutical fentanyl prescribing rates, suggesting that the increases were largely due to IMF.[3] In a recent report, fentanyl was detected in at least half of the opioid overdose deaths from July to December 2016 in 7 of the 10 states examined.[4]

Traditionally, the Centers for Disease Control and Prevention (CDC) and others have included synthetic opioid deaths in estimates of "prescription" opioid deaths. However, with IMF likely being involved more recently, estimating prescription opioid–involved deaths with the inclusion of synthetic opioid–involved deaths could significantly inflate estimates.

MORE CONSERVATIVE ESTIMATION APPROACH

A new, more conservative estimation of prescription opioid–involved deaths is proposed to better differentiate deaths involving prescription (pharmaceutically manufactured) opioids from deaths involving illicit opioids (heroin, IMF). Pharmaceutically manufactured opioids are considered prescription opioids for estimation purposes because most persons misusing them reported obtaining them in a way that originated with a prescription (misusing own prescription or obtaining from friends or relatives). Only 4.9% bought opioids from a drug dealer or stranger, and 5.6% reported obtaining them by stealing from a doctor's office, clinic, hospital, or pharmacy or in some other way.[5]

The National Vital Statistics System (NVSS) multiple cause-of-death mortality files record drug overdose deaths, which are identified with the *International Classification of Diseases, 10th Revision* (*ICD-10;* Geneva, Switzerland: World Health Organization; 1992), according to the underlying cause-of-death codes X40 to X44 (unintentional), X60 to X64 (suicide), X85 (homicide), or Y10 to Y14 (undetermined intent). Among deaths with drug overdose as the underlying cause, the type of opioid is indicated by the following *ICD-10* multiple cause-of-death codes: opium (T40.0); heroin (T40.1); natural and semisynthetic opioids (T40.2); methadone (T40.3); synthetic opioids other than methadone (T40.4); and other and unspecified narcotics (T40.6).

Under the CDC's traditional method of calculating prescription opioid overdose deaths with NVSS, deaths involving natural and semisynthetic opioids and synthetic opioids as well as methadone are included. Under a more conservative method, deaths involving only natural and semisynthetic opioids and methadone are included. Deaths involving synthetic opioids are removed and calculated separately because of the high proportion of deaths that likely involve IMF.

With the traditional method, an estimated 32 445 prescription opioid–involved deaths occurred in 2016. With the more conservative method, 17 087 prescription opioid–involved deaths occurred in 2016 (Table 1). Longitudinal trends indicated a rapid increase in death rates involving synthetic opioids from 2013 to 2016 (annual percent change = 87.7%), whereas death rates involving natural and

ABOUT THE AUTHORS

All of the authors are with the Division of Unintentional Injury Prevention, Centers for Disease Control and Prevention, Atlanta, GA.

Correspondence should be sent to Puja Seth, PhD, Division of Unintentional Injury Prevention, Centers for Disease Control and Prevention, 4770 Buford Hwy NE, MS F-62, Atlanta, GA 30341 (e-mail: pseth@cdc.gov). Reprints can be ordered at http://www.ajph.org by clicking the "Reprints" link.

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Note. *The findings and conclusions of this editorial are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.*

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Update on proposed changes to coverage of treatments for certain chronic pain conditions for the Oregon Health Plan

The Oregon Health Authority (OHA) is committed to transforming health care to improve the health of Oregonians. The Health Evidence Review Commission (HERC), a volunteer panel of health leaders and experts, plays a critical role in fulfilling this mission by prioritizing health services covered by the Oregon Health Plan. In recent months, OHA staff has been working in collaboration with the advisory Chronic Pain Task Force, to prepare a proposal for the HERC's consideration to expand treatment options for certain chronic pain conditions and protect against overprescribing of opioid painkillers.

The CPTF and OHA staff completed the development of a proposal in December 2018 to enhance coverage of treatments for fibromyalgia and four other diagnoses related to chronic pain. The goal of this proposal is to expand treatment options for patients with chronic pain conditions that are currently not covered in the Oregon Health Plan, with the goal of improving patient health and safety. At its May 16, 2019 meeting, the HERC and its Value-based Benefits Subcommittee (VbBS) must consider this proposal as it relates to the entire benefit package for the Oregon Health Plan.

This proposed benefit expansion includes a menu of pharmacologic and non-pharmacologic pain treatment services that are currently not covered for these conditions. If adopted, it would take effect January 1, 2020. Additional options will be considered by the HERC, including not adopting the proposal. HERC will use its prioritization methodology to weigh the potential options based on the evidence of benefit, cost impact and public input.

Questions and answers

I've just learned of this proposal. How did we get to this point? The Chronic Pain Task Force met seven times between September, 2017 and December, 2018. The task force's recommendations were initially presented to the VbBS in August, 2018. The VbBS began reviewing a revised proposal based on additional evidence, public testimony and implementation concerns on January 17, 2019. At the March 9, 2019 meeting no discussion of the topic was held due to a pause ordered by OHA leadership, but public testimony was heard. Meeting materials and minutes are available on our Meeting Archives page. All meetings were public, and members of the task force received extensive written and oral public input on the proposal, including testimony from national experts on pain management and opioid tapering.

What is the current proposal? The proposal to be considered May 16, 2019 will be similar to what was considered at VbBS and HERC on January 17, 2019. The HERC will also consider an option not to adopt the proposal.

The critical component of the modified CPTF proposal is to reprioritize five chronic pain diagnosis codes to their own line on the Prioritized List. In addition, there are proposed additions to related guidelines. The new line would include:

- Fibromyalgia and four broad chronic pain diagnoses (G89.21 Chronic pain due to trauma, G89.28 Other chronic postprocedural pain, G89.29 Other chronic pain, and G89.4 Chronic pain syndrome) moved to the funded region.

- Nonpharmacologic treatments including exercise therapy, acupuncture, tai chi, acupuncture, physical therapy and cognitive behavioral therapy.
- Non-opioid medications, with a requirement the patient also be treated with active therapy or continuing self-maintenance of strategies learned in active therapy.
- Opioid medications for these conditions. Since the March meeting staff has developed alternatives for Commission consideration around fibromyalgia and one that would allow "grandfathered" coverage for patients already on long-term opioid therapy, but not newly-initiated treatment. Some of these options include requiring taper plans for continued coverage for patients for whom opioid prescribing does not align with the guideline. Unlike previous versions, this version of the taper plan does not include a recommended taper rate or the requirement that the plan include a goal of zero.

There is also an option to not make any changes to the current prioritization of fibromyalgia and certain other chronic pain conditions due to the low level of effectiveness for various therapies and due to the other consequences of reprioritizing these diagnoses in the funded region, such as an increase in coverage for opioid medications.

Would the proposal take away all opioids for all chronic pain patients? No. At no time has the proposal affected opioids being prescribed for other funded conditions under the Oregon Health Plan (e.g. arthritis, cancer, end-of-life care, etc).

The HERC has had a long-term guideline that opioids are not intended to be covered for fibromyalgia due to their lack of effectiveness and risk of harm. For patients who are currently receiving opioids for fibromyalgia despite this guideline, depending on the option adopted, the new coverage proposal may result in them being required to begin an individualized taper plan.

Depending on the option selected, patients receiving opioids for the other four chronic pain conditions under consideration could be required to taper as part of Oregon Health Plan coverage, but only if their current prescriptions do not align (or cannot be adjusted to align) with safe and effective prescribing as outlined in the Oregon Opioid Prescribing Guidelines. Decisions about the pace of any taper plan would be made by prescribers, not health plans, and taper plans could be paused if needed. As has always been the case, providers may refuse to prescribe opioids, or decide to initiate a taper plan based on their clinical judgement.

If the HERC chooses not to change the prioritization of fibromyalgia and certain other chronic pain conditions, then these conditions will continue to be "below the line" and will continue to not be eligible for opioid prescriptions if the patient's CCO has prescription controls on opioids.

I am an OHP member and I have a chronic pain condition that is currently "not covered" or "below the (funding) line"; however my opioids ARE being covered. How can this be? Health plans identify many medications, including opioids as "preferred". Such prescriptions are paid for by plans automatically, without review to see if they are being prescribed for a funded condition. In other cases plans allow coverage by exception. Plans can change their criteria for a variety of reasons, including but not limited to Prioritized List guidelines.

How many people could this proposal impact? During calendar year 2017, OHA's Actuarial Services Unit (ASU) found approximately 90,000 OHP recipients had a claim including one of the diagnoses affected by

the proposal. Of these, approximately 63,000 also had a diagnosis of back or spine pain, meaning they would already be eligible for a package of services similar to those proposed under the CPTF proposal. This leaves about 27,000 recipients who might be eligible for the new nonpharmacologic benefits, though some of these might already have access to certain benefits such as physical therapy because of other orthopedic conditions. Of the 90,000 recipients, about 40,000 had at least one opioid prescription during the time period.

What will it cost? OHA's Actuarial Service Unit (ASU) estimates the cost of the nonpharmacologic therapies to be $10.8 to $17.3 million for all of the Oregon Health Plan in 2020. These cost adjustments assume limited impact on pharmaceutical costs, as most of the patients receiving opioids would already be eligible to receive them due to a comorbid funded diagnosis. The top end of this estimate is higher than presented at the March meeting due to the fact that the availability of Lyrica in generic form may be delayed.

What factors will the Commission consider as it prioritizes these treatments? The Commission's legislative mandate is to rank services "by priority, from the most important to the least important, representing the comparative benefits of each service to the population to be served." The Commission will use its Prioritization Methodology, which includes consideration of several factors including the effectiveness of the treatments, the proportion of affected patients who need the services, pain and suffering caused by the condition, the overall effect of the condition on a person's healthy life and the ability of the treatment to prevent acute exacerbations of the chronically painful condition. These are used to determine a score which ranks the line under consideration relative to other lines on the Prioritized List.

What options does the Commission have in addressing the proposal? The Commission could choose to accept the proposal as presented or to adopt a modified version. Alternately, it could decide not to create a new line for the reprioritization of these services at all.

Whether or not the Commission creates the new line, the Commission will consider modifying Guideline Note 60, Opioids for Conditions of the Back and Spine, to remove the existing reference to an end date for tapering that has already passed (January 1, 2018) and to update language related to tapering in light of the work of the Chronic Pain Task Force.

Why are back and spine pain guidelines being addressed as part of this work?

HERC reviewed the evidence for a variety of nonpharmacologic and pharmacologic interventions for back pain starting in 2013. They decided to reprioritize back pain to the funded region of the Prioritized List which allowed access to evidence-based treatments, but also restricted opioid coverage because of a lack of evidence of benefit, and concerns given the opioid epidemic. This back pain policy went into effect July 1, 2016 and is not a new HERC policy. The new suggested changes to the back and spine guidelines are to remove references to dates that have passed and to consider adding language allowing for a more individualized taper plan.

How can I participate or get updates on HERC's activities?
You can subscribe at the HERC website at https://www.oregon.gov/oha/HPA/DSI-HERC/Pages/ to receive notifications of future meetings and look at materials being discussed. Materials for the March 14th meetings will be posted on Thursday, March 7th at https://www.oregon.gov/oha/HPA/DSI-

HERC/Pages/Meetings-Public.aspx. You can attend the meetings, which are open to the public, and speak during time set aside for public comment. You can listen to the meetings by dialing 1-888-204-5984, participant code 801373 and also register for the meeting webinar at https://attendee.gotowebinar.com/rt/4563145172385374211. You can also send written comment of up to 1,000 words to HERC.Info@state.or.us by 12:00 PM PDT, Tuesday, March 12th. See https://www.oregon.gov/oha/HPA/DSI-HERC/Pages/Policy-Comment-Current-Topics.aspx for further details on HERC's policies for providing verbal or written comments.

Everyone has a right to know about and use Oregon Health Authority (OHA) programs and services. OHA provides free help. Some examples of the free help OHA can provide are:

- Sign language and spoken language interpreters
- Written materials in other languages
- Braille
- Large print
- Audio and other formats

If you need help or have questions, please contact Daphne Peck at 503-373-1985, 711 TTY or herc.info@state.or.us at least 48 hours before the meeting.

Liver Transplant for Hepatic Malignancies

Question: Should liver transplant for hepatic malignancies be moved to a higher priority line?

Question sources:

1) Pippa Newell, MD, Providence hepatobiliary surgeon: adult hepatocellular carcinoma (HCC)
2) Stanford University transplant program: pediatric liver malignancies, specifically hepatoblastoma

Issue: Currently, liver transplant for hepatic malignancies is on line 560 for both adult and pediatric malignancies, which is well below the funding line. Other liver conditions, such as biliary atresia, acute necrosis of the liver, cirrhosis of the liver, and inborn errors of metabolism are paired with liver transplant on covered lines.

The low prioritization of the liver transplant line for hepatic malignancies dates from the beginning of the Prioritized List. In the 1980's and 1990's, liver transplant for HCC was reported to have very poor outcomes. In 1994, the OHSU liver transplant program testified that there were a small subset of hepatic malignancies which benefited from transplant, but the pairing was appropriate for placement on a very low line. Liver transplant was reviewed again as a group in 2000, and at that time, UNOS did not list any hepatic malignancies as indications for transplant. This topic was again touched upon in 2002, and it was noted that survival rates (presumably 5-year survival) with transplant for hepatocellular carcinoma were about 6% and the low prioritization of the line was continued. However, since that time, outcomes of liver transplant for certain liver malignancies have greatly improved and transplant become standard of care for many types of malignancies in appropriate clinical situations.

At the November, 2018 VBBS meeting, the liver surgeons who presented regarding yttrium 90 therapy for hepatocellular carcinoma testified that liver transplant for this condition was standard of care for patients meeting certain criteria. They requested that the HERC reconsider reprioritization of this pairing. However, the liver surgeons noted that most patients with HCC also had cirrhosis, and so were able to access liver transplant using that covered diagnosis. Subsequently, the HERC was contacted by the Stanford University transplant program about lack of coverage for liver transplant for hepatoblastoma, a rare liver malignancy in children. Liver transplant is the usual treatment for children with certain forms of this cancer.

Currently, surgical resection, chemotherapy, radiation, yttrium-90 therapy for certain patients, and other medical therapies are available to adult patients with HCC and children with cancers like hepatoblastoma on line 315 CANCER OF LIVER. According to recent reviews on the treatment of HCC (see **Forner 2018**), liver transplantation is a standard therapy with improvement in survival for certain types of patients. Forner et al (2018) note that "Milan criteria (a single nodule ≤5 cm or up to three nodules ≤3 cm) are the benchmark to offer the best post liver transplantation survival in hepatocellular carcinoma (>70% 5-year survival with a recurrence rate of <10–15%). These restricted criteria have become the accepted selection criteria in the USA and Europe."

The current liver transplant line (line 560) contains the diagnosis codes for HCC and hepatoblastoma, as well as rarer tumor types such as sarcomas (usually found in children), angiosarcoma, and intrahepatic bile duct carcinoma. Of note, when liver transplant for cancer was discussed in 2002, it was recommended to move medical and surgical treatment (other than transplant) of intrahepatic bile duct carcinomas from the liver cancer line to the line for cancer of the gall bladder, which is now 433 CANCER OF GALLBLADDER AND OTHER BILIARY, due to this type of cancer having a much worse prognosis than other liver cancers.

Liver Transplant for Hepatic Malignancies

Current Prioritized List status:

Diagnoses included on line 560

ICD10 Code	Code Description	Subdiagnoses
C22.1	Intrahepatic bile duct carcinoma	
C22.2	Hepatoblastoma	
C22.3	Angiosarcoma of liver	
C22.4	Other sarcomas of liver	Mesodermal tumor of liver
C22.7	Other specified carcinomas of liver	Embryonal carcinoma of liver Embryonal teratocarcinoma of liver Teratocarcinoma of liver Mixed embryonal tumor of liver
C22.8	Malignant neoplasm of liver, primary, unspecified as to type	

Note: colorectal cancer metastatic to the liver (ICD10 C78.6 Secondary malignant neoplasm of liver and intrahepatic bile duct) is only on line 589 SECONDARY AND ILL-DEFINED MALIGNANT NEOPLASMS and is not currently eligible for transplant.

Line scoring

	Line 307	Line 315	Line 560
Category (Non-Fatal Condition)	6	6	6
Healthy Life Years (0-10)	7	8	7
Suffering (0-5)	2	5	4
Population effects (0-5)	0	0	0
Vulnerable population (0-5)	0	0	0
Tertiary prevention (0-5)	0	0	0
Effectiveness (0-5)	3	2	1
Need for service (0-1)	1	1	0.1
Net cost	0	1	0
Score	1080	1040	44
Approximate line	307	315	560

- Line 162 BILIARY ATRESIA Treatment LIVER TRANSPLANT
- Line 240 SHORT BOWEL SYNDROME - AGE 5 OR UNDER Treatment INTESTINE AND INTESTINE/LIVER TRANSPLANT
- Line 242 ACUTE AND SUBACUTE NECROSIS OF LIVER; SPECIFIED INBORN ERRORS OF METABOLISM (E.G., MAPLE SYRUP URINE DISEASE, TYROSINEMIA) Treatment LIVER TRANSPLANT
- Line 307 CIRRHOSIS OF LIVER OR BILIARY TRACT; BUDD-CHIARI SYNDROME; HEPATIC VEIN THROMBOSIS; INTRAHEPATIC VASCULAR MALFORMATIONS; CAROLI'S DISEASE Treatment LIVER TRANSPLANT, LIVER-KIDNEY TRANSPLANT
- Line 315 CANCER OF LIVER Treatment MEDICAL AND SURGICAL TREATMENT, WHICH INCLUDES CHEMOTHERAPY AND RADIATION THERAPY
- Line 560 CANCER OF LIVER AND INTRAHEPATIC BILE DUCTS Treatment LIVER TRANSPLANT

Evidence

Liver transplant for HCC

1) **Golabi 2017:** database review of liver transplant vs resection outcomes for HCC
    a. Used data from the Surveillance, Epidemiology and End Results (SEER)-Medicare database between 2001 and 2009.
    b. Total of 11,187 cases were included (mean age at diagnosis: 72 years, 69% male, 67% White). HCC patients who underwent liver transplant were younger (61 vs 71 years), sicker (presence of decompensated cirrhosis: 80% vs 23%), and less likely to die within 2 years (29% vs 44%, all P<0.01), compared to surgical resection patients. In multivariate analysis, older age (HR: 1.01 [95% CI=1.01–1.01]), stage of HCC other than local (HR: 1.81[95%CI=1.70–1.91]), and being treated with surgical resection (HR: 1.95 [95%CI=1.55–2.46]) were independent predictors of mortality within 2 years. Furthermore, the presence of decompensated cirrhosis (HR: 1.84 [95%CI=1.73–1.96]) and alcoholic liver disease (HR: 1.19[95%CI=1.11–1.28]) increased within 2 years of mortality.
    c. Mortality within 2 years postdiagnosis of HCC was significantly higher in patients treated with surgical resection than liver transplant.
2) **Chapman 2015:** retrospective analysis of liver transplantation vs resection for HCC
    a. N=1765 patients (884 resection, 881 transplantation)
        i. Comparison of transplant eligible patients who had resection vs transplantation
    b. Overall, 248 (28.1%) resected patients were transplant eligible (1 tumor <5 cm or 2 to 3 tumors all <3 cm, no major vascular invasion); these were compared with 496 transplant patients, matched based on year of transplantation and tumor status.
    c. Overall survivals at 5 and 10 years were significantly improved for transplantation patients (74.3% vs 52.8% and 53.7% vs 21.7% respectively, $p < 0.001$), with greater differences in disease-free survival (71.8% vs 30.1% at 5 years and 53.4% vs 11.7% at 10 years, $p < 0.001$).
    d. CONCLUSIONS: Although transplantation results in better long-term survival, limited donor availability precludes widespread application.
3) **Dhir 2012**: meta-analysis of liver transplantation vs resection for HCC
    a. N=10 studies (1763 patients) with early HCC
    b. The 5-year overall survival (OS) for all patients was 58% (transplantation: 63%; resection: 53%). Meta-analysis of all 10 studies revealed a survival advantage for transplantation [odds ratio (OR) 0.581, 95% confidence interval (CI) 0.359–0.939; *P* = 0.027]. Analysis of only those reports that utilized an 'intention-to-treat' strategy failed to demonstrate a survival advantage for either treatment approach (OR 0.600, 95% CI 0.291–1.237; *P* = 0.166).
    c. Conclusions: The current study demonstrates a favorable outcome in patients with early HCC treated by either transplantation or resection. Although transplantation was noted to have a survival advantage in some settings, resection continues to be a viable treatment approach.

Liver transplant for hepatoblastoma and other pediatric liver malignancies

1) **Ezekian 2018**, database study on survival after transplantation for hepatoblastoma
    a. N=741 (599 hepatoblastoma (HB), 141 HCC)
        i. Analysis of UNOS database

   ii. Subjects were divided into historic (transplant before 2010) and contemporary (transplant since 2010) cohorts.
   b. 599 children with HB received liver transplant (LT) (320 historic vs 279 contemporary) LT. Concurrently, 141 children with HCC received LT (92 historic vs 49 contemporary). In the historic cohorts, patients with HB had a 1-year and 5-year OS of 84.6% and 75.1%, respectively. Survival for HCC was 84.4% and 59.9%, respectively. Outcomes improved in the contemporary era to 89.1% and 82.6% for HB, and 94.7% and 80.8% for HCC, respectively (both log-rank test P < 0.0001).
   c. Conclusion: Outcomes of LT have improved significantly, with contemporary survival now equivalent between these tumors and exceeding 80% 5-year OS.
2) **Vinayak 2017**: retrospective database study of outcomes of liver transplant for pediatric hepatic malignancies
   a. US Scientific Registry of Transplant Recipients, data from the Children's Hospital of Pittsburgh
   b. 149 HCC cases experienced 10-year patient survival similar to 15,710 adult HCC LT recipients (51.6% versus 49.6%; P=0.848, not significant [NS], log-rank test).
   c. Actuarial 10-year patient survival for 17 embryonal tumors (EMBs), 10 metastatic liver tumors (METS), and 6 leiomyosarcoma patients exceeded 60%.
   d. Conclusion: Among children, LT can be curative for unresectable HCC confined to the liver and without vascular invasion, incidental HCC, embryonal tumors, and metastatic neuroendocrine tumor

Liver transplant for cholangiocarcinoma (bile duct cancer)

1) **Gu 2012**, systematic review and meta-analysis of liver transplant for cholangiocarcinoma
   a. N=14 trials (605 patients)
   b. The overall 1-, 3- and 5-year pooled survival rates were 0.73 [95% confidence interval (CI) 5 0.65–0.80], 0.42 (95% CI 5 0.33–0.51) and 0.39 (95% CI 5 0.28–0.51), respectively. In comparison to curative resection of cholangiocarcinoma with the 5-year survival rate reported from 20 to 40%, the role of liver transplantation alone is limited.
   c. The overall pooled incidence of complications in the above subgroups was 0.62 (95% CI ¼ 0.44–0.78); postoperative incidence of complications included biliary leakage, pancreatic leakage and vascular complications
   d. The results from our study were discouraging even for early stages of the disease. The overall 5-year pooled survival rate of OLT for cholangiocarcinoma from 13 studies was only 36%, which was not expectedly superior to the long-term outcome of liver resection

Liver transplant for angiosarcoma

1) **Li 2018**, systematic review of liver transplant for angiosarcoma
   a. N=75 articles (186 patients)
   b. The median overall survival (OS) was 8 months, with 1-, 3-, and 5-year OS rates of 36.6%, 22.3%, and 12.0%, respectively. The median OS after partial hepatectomy (*n* = 86), chemotherapy (*n* = 36), liver transplantation (*n* = 17), and supportive care (*n* = 46) were 15, 10, 5 and 1.3 months, respectively.
   c. *Conclusions:* Despite the dismal prognosis, partial hepatectomy could prolong the survival of hepatic angiosarcoma patients, particularly those with tumors < 10 cm. Chemotherapy could be an option for unresectable disease. Liver transplantation is not a recommendable option for the management of this malignancy.

Expert guidelines

1) **NCCN 2019,** guideline for the management of hepatobiliary cancers
    a. Hepatocellular carcinoma—liver transplant is a major pathway of their treatment algorithm
        i. Refer patients meeting UNOS criteria to transplant:
            1. tumor 2-5 cm in diameter or 2-3 tumors $\leq$ 3cm each
            2. no macrovascular involvement
            3. no extrahepatic disease
            4. adequate performance status
    b. Intrahepatic cholangiocarcinoma: liver transplant in not mentioned in the algorithm
    c. Angiosarcoma of the liver is not included in this guideline
2) **Vogel 2018**, European Society for Medical Oncology (ESMO) guidelines for management of HCC
    a. The Milan criteria (one lesion < 5 cm; alternatively, up to three lesions, each < 3 cm; no extrahepatic manifestations; no evidence of macrovascular invasion) are currently the benchmark for the selection of patients with HCC for orthotopic liver transplant (OLT). OLT is recommended for patients that fit the Milan criteria, for which < 10% recurrence and 70% 5-year survival are expected [II, A]
3) **Squires 2014**, practice guideline by the American Association for the Study of Liver Diseases, American Society of Transplantation and the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition for pediatric liver transplantation
    a. Children with nonmetastatic and otherwise unresectable hepatoblastoma (HB) should be referred for liver transplantation (LT) evaluation at the time of diagnosis or no later than after 2 rounds of chemotherapy. (1-B)
    b. Patients with HB and pulmonary metastases can be considered for LT if, following chemotherapy, a chest CT is clear of metastases or, if a tumor is identified, the pulmonary wedge resection reveal the margins are free of the tumor. (1-B)
    c. Prompt referral to a liver transplant center should occur for children with or suspected to have hepatocellular carcinoma. (2-B)
    d. Liver transplant evaluation for infantile hemangioma (IH) is indicated if the hemangioendothelioma is not responding to treatment or is associated with life-threatening complications. (1-B)

Other payer policies:

All other major insurance payers are covering liver transplantation for HCC and pediatric liver malignancies for appropriate patients.

HERC staff summary

Liver transplantation for patients with HCC meeting the Milan criteria have 5 year survival rates >70%, Compared to resection (which is currently covered on the Prioritized List for HCC), liver transplantation has at least equivalent and possibly higher 5 year survival rates for appropriate patients. Liver transplant is considered standard of care in all expert guidelines for HCC including NCCN, for patients who meet transplant criteria. Liver transplantation for hepatoblastoma and other rare pediatric liver malignancies has five year survival rates of 60-95% depending on the type of malignancy and other patient characteristics. Liver transplant is recommended by expert groups for children with liver malignancies who meet certain criteria. These outcomes are significantly different that the poor outcomes last reviewed for liver transplant for hepatic malignancies over 15 yrs ago. Transplant criteria are determined by UNOS and the transplant centers; donor livers are scarce and these criteria are unlikely to be inappropriate or too liberal.

Liver transplant is not currently recommended for angiosarcoma of the liver, due to a 5 yr survival rate of 12%. It is also not recommended for bile duct cancers, due to a 5 yr survival rate of 40% vs a cure for surgical resection, and is not included in the NCCN treatment algorithm for cholangiocarcinoma.

Liver Transplant for Hepatic Malignancies

HERC staff recommendations:

1) Create a new line for liver transplantation for hepatic malignancies as shown below, effective January 2020
    a. Include all ICD-10 codes currently on line 560, except the following diagnoses due to lack of evidence of effectiveness with liver transplant:
        i. ICD10 C22.1 Intrahepatic bile duct carcinoma
        ii. ICD10 C22.3 Angiosarcoma of liver
    b. Include all CPT and HCPCS codes currently on line 560
    c. Attach GN64 and 65 (telephone and email encounters)
    d. Do not add a guideline: transplant criteria to be determined by UNOS and the transplant centers
2) Keep the original line, including only the ICD-10 codes for intrahepatic bile duct carcinoma and angiosarcoma of the liver, with current line prioritization, as shown below

Line: XXX

Condition: CANCER OF LIVER OTHER THAN ANGIOSARCOMA (See Guideline Notes 64,65)
Treatment: LIVER TRANSPLANT
ICD-10: C22.0 [Liver cell carcinoma], C22.2 [Hepatoblastoma], C22.4 [Other sarcomas of liver], C22.7 [Other specified carcinomas of liver], C22.8 [Malignant neoplasm of liver, primary, unspecified as to type],T86.40-T86.49,Z48.23,Z51.11,Z52.6 [transplant rejection codes, post transplant care visit codes]
CPT: 47133-47147,86825-86835,93792,93793,98966-98969,99051,99060,99070,99078,99184, 99201-99239,99281-99285,99291-99404,99408-99449,99451,99452,99468-99480,99487-99491,99495-99498,99605-99607
HCPCS: G0068,G0071,G0248-G0250,G0396,G0397,G0406-G0408,G0425-G0427,G0463-G0467, G0490,G0508-G0511,G0513,G0514,G2010-G2012

Scoring

	Line XXX	**Line 307**	**Line 315**	**Line 560**
Category (Non-Fatal Condition)	6	6	6	6
Healthy Life Years (0-10)	7	7	8	7
Suffering (0-5)	4	2	5	4
Population effects (0-5)	0	0	0	0
Vulnerable population (0-5)	0	0	0	0
Tertiary prevention (0-5)	0	0	0	0
Effectiveness (0-5)	3	3	2	1
Need for service (0-1)	1	1	1	0.1
Net cost	0	0	1	0
Score	1320	1080	1040	44
Approximate line	264	307	315	560

• Line 307 CIRRHOSIS OF LIVER OR BILIARY TRACT; BUDD-CHIARI SYNDROME; HEPATIC VEIN THROMBOSIS; INTRAHEPATIC VASCULAR MALFORMATIONS; CAROLI'S DISEASE Treatment LIVER TRANSPLANT, LIVER-KIDNEY TRANSPLANT
• Line 315 CANCER OF LIVER Treatment MEDICAL AND SURGICAL TREATMENT, WHICH INCLUDES CHEMOTHERAPY AND RADIATION THERAPY
• Line 560 CANCER OF LIVER AND INTRAHEPATIC BILE DUCTS Treatment LIVER TRANSPLANT

Line: 560

Condition: ~~CANCER~~ ANGIOSARCOMA OF LIVER; ~~AND~~ INTRAHEPATIC BILE DUCT~~S~~ CARCINOMA

Treatment: LIVER TRANSPLANT

ICD-10: ~~C22.0 [Liver cell carcinoma],~~ C22.1 [Intrahepatic bile duct carcinoma],~~ C22.2 [Hepatoblastoma],~~ C22.3 [Angiosarcoma of liver], ~~C22.4 [Other sarcomas of liver], C22.7 [Other specified carcinomas of liver], C22.8 [Malignant neoplasm of liver, primary, unspecified as to type],~~T86.40-T86.49,Z48.23,Z51.11,Z52.6 [transplant care visit codes]

CPT: 47133-47147,86825-86835,93792,93793,98966-98969,99051,99060,99070,99078,99184, 99201-99239,99281-99285,99291-99404,99408-99449,99451,99452,99468-99480,99487-99491,99495-99498,99605-99607

HCPCS: G0068,G0071,G0248-G0250,G0396,G0397,G0406-G0408,G0425-G0427,G0463-G0467, G0490,G0508-G0511,G0513,G0514,G2010-G2012

Hepatocellular carcinoma

Alejandro Forner, María Reig, Jordi Bruix

Hepatocellular carcinoma appears frequently in patients with cirrhosis. Surveillance by biannual ultrasound is recommended for such patients because it allows diagnosis at an early stage, when effective therapies are feasible. The best candidates for resection are patients with a solitary tumour and preserved liver function. Liver transplantation benefits patients who are not good candidates for surgical resection, and the best candidates are those within Milan criteria (solitary tumour ≤5 cm or up to three nodules ≤3 cm). Image-guided ablation is the most frequently used therapeutic strategy, but its efficacy is limited by the size of the tumour and its localisation. Chemoembolisation has survival benefit in asymptomatic patients with multifocal disease without vascular invasion or extrahepatic spread. Finally, sorafenib, lenvatinib, which is non-inferior to sorafenib, and regorafenib increase survival and are the standard treatments in advanced hepatocellular carcinoma. This Seminar summarises the scientific evidence that supports the current recommendations for clinical practice, and discusses the areas in which more research is needed.

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Barcelona Clinic Liver Cancer group, Liver Unit, IDIBAPS, Hospital Clínic, University of Barcelona, Barcelona, Spain (A Forner MD, M Reig MD, Prof J Bruix MD); **and Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas, Madrid, Spain** (A Forner, M Reig, Prof J Bruix)

Correspondence to:
Dr Alejandro Forner, Barcelona Clinic Liver Cancer group, Liver Unit, IDIBAPS, Hospital Clínic, 08036 Barcelona, Spain
aforner@clinic.ub.es

Introduction

Hepatocellular carcinoma is the most frequent primary liver cancer and is an important medical problem. With 782 000 cases diagnosed and 746 000 deaths in 2012, and an age-adjusted worldwide incidence of 10·1 cases per 100 000 person-years, hepatocellular carcinoma is ranked as the sixth most common neoplasm and the third leading cause of cancer death. Hepatocellular carcinoma has been recognised as a leading cause of death among patients with cirrhosis, and its incidence is expected to increase in the future.[1] Together with the recognition of its clinical relevance, major progress has been made in prevention, detection, diagnosis, and treatment. In this Seminar, we summarise the knowledge that has emerged since our last update in 2012.[2]

Epidemiology

The development of hepatocellular carcinoma is closely related to the presence of chronic liver disease. The worldwide incidence is heterogeneous because of the variable prevalence of the risk factors. Most hepatocellular carcinoma cases (80%) occur in sub-Saharan Africa and eastern Asia, where the main risk factors are chronic hepatitis B and aflatoxin B1 exposure.[3] In patients with hepatitis B, the incidence of hepatocellular carcinoma increases with viral load, duration of infection, and severity of the liver disease.[4] Occult hepatitis B virus infection is also associated with increased risk because of DNA damage induced by virus integration.[5] In the USA, Europe, and Japan, hepatitis C is the main risk factor,[3] together with excessive alcohol intake.[6] The epidemiology of hepatocellular carcinoma is characterised by dynamic temporal trends. In Japan and Europe, where spread of hepatitis C virus occurred earlier than in the USA, the incidence of hepatocellular carcinoma has almost reached a plateau and in some areas it is declining.[7,8] By contrast, in the USA, where hepatitis C virus spread occurred later, the incidence is still increasing and is predicted to stabilise by 2020.[8] Non-alcoholic fatty liver disease is becoming an important cause of hepatocellular carcinoma in developed regions.[9,10] Future prospective studies should clarify to what extent non-alcoholic fatty liver disease overlaps with alcohol-related liver disease as a risk factor for hepatocellular carcinoma.[11] Growing evidence based on retrospective assessments supports the association between metabolic syndrome, diabetes, and obesity and hepatocellular carcinoma in patients with non-alcoholic fatty liver disease. Diabetes is an independent risk factor for hepatocellular carcinoma,[12,13] and liver cancer mortality is five times greater among men with a high baseline body-mass index than among men with a normal body-mass index.[14] Tobacco use is associated with an increased risk,[15] whereas coffee is associated with reduced risk.[16] Co-infection of HIV with either hepatitis B virus or hepatitis C virus might be associated with rapidly progressive liver disease, and the risk of hepatocellular carcinoma increases on cirrhosis development.[17]

Hepatocellular carcinoma-related mortality can be prevented by avoiding the risk factors. Nationwide hepatitis B virus vaccination of infants in Taiwan reduced the incidence of hepatocellular carcinoma per 10^5 person-years from 0·92 in the unvaccinated cohort to 0·23 in the vaccinated birth cohorts.[18] Once chronic infection is acquired, elimination of viral replication by antiviral agents prevents progression of liver disease and probably development of hepatocellular carcinoma.[19] Prevention of hepatitis C virus infection relies on avoiding transmission through contaminated blood. Once infection is acquired, effective antiviral therapy should prevent the progression to cirrhosis and, ultimately, the development of

Search strategy and selection criteria

We searched in MEDLINE, Embase, and Cochrane Library (between Jan 1, 2005, and April 30, 2017), using hepatocellular carcinoma, liver cancer, and primary liver carcinoma as free text words. We also did a manual search and review of reference lists. We largely selected publications in the past 5 years, but did not exclude commonly referenced and highly regarded older publications. Only articles published in English were selected.

Observational Study

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Mortality assessment of patients with hepatocellular carcinoma according to underlying disease and treatment modalities

Pegah Golabi, MD[a], Sofie Fazel, BS[a], Munkhzul Otgonsuren, MPH[a], Mehmet Sayiner, MD[a], Cameron T. Locklear, MD, MPH[b], Zobair M. Younossi, MD, MPH[a,b,*]

Abstract

Hepatocellular carcinoma (HCC) is among the most common types of cancer. Liver transplantation (LT) and surgical resection (SR) are primary surgical treatment options for HCC.

The aim of the study was to assess mortality within 2 years postdiagnosis among patients with HCC according to their treatment modalities.

We examined data from the Surveillance, Epidemiology and End Results (SEER)-Medicare database between 2001 and 2009. SEER registries collect demographics, cancer stage and historical types, and treatments. Medicare claims include diagnoses, procedures, and survival status for each beneficiary. Patients with HCC were identified using the International Classification of Disease Oncology, Third Edition Site code C22.0 and Histology Code 8170-8175. Treatment modalities were LT, SR, or nonsurgical treatment.

Total of 11,187 cases was included (age at diagnosis: 72 years, 69% male, 67% White). HCC patients who underwent LT were younger (61 vs 71 years), sicker (presence of decompensated cirrhosis: 80% vs 23%), and less likely to die within 2 years (29% vs 44%, all $P < 0.01$), compared to SR patients. In multivariate analysis, older age (HR: 1.01 [95% CI = 1.01–1.01]), stage of HCC other than local (HR: 1.81[95%CI = 1.70–1.91]), and being treated with SR (HR: 1.95 [95%CI = 1.55–2.46]) were independent predictors of mortality within 2 years. Furthermore, the presence of decompensated cirrhosis (HR: 1.84 [95%CI = 1.73–1.96]) and alcoholic liver disease (HR: 1.19[95%CI = 1.11–1.28]) increased within 2 years mortality.

Mortality within 2 years postdiagnosis of HCC was significantly higher in patients treated with SR than LT.

Abbreviations: HBV = hepatitis B virus, HCC = hepatocellular carcinoma, HCV = hepatitis C virus, ICD = International Classification of Disease, LT = liver transplantation, NAFLD = Non-alcoholic fatty liver disease, SEER = Surveillance, Epidemiology and End Results, SR = surgical resection, TACE = transarterial chemoembolization.

Keywords: hepatocellular carcinoma, liver transplantation, mortality, surgical resection

1. Introduction

Cancer is among the leading causes of morbidity and mortality worldwide, accounting for 14 million new cases and 8.2 million deaths in 2012.[1,2] Globally, liver cancer is the fifth most common type of cancer and third most common cause of cancer mortality.[3] With an estimated 746,000 deaths in 2012, liver cancer is the second most common cancer-related deaths, worldwide.[4] In the United States (US), according to the Surveillance, Epidemiology, and End Results Program (SEER) estimates, in 2015, liver cancer accounted for 2.2% of all new cancer cases and 4.2% of all cancer deaths.[5] Although metastatic tumors are the most frequently seen type of cancer of the liver, hepatocellular carcinoma (HCC) is the most common primary liver cancer, accounting for nearly 80% of all primary liver cancers.[6,7]

In the United States, hepatocellular carcinoma has been recognized as the ninth leading cause of cancer-related deaths.[7–10] Furthermore, HCC incidence and mortality rates have been increasing for decades.[11,12] Unfortunately, HCC is typically diagnosed late in its course, with a median survival following diagnosis of approximately 6 to 20 months. In the United States, 2 years survival is less than 50% and 5-year survival is only 10%.[13–15]

The effective management of HCC involves a multidisciplinary approach, involving hepatologists, surgeons, radiologists, and liver transplant team. In this context, treatment modalities for HCC patients include surgical resection, radiofrequency ablation, microwave ablation, percutaneous ethanol or acetic acid injection, transarterial chemoembolization (TACE), liver transplantation (LT) and, rarely, systemic chemotherapy.[16,17] The

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[a] Betty and Guy Beatty Center for Integrated Research, Inova Health System, Falls Church, [b] Center For Liver Disease, Department of Medicine, Inova Fairfax Hospital Falls Church, VA.

[*] Correspondence: Zobair M. Younossi, Betty and Guy Beatty Center for Integrated Research, Claude Moore Health Education and Research Building, Falls Church, VA (e-mail: Zobair.Younossi@inova.org).

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ORIGINAL ARTICLE

Comparison of outcomes of transplantation and resection in patients with early hepatocellular carcinoma: a meta-analysis

Mashaal Dhir[1], Elizabeth R. Lyden[2], Lynette M. Smith[2] & Chandrakanth Are[1,3]

[1]Department of Surgery, Division of Surgical Oncology, Eppley Cancer Center, [2]Department of Epidemiology and Biostatistics, College of Public Health and [3]Department of Genetics, Cell Biology and Anatomy, University of Nebraska Medical Center, Omaha, NE, USA

Abstract

Objectives: Surgical decision making for patients with early hepatocellular carcinoma (HCC) and well-compensated cirrhosis remains controversial. The aim of the current study was to conduct a meta-analysis of published reports to compare survival outcomes after transplantation and resection, respectively, in patients with early HCC [i.e. HCC falling within the Milan Criteria (a solitary lesion measuring ≤5 cm or fewer than three lesions with a largest diameter of ≤3 cm, and absence of macroscopic vascular invasion or extrahepatic disease)] and well-compensated cirrhosis.

Methods: A total of 990 abstracts were identified through a PubMed-based search. Ten articles comparing transplantation and resection in patients with early HCC were included in the meta-analysis. Meta-analysis was performed using STATA 9.2 statistical software.

Results: Outcomes were analysed for a total of 1763 patients with early HCC. The 5-year overall survival (OS) for all patients was 58% (transplantation: 63%; resection: 53%). Meta-analysis of all 10 studies revealed a survival advantage for transplantation [odds ratio (OR) 0.581, 95% confidence interval (CI) 0.359–0.939; $P = 0.027$]. Analysis of only those reports that utilized an 'intention-to-treat' strategy failed to demonstrate a survival advantage for either treatment approach (OR 0.600, 95% CI 0.291–1.237; $P = 0.166$).

Conclusions: The current study demonstrates a favourable outcome in patients with early HCC treated by either transplantation or resection. Although transplantation was noted to have a survival advantage in some settings, resection continues to be a viable treatment approach.

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Correspondence

Chandrakanth Are, Associate Professor, Division of Surgical Oncology, Department of Surgery, Genetics, Cell Biology and Anatomy, Program Director-General Surgery Residency, University of Nebraska Medical Center, Omaha, NE 68198, USA. Tel: + 1 402 559 8941. Fax: + 1 402 559 7900. E-mail: care@unmc.edu

Introduction

Worldwide, hepatocellular carcinoma (HCC) is the fifth most common cancer, with an estimated 748 300 new cases diagnosed in 2008, and is also a leading cause of mortality, accounting for an estimated 695 900 cancer deaths in 2008.[1] Although HCC is much more frequent in eastern Asia, its incidence continues to rise in the United States (US) as a result of major risk factors such as hepatitis C virus (HCV)-induced cirrhosis and non-alcoholic steatohepatitis (NASH).[1–3] In 2011, an estimated 26 190 new cases and 19 590 deaths from liver and intrahepatic bile duct cancers were expected in the US.[4]

Several treatment options are available to patients with HCC and the ideal option is determined based on the burden of tumour and extent of underlying liver disease.[5,6] Transplantation and resection remain the major therapeutic options available to patients with HCC.[5–7] Patients with early-stage disease [i.e. HCC falling within the Milan Criteria (a solitary lesion measuring ≤5 cm or up to three lesions with a largest diameter of ≤3 cm, and absence of macroscopic vascular invasion or extrahepatic disease)] and advanced cirrhosis, including Child–Pugh class B/C disease and portal hypertension, are thought to be candidates for transplantation, whereas resection remains the treatment of choice in patients without underlying liver disease. However, significant controversy exists regarding the choice between transplantation and resection in the management of patients with well-compensated cirrhosis (i.e. patients with Child–Pugh class A disease and selected patients with class B disease) and early HCC.

Surgical Treatment of Hepatocellular Carcinoma in North America: Can Hepatic Resection Still Be Justified?

William C Chapman, MD, FACS, Goran Klintmalm, MD, FACS, Alan Hemming, MD, FACS, Neeta Vachharajani, BS, Maria B Majella Doyle, MD, Ron DeMatteo, MD, FACS, Victor Zaydfudim, MD, Haniee Chung, MD, Keith Cavaness, MD, FACS, Robert Goldstein, MD, FACS, Ivan Zendajas, MD, Laleh G Melstrom, MD, David Nagorney, MD, FACS, William Jarnagin, MD, FACS

BACKGROUND: The incidence of hepatocellular cancer (HCC) is increasing dramatically worldwide. Optimal management remains undefined, especially for well-compensated cirrhosis and HCC.

STUDY DESIGN: This retrospective analysis included 5 US liver cancer centers. Patients with surgically treated HCC between 1990 and 2011 were analyzed; demographics, tumor characteristics, and survival rates were included.

RESULTS: There were 1,765 patients who underwent resection (n = 884, 50.1%) or transplantation (n = 881, 49.9%). Overall, 248 (28.1%) resected patients were transplant eligible (1 tumor <5 cm or 2 to 3 tumors all <3 cm, no major vascular invasion); these were compared with 496 transplant patients, matched based on year of transplantation and tumor status. Overall survivals at 5 and 10 years were significantly improved for transplantation patients (74.3% vs 52.8% and 53.7% vs 21.7% respectively, $p < 0.001$), with greater differences in disease-free survival (71.8% vs 30.1% at 5 years and 53.4% vs 11.7% at 10 years, $p < 0.001$). Ninety-seven of the 884 (11%) resected patients were within Milan criteria and had cirrhosis; these were compared with the 496 transplantation patients, with similar results to the overall group. On multivariate analysis, type of surgery was an independent variable affecting all survival outcomes.

CONCLUSIONS: The increasing incidence of HCC stresses limited resources. Although transplantation results in better long-term survival, limited donor availability precludes widespread application. Hepatic resection will likely remain a standard therapy in selected patients with HCC. In this large series, only about 10% of patients with cirrhosis were transplant-eligible based on tumor status. Although liver transplantation results are significantly improved compared with resection, transplantation is available only for a minority of patients with HCC. (J Am Coll Surg 2015;220:628–637. © 2015 by the American College of Surgeons)

Hepatocellular cancer (HCC) is the fifth most common cause of malignancy worldwide and is one of the leading causes of cancer-related mortality. Liver transplantation (LT) and liver resection (LR) are the mainstays of surgical therapy for HCC, which occurs in the setting of chronic liver disease in the majority of patients (65% to 85%), limiting consideration of hepatic resection because of the risk of postoperative liver failure. Many patients also present with advanced stages of disease that often preclude consideration of LT.[1] For these reasons, only highly selected patients receive curative therapy for HCC; overall curative therapy occurs in 25% to 40% of American patients after presentation.[1]

Liver resection with partial hepatectomy is the first-line approach for all patients with resectable tumors in the

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From the Department of Surgery, Section of Abdominal Transplantation, Washington University School of Medicine, St Louis, MO (Chapman, Vachharajani, Doyle, Chung) and the Departments of Surgery, Baylor University, Waco, TX (Klintmalm, Cavaness, Goldstein); University of California San Diego Health System, San Diego, CA (Hemming); Memorial Sloan-Kettering Cancer Center, New York, NY (DeMatteo, Jarnagin); University of Virginia Health System, Charlottesville, VA (Zaydfudim); The Cancer Institute of New Jersey, Rutgets Robert Wood Johnson Medical School, New Brunswick, NJ (Melstrom); University of Florida Health, Gainesville, FL (Zendajas); and Mayo Clinic, Rochester, MN (Nagorney). Correspondence address: William C Chapman, MD, FACS, Washington University School of Medicine, 660 S Euclid Ave, Campus Box 8109, St Louis, MO 63110. email: chapmanw@wustl.edu

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Pediatric Liver Transplantation for Hepatocellular Cancer and Rare Liver Malignancies: US Multicenter and Single-Center Experience (1981-2015)

Rohan Vinayak,[1]* Ruy J. Cruz Jr.,[2]* Sarangarajan Ranganathan,[3] Ravi Mohanka,[4] George Mazariegos,[3] Kyle Soltys,[3] Geoff Bond,[3] Sameh Tadros,[3] Abhinav Humar,[2] J. Wallis Marsh,[2] Robert R. Selby,[5] Jorge Reyes,[6] Qing Sun,[3] Kimberly Haberman,[2] and Rakesh Sindhi[3]

[1]Department of Surgery, College of Medicine, Medical University of South Carolina, Charleston, SC; [2]Thomas E. Starzl Transplantation Institute, University of Pittsburgh Medical Center, Montefiore, Pittsburgh, PA; [3]Thomas E. Starzl Transplantation Institute, Children's Hospital of Pittsburgh, University of Pittsburgh Medical Center, Pittsburgh, PA; [4]Liver Transplant and Hepatobiliary Surgery, Global Hospitals, Mumbai, India; [5]Department of Surgery, Keck School of Medicine, University of Southern California, Los Angeles, CA; and [6]Kidney, Liver, Intestinal Care Services, University of Washington Medical Center, Seattle, WA

A tenth of all pediatric liver transplantations (LTs) are performed for unresectable liver malignancies, especially the more common hepatoblastoma (HBL). Less understood are outcomes after LT for the rare hepatocellular carcinoma, nonhepatoblastoma embryonal tumors (EMBs), and slow growing metastatic neuroendocrine tumors of childhood. Pediatric LT is increasingly performed for rare unresectable liver malignancies other than HBL. We performed a retrospective review of outcomes after LT for malignancy in the multicenter US Scientific Registry of Transplant Recipients (SRTR; n = 677; 1987-2015). We then reviewed the Children's Hospital of Pittsburgh (CHP; n = 74; 1981-2014) experience focusing on LT for unresectable hepatocellular cancer (HCC), EMBs, and metastatic liver tumors (METS). HBL was included to provide reference statistics. In the SRTR database, LT for HCC and HBL increased over time ($P < 0.001$). Compared with other malignancies, the 149 HCC cases received fewer segmental grafts ($P < 0.001$) and also experienced 10-year patient survival similar to 15,710 adult HCC LT recipients (51.6% versus 49.6%; $P = 0.848$, not significant [NS], log-rank test). For 22 of 149 cases with incidental HCC, 10-year patient survival was higher than 127 primary HCC cases (85% [95% confidence interval (CI), 70.6%-100%] versus 48.3% [95% CI, 38%-61%]; $P = 0.168$, NS) and similar to 3392 biliary atresia cases (89.9%; 95% CI, 88.7%-91%). Actuarial 10-year patient survival for 17 EMBs, 10 METS, and 6 leiomyosarcoma patients exceeded 60%. These survival outcomes were similar to those seen for HBL. At CHP, posttransplant recurrence-free and overall survival among 25 HCC, 17 (68%) of whom had preexisting liver disease, was 16/25 or 64%, and 9/25 or 36%, respectively. All 10 patients with incidental HCC and tumor-node-metastasis stage I and II HCC survived recurrence-free. Only vascular invasion predicted poor survival in multivariate analysis ($P < 0.0001$). A total of 4 of 5 EMB patients (80%) and all patients with METS (neuroendocrine-2, pseudopapillary pancreatic-1) also survived recurrence-free. Among children, LT can be curative for unresectable HCC confined to the liver and without vascular invasion, incidental HCC, embryonal tumors, and metastatic neuroendocrine tumors.

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Abbreviations: AFP, alpha-fetoprotein; BA, biliary atresia; BDCA, bile duct carcinoma; CHP, Children's Hospital of Pittsburgh; CI, confidence interval; CIT, cold ischemia time; EMB, nonhepatoblastoma embryonal tumor; HBL, hepatoblastoma; HCC, hepatocellular carcinoma; LD, living donor; LT, liver transplantation; METS, metastatic liver tumors; NA, not applicable; NS, not significant; PTLD, posttransplant lymphoproliferative disease; PV, portal vein; SARC, leiomyosarcoma; SEC, sinusoidal endothelial cell; SRTR,

SEE EDITORIAL ON PAGE 1501

Although malignant liver tumors in children make up 1% of all pediatric tumors, those liver malignancies which are unresectable account for a tenth of all liver transplantations (LTs) performed in children in the United States.[1,2] Three-fourths of these LTs are

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Efficacy and safety of liver transplantation in patients with cholangiocarcinoma: a systematic review and meta-analysis

Jinyang Gu[1,2], Jianling Bai[3], Xiaolei Shi[1,2], Jianxin Zhou[1,2], Yudong Qiu[1,2], Yafu Wu[1,2], Chunping Jiang[1,2], Xitai Sun[1,2], Fanggui Xu[4], Yue Zhang[4] and Yitao Ding[1,2]

[1] Department of Hepatobiliary Surgery, Affiliated DrumTower Hospital of Nanjing University Medical School, Nanjing, China
[2] Jiangsu Province's Key Medical Center for Hepatobiliary Disease, Nanjing, China
[3] Department of Epidemiology and Biostatistics, School of Public Health, Nanjing Medical University, Nanjing, China
[4] Department of Hepatobiliary Surgery, Clinical Medical College of Nanjing Medical University, Nanjing, China

The aim of our study was to evaluate the efficacy and safety of liver transplantation in patients with cholangiocarcinoma. According to the requirements of Cochrane systematic review, a thorough literature search was performed in PubMed/Medline, Embase and Cochrane electronic databases between 1995 and 2009 in terms of the key words "liver transplantation" and "cholangiocarcinoma," "cholangiocellular carcinoma" or "bile duct cancer," with restricted articles for the English language. Data were processed for a meta-analysis by Stata 10 software. Altogether 14 clinical trials containing 605 transplanted patients of bile duct cancers were finally enrolled in our study. The overall 1-, 3- and 5-year pooled survival rates were 0.73 [95% confidence interval (CI) = 0.65–0.80], 0.42 (95% CI = 0.33–0.51) and 0.39 (95% CI = 0.28–0.51), respectively. Of note, preoperative adjuvant therapies [orthotopic liver transplantation (OLT)-PAT group] rendered the transplanted individuals with comparably favorable outcomes with 1-, 3- and 5-year pooled survival rates of 0.83 (95% CI = 0.57–0.98), 0.57 (95% CI = 0.18–0.92) and 0.65 (95% CI = 0.40–0.87). In addition, the overall pooled incidence of complications was 0.62 (95% CI = 0.44–0.78), among which that of OLT-PAT group (0.58; 95% CI = 0.20–0.92) was relatively acceptable compared to those of liver transplantation alone (0.61; 95% CI = 0.33–0.85) and liver transplantation with extended bile duct resection (0.78; 95% CI = 0.55–0.94). In comparison to curative resection of cholangiocarcinoma with the 5-year survival rate reported from 20 to 40%, the role of liver transplantation alone is so limited. In the future, attention will be focused on liver transplantation following neoadjuvant radiochemotherapy, which requires a well-designed, prospective randomized controlled study.

Bile duct cancer or cholangiocarcinoma, which arises from the epithelium of bile ducts, is the second most common primary malignant tumor of the liver after hepatocellular carcinoma.[1] Although hepatic resection represents the primary treatment for cholangiocarcinoma, extensive perineural and lymphatic invasion, bilateral liver involvement and vascular encasement frequently preclude potentially complete resection.[2] In addition, extensive surgical resection is not tolerated in patients with primary sclerosing cholangitis (PSC) because of the underlying liver dysfunction.[3] Even if curative resection is achieved, cholangiocarcinoma, to date, remains a devastating and challenging disease with 5-year survival rates reported from 20 to 40%.[4] As for palliative modalities including biliary drainage, irradiation or chemotherapy and photodynamic therapy, the median survival for unresectable individuals is less than 12 months.[1]

Since the late 1990s, orthotopic liver transplantation (OLT) has been established for end-stage liver disease as well as hepatocellular carcinoma.[5] Total hepatectomy followed by subsequent OLT seems to offer a chance for significant prolongation of survival with wide tumor-free margins and without underlying liver disease.[6] Taken into consideration, OLT was initially proposed as an optimal solution for patients with irresectable cholangiocarcinoma.[7–10] Despite sound theoretical argument in favor of liver transplantation, the early experience with OLT alone for bile duct cancer was uniformly disappointing because of frequent tumor relapse.[11–13] Reports from Hannover in 1996 described that 1-, 3- and 5-year survival rates for 25 liver transplants of proximal bile duct cancer were 60, 21.4 and 17.1%, respectively.[11] No significant difference was observed with comparison to survival after resection.[11] Spanish experience in liver transplantation for hilar and peripheral cholangiocarcinoma revealed that

Key words: cholangiocarcinoma, liver transplantation, extended bile duct resection, neoadjuvant therapy, systematic review, meta-analysis
Abbreviation:: CI: confidence interval
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Correspondence to: Yitao Ding, Department of Hepatobiliary Surgery, Affiliated DrumTower Hospital of Nanjing University Medical School, No. 321 Zhongshan Road, Nanjing, China, E-mail: yitaoding@hotmail.com

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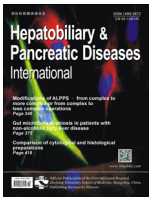

Review Article

A pooled analysis of treatment and prognosis of hepatic angiosarcoma in adults

De-Bang Li[a], Xiao-Ying Si[b], Tao Wan[b], Yan-Ming Zhou[b,*]

[a] Department III of General Surgery, The First Hospital of Lanzhou University, Lanzhou 730000, China
[b] Department of Hepatobiliary & Pancreatovascular Surgery, First Affiliated Hospital of Xiamen University, Xiamen 361003, China

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ABSTRACT

Background: Hepatic angiosarcoma is a rare malignant vascular tumor presenting unique treatment challenges. The aim of the present study was to determine the treatment and prognosis of this entity.
Data sources: A systematic literature search was conducted using PubMed, Embase and Chinese Biomedical Literature database, to identify articles published from January 1980 to July 2017. Search terms were "hepatic angiosarcoma" and "liver angiosarcoma". Additional articles were retrieved through manual search of bibliographies of the relevant articles. Pooled individual data concerning the prognosis following various therapeutic modalities were analyzed.
Results: A total of 75 articles involving 186 patients were eligible for inclusion. The median overall survival (OS) was 8 months, with 1-, 3-, and 5-year OS rates of 36.6%, 22.3%, and 12.0%, respectively. The median OS after partial hepatectomy ($n=86$), chemotherapy ($n=36$), liver transplantation ($n=17$), and supportive care ($n=46$) were 15, 10, 5 and 1.3 months, respectively. Small tumor size (<10 cm) was the only significant favorable factor for OS after partial hepatectomy ($P=0.012$).
Conclusions: Despite the dismal prognosis, partial hepatectomy could prolong the survival of hepatic angiosarcoma patients, particularly those with tumors <10 cm. Chemotherapy could be an option for unresectable disease. Liver transplantation is not a recommendable option for the management of this malignancy.

Introduction

Hepatic angiosarcoma (HAS) is a rare malignancy of vascular origin representing less than 2% of all primary liver tumors. Unlike most primary hepatocellular carcinomas (HCC) occurring in a background of chronic liver disease, the etiologic factors for HAS remain unclear in most cases, and only a few cases were reported to be associated with exposure to chemical carcinogens such as thorium dioxide, vinyl chloride, arsenic and radiation. However, most HAS cases had no known etiology [1]. Partial hepatectomy, chemotherapy, and liver transplantation have been used in the treatment of HAS patients. But given the rarity of this entity, it is difficult to provide sufficient evidence to draw a conclusion about the efficacy of a particular therapy. The aim of this systematic review is to evaluate the prognosis following various therapeutic modalities by pooling data from all individually documented patients with HAS.

Methods

The present study was conducted according to the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement [2]. The level of evidence of each study was classified according to the Oxford Centre for Evidence-Based Medicine levels of evidence [3].

Literature review

A systematic literature search was conducted using PubMed, Embase and Chinese Biomedical Literature database, to identify articles published from January 1980 to July 2017. Search terms were "hepatic angiosarcoma" and "liver angiosarcoma". Additional articles were retrieved through manual search of bibliographies of the relevant articles.

Inclusion criteria: (i) articles that included patients who underwent partial hepatectomy, or any other treatments for HAS; (ii) original data published; (iii) availability of survival data; and (iv) articles published in either the Chinese or English language.

* Corresponding author.
E-mail address: zhouymsxy@sina.cn (Y.-M. Zhou).

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CLINICAL PRACTICE GUIDELINES

Hepatocellular carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

A. Vogel[1], A. Cervantes[2], I. Chau[3], B. Daniele[4], J. M. Llovet[5,6,7], T. Meyer[8,9], J.-C. Nault[10], U. Neumann[11], J. Ricke[12], B. Sangro[13], P. Schirmacher[14], C. Verslype[15], C. J. Zech[16], D. Arnold[17] & E. Martinelli[18], on behalf of the ESMO Guidelines Committee*

[1]Department of Gastroenterology, Hepatology and Endocrinology, Medical School Hannover, Hannover, Germany; [2]Department of Medical Oncology, Biomedical Research Institute INCLIVA, University of Valencia, Valencia, Spain; [3]Department of Medicine, Royal Marsden Hospital, Surrey, UK; [4]Dipartimento di Oncologia, A. O. G. Rummo, Benevento, Italy; [5]Division of Liver Diseases, Icahn School of Medicine at Mount Sinai, Mount Sinai Liver Cancer Program, New York, USA; [6]Barcelona-Clínic Liver Cancer Group (BCLC), Unitat d'Hepatologia, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Hospital Clínic, Universitat de Barcelona, Barcelona; [7]Institució Catalana de Recerca i Estudis Avançats (ICREA), Barcelona, Spain; [8]Oncology, Royal Free Hospital, London; [9]UCL Cancer Institute, University College London, London, UK; [10]Service d'hépatologie, Hôpital Jean Verdier, Bondy, France; [11]Klinik für Allgemein- und Viszeralchirurgie, Medizinische Fakultät der RWTH Aachen; [12]Klinik und Poliklinik für Radiologie, Ludwig-Maximilians-Universität München, Munich, Germany; [13]Liver Unit, Clinica Universidad de Navarra-IDISNA and CIBEREHD, Pamplona, Spain; [14]Institute of Pathology, University Hospital, Heidelberg, Germany; [15]Campus Gasthuisberg, UZ Leuven, Leuven, Belgium; [16]Klinik für Radiologie und Nuklearmedizin Universität Basel, Basel, Switzerland; [17]Department Oncology, Section Hematology and Palliative Care AK Altona, Asklepios Tumorzentrum Hamburg, Hamburg, Germany; [18]Faculty of Medicine, Università della Campania L. Vanvitelli Naples, Caserta, Italy

**Correspondence to*: ESMO Guidelines Committee, ESMO Head Office, Via Ginevra 4, 6900 Lugano, Switzerland. E-mail: clinicalguidelines@esmo.org

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Incidence and epidemiology

The incidence of hepatocellular carcinoma (HCC) has been rising worldwide over the last 20 years and is expected to increase until 2030 in some countries including the United States, while in other countries, such as Japan, the incidence has started to decline [1–3]. In 2012, liver cancer represented the fifth most common cancer in men (554 000 new cases) and the ninth in women (228 000 new cases) and the second most common cause of cancer-related death (746 000 estimated deaths), worldwide [3]. The incidence varies from 3/100 000 in Western countries, to 78.1/100 000 in Mongolia, with the highest incidence in Africa and Asia, mapping the geographical distribution of viral hepatitis B (HBV) and hepatitis C (HCV), the most important causes of chronic liver disease and HCC [4]. In Europe, in 2012 the estimated incidence rate was 10.0 in men and 3.3 in women per 100 000, respectively, while the estimated mortality rate was 9.1 and 3.3 per 100 000 in men and women, respectively [3]. The incidence of HCC shows a strong male preponderance and increases progressively with advancing age in all populations. The association of chronic liver disease and HCC represents the basis for preventive strategies, including universal vaccination at birth against HBV [I, A] [5] and early antiviral treatment of viral HBC and HCV [III, A] [6–8].

The prevalence of obesity and type 2 diabetes has greatly increased in the past decades, leading to a rising incidence of non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH), which can lead to fibrosis and cirrhosis and, eventually, HCC [9]. HCC related to NAFLD/NASH is probably underestimated [10] and is expected to rise in the future, possibly overtaking the other aetiologies in some areas of the world [11]. A significant proportion of patients with NAFLD/NASH-associated HCC do not have histological evidence of cirrhosis [12].

The control of other risk factors for chronic liver disease and cancer is more difficult to implement, such as cutting down on the consumption of alcohol and programmes aiming at a healthier lifestyle in the light of the obesity pandemic [13, 14]. In Africa, reduction of exposure to aflatoxin B1, especially in HBV-infected individuals, may lower the risk of HCC. HCC may evolve from subclasses of adenomas; in $< 10\%$ of cases HCC occurs in an otherwise normal liver.

Surveillance

Surveillance of HCC involves the repeated application of screening tools in patients at risk for HCC and aims for the reduction in mortality of this patient population. The success of surveillance is influenced by the incidence of HCC in the target population, the availability and acceptance of efficient diagnostic tests and the availability of effective treatment. Cost-effectiveness studies suggest surveillance of HCC is warranted in all cirrhotic patients

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AASLD PRACTICE GUIDELINE

Evaluation of the Pediatric Patient for Liver Transplantation: 2014 Practice Guideline by the American Association for the Study of Liver Diseases, American Society of Transplantation and the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition

Robert H. Squires,[1] Vicky Ng,[2] Rene Romero,[3] Udeme Ekong,[4] Winita Hardikar,[5] Sukru Emre,[6] and George V. Mazariegos[7]

This practice guideline has been approved by the American Association for the Study of Liver Diseases, the American Society of Transplantation and the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition.

Abbreviations: ALF, acute liver failure; GRADE, Grading of Recommendation Assessment, Development, and Evaluation; HB, hepatoblastoma; HCC, hepatocellular carcinoma; HPE, hepatoportoenterostomy; LT, liver transplantation; OTPN, Organ Procurement and Transplantation Network; PFIC, progressive familial intrahepatic cholestasis; TIPS, transjugular intrahepatic portosystemic shunt.

From the [1]Department of Pediatrics, University of Pittsburgh School of Medicine; Division of Pediatric Gastroenterology, Hepatology and Nutrition, Children's Hospital of Pittsburgh of UPMC, Pittsburgh, PA; [2]Department of Pediatrics, University of Toronto; Division of Pediatric Gastroenterology, Hepatology and Nutrition, SickKids Transplant and Regenerative Medicine Center, Hospital for Sick Children, Toronto, Canada; [3]Department of Pediatrics, Division of Pediatric Gastroenterology, Hepatology, and Nutrition, Emory University School of Medicine; Children's Healthcare of Atlanta, Atlanta, GA; [4]Department of Pediatrics, Division of Pediatric Gastroenterology and Hepatology, Yale School of Medicine, New Haven, CT; [5]Department of Paediatrics, University of Melbourne; Department of Gastroenterology, Royal Children's Hospital, Melbourne, Australia; [6]Department of Surgery, Section of Transplantation and Immunology, Yale School of Medicine, New Haven, CT; [7]Department of Surgery, University of Pittsburgh School of Medicine; Division of Pediatric Transplantation, Hillman Center for Pediatric Transplantation, Children's Hospital of Pittsburgh of UPMC, Pittsburgh, PA.

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All AASLD Practice Guidelines are updated annually. If you are viewing a Practice Guideline that is more than 12 months old, please visit www.aasld.org for an update in the material.

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Address reprint requests to: Robert H. Squires, M.D., Professor of Pediatrics, University of Pittsburgh, Children's Hospital of Pittsburgh of UPMC, 4401 Penn Ave., Pittsburgh, PA 15224. E-mail: squiresr@upmc.edu

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Preamble

Current American Association for the Study of Liver Diseases (AASLD) liver transplant evaluation guidelines include both adult and pediatric patients.[1] While pediatric liver transplants account for ~7.8% of all liver transplants in the United States, sufficient differences between pediatric and adult patients seeking liver transplantation (LT) now require independent, yet complementary documents. This document will focus on pediatric issues at each level of the evaluation process. Disease categories suitable for referral to a pediatric LT program are similar to adults: acute liver failure, autoimmune, cholestasis, metabolic or genetic, oncologic, vascular, and infectious. However, specific etiologies and outcomes differ widely from adult patients, justifying independent pediatric guidelines. Data supporting our recommendations are based on a Medline search of the English language literature from 1997 to the present.

Intended for use by physicians, these recommendations suggest preferred approaches to the diagnostic, therapeutic, and preventive aspects of care. They are intended to be flexible, in contrast to standards of care, which are inflexible policies to be followed in every case. Specific recommendations are based on relevant published information.

To more fully characterize the available evidence supporting the recommendations, the AASLD Practice Guidelines Committee has adopted the classification used by the Grading of Recommendation Assessment, Development, and Evaluation (GRADE) workgroup with minor modifications (Table 1). The classifications and recommendations are based on three categories: the source of evidence in levels I through III; the

Section 5.0

New Discussion Items

The use of functional MRI in presurgical planning for epilepsy

Question: Should coverage of functional MRI be modified for patients with epilepsy who are being evaluated for epilepsy surgery?

Question source: David Spencer, MD, Director OHSU Epilepsy Program

Issue:

From Dr. Spencer

> I am writing to you as the director of the OHSU Epilepsy Program. We care for a large group of Medicaid patients with epilepsy and a small subset of these patients have medically refractory epilepsy and are referred to us for evaluation for epilepsy surgery.
>
> There are two key pieces of the surgical workup that are presently being routinely denied or not even considered for coverage: neuropsychological testing and functional MRI (fMRI). Thus we have a growing pool of patients who have undergone a great deal of testing (e.g. video-EEG monitoring, MRI scans, PET scans, etc.) and are ready to proceed to surgery but are unable to progress because of the inability to complete these final tests. We are spending a great deal of time writing appeals and trying to set up peer-to-peer discussions with little progress, and it has become clear that this issue needs to be addressed at a higher level.
>
> Functional MRI is used to establish hemispheric language dominance and predict language and memory risk prior to epilepsy surgery. If we are unable to perform fMRI, we have to put more patients through a more invasive and more costly procedure (Wada test) which could be obviated by doing the fMRI study.
>
> These patients with medically refractory epilepsy are at high risk for sudden unexpected death in epilepsy (SUDEP) and we are very uncomfortable drawing out the length of the evaluations or not progressing at all to highly effective surgery in these patients.

Prioritized List Status:

Line:	**30**
Condition:	EPILEPSY AND FEBRILE CONVULSIONS (See Guideline Notes 64,65,84)
Treatment:	MEDICAL THERAPY
ICD-10:	G40.001-G40.919,R56.00-R56.9
CPT:	93792,93793,96150-96155,97535,97802-97804,98966-98969,99051,99060, 99070,99078,99184,99201-99239,99281-99285,99291-99404,99408-99449, 99451,99452,99468-99480,99487-99491,99495-99498,99605-99607
HCPCS:	G0068,G0071,G0248-G0250,G0396,G0397,G0406-G0408,G0425-G0427, G0463-G0467,G0490,G0508-G0511,G0513,G0514,G2010-G2012

Line: 174

Condition: GENERALIZED CONVULSIVE OR PARTIAL EPILEPSY WITHOUT MENTION OF IMPAIRMENT OF CONSCIOUSNESS (See Coding Specification Below)

Treatment: SINGLE FOCAL SURGERY

ICD-10: G40.001-G40.219,G40.309-G40.319,Z45.42-Z45.49,Z46.2

CPT: 61531-61537,61540-61543,61566,61567,61720,61735,61760,61850,61860, 61870,61885,61888,64553,64568-64570,93792,93793,95836,95976,95977, 95983,95984,96150-96155,98966-98969,99051,99060,99070,99078,99184, 99201-99239,99281-99285,99291-99404,99408-99449,99451,99452, 99468-99480,99487-99491,99495-99498,99605-99607

HCPCS: C1767,C1778,C1816,C1820,C1822,C1823,C1897,G0068,G0071,G0235, G0248-G0250,G0396,G0397,G0406-G0408,G0425-G0427,G0463-G0467, G0490,G0508-G0511,G0513,G0514,G2010-G2012

CPT 61885 is included on this line only for vagal nerve stimulation. It is not included on this line for deep brain stimulation.

GUIDELINE NOTE 84, MEDICAL NUTRITION THERAPY FOR EPILEPSY

Line 30

Medical Nutrition Therapy (CPT 97802-97804) is included on this line only for training in the ketogenic diet for children with epilepsy in cases where the child has failed or not tolerated conventional therapy.

DIAGNOSTIC GUIDELINE D22, PET SCAN GUIDELINES *(excerpt related to epilepsy*)

PET scans are also indicated for preoperative evaluation of the brain in patients who have intractable seizures and are candidates for focal surgery.

Codes:

Code	Code Description	Current Line placement
70554	Magnetic resonance imaging, brain, functional MRI; including test selection and administration of repetitive body part movement and/or visual stimulation, not requiring physician or psychologist administration	660 CONDITIONS FOR WHICH CERTAIN INTERVENTIONS ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS
70555	Magnetic resonance imaging, brain, functional MRI; requiring physician or psychologist administration of entire neurofunctional testing	660 CONDITIONS FOR WHICH CERTAIN INTERVENTIONS ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT

Code	Code Description	Current Line placement
		BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS
95958	Wada activation test for hemispheric function, including electroencephalographic (EEG) monitoring	Diagnostic Procedures File
96020	Neurofunctional testing selection and administration during noninvasive imaging functional brain mapping, with test administered entirely by a physician or other qualified health care professional (ie, psychologist), with review of test results and report	660 CONDITIONS FOR WHICH CERTAIN INTERVENTIONS ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS

Clinical Background

From Bauer, 2014
The Wada test (intracarotid amobarbital test or intracarotid amobarbital procedure, respectively, IAT or IAP) is considered the gold standard for preoperative assessment of lateralisation of language and memory function. This test consists of an amobarbital injection in the internal carotid artery, which causes functional disruption of the ipsilateral cerebral hemisphere for 3–5 min. Meanwhile, the patient is asked to perform language tasks. If (s)he can do this without problems, language is probably located on the contralateral side. If the patient becomes aphasic, language is considered to be lateralised to the injected hemisphere. There are several drawbacks to this test: (i) it is invasive and in a vascular compromised population angiography has a complication rate of 1.3%–11%, of which about 0.6% are permanent; (ii) during and shortly after testing amobarbital may cause somnolence, agitation and confusion, which can be distressing for the patient and which can obscure test results; (iii) the tests have to be carried out within 3–5 min because of the duration of the effect of amobarbital; and (iv) it can give unreliable results, possibly due to anatomical variations in the brain vascularisation.

In healthy individuals, language function is lateralised to the left hemisphere in 73%–96% of cases. In epilepsy patients, however, atypically represented language (bilateral or right-dominant) occurs more often.

Functional MRI (fMRI) is one of the emergent non-invasive techniques that could offer a safe, non-invasive and relatively rapid alternative to the Wada test, which offers the possibility to conduct a retest, is less distressing for the patient and costs a third of the Wada test. An optimal fMRI protocol for language testing has not yet been developed, and protocols used both for fMRI and the Wada test differ widely between centres.

If a patient is incorrectly labelled by fMRI as having left language lateralization in the case of a right-sided operation, or incorrectly classified as having right/mixed language lateralisation in the case of a left-sided operation, these incorrect results have grave consequences because the operation will be carried out without further testing.

Evidence review:

Schmid, 2018

- Systematic review of the diagnostic accuracy of functional magnetic resonance imaging, Wada test, magnetoencephalography, and functional transcranial Doppler sonography for memory and language outcome after epilepsy surgery
- Purpose to develop EU guidelines
- 28 papers
- Limitations: high heterogeneity
- Wada Tests (n=17) for memory outcomes
    - Best case sensitivity, specificity (0.79, 0.65)
    - Worst case sensitivity, specificity (0.65, 0.46)
    - The overall quality of evidence was very low
- fMRI (n=4) meta-analysis was not feasible due to small numbers of studies
- Conclusions: Meta-analyses could only be conducted in a few subgroups for the Wada test with low-quality evidence. Thus, more evidence from high-quality studies and improved data reporting are required.

Collinge, 2017

- Review of advanced functional neuroimaging (functional magnetic resonance imaging [fMRI]) and magnetoencephalography (MEG) for pediatric epilepsy surgery candidates
- 34 papers, 353 patients, with an age range of 5 months-19 years
- fMRI language laterilisation with validation: Sensitivity 0.72 (95% CI 0.52–0.86) and specificity 0.60 (95% CI 0.35–0.92) values with a Positive Predictive Value of 74% (95% CI 61–87) and a Negative Predictive Value of 65% (95% CI 52–78)
- Retrieved studies indicate evidence that both fMRI and MEG are able to provide information lateralising and localising motor and language functions. A PPV of 74% (95% CI 61–87) for ‘typical’ lateralisation of language fMRI with validation was demonstrated from available data. The retrieved studies provide evidence that these non-invasive methods are of benefit. However, there is no clear standardised guidance for clinicians regarding which patients are most likely to benefit from a particular modality. Evidence indicates these modalities should not be used as screening tests but should be used to help answer specific questions. For focal lesions this is usually for establishing the relationship of the lesion to the specific eloquent cortex and for mesial temporal epilepsy, assessment of language. Wada is a test that may be failed, providing an indication for likely significant detriment to post-operative memory. The retrieved literature does not provide criteria for failure.

- The majority of studies (76%) achieved Level 3 evidence status
- There is strong preliminary evidence that fMRI and MEG can be used to lateralise and localise language and motor function in paediatric epilepsy surgery candidates and therefore support treatment decisions.
- Authors Conclusions: For children, it remains unclear which language and memory paradigms produce optimal activation and how these should be quantified in a statistically robust manner. Larger scale studies are required to produce patient series data which clinicians may refer to interpret results objectively. If functional imaging techniques are to be the viable alternative for pre-surgical mapping of eloquent cortex for children, paradigms and analyses demonstrating concordance with independent measures must be developed.

Bauer, 2014

- Systematic review and meta-analysis comparing fMRI and Wada testing for presurgical assessment of language lateralization
- 22 studies (504 patients) were included
- 81% of patients were correctly classified with fMRI as having left or right language dominance or mixed language representation. Techniques were discordant in 19% of patients. fMRI and Wada test agreed in 94% for typical language lateralisation and in 51% for atypical language lateralisation.
- Language production or language comprehension tasks and different regions of interest did not yield statistically significant different results.
- It can be concluded that fMRI is reliable when there is strong left lateralised language. The Wada test is warranted when fMRI fails to show clear left-lateralisation.

Benjamin, 2018

- Evaluation of current clinical use of fMRI in presurgical planning
- Survey of surgical epilepsy programs worldwide
    - US (61%) academic programs (85%), and evaluated adults (44%), adults and children (40%), or children only (16%).
- fMRI is used to guide surgical margins (44% of programs) as well as lateralize language (100%). Sites using fMRI for localization most often use a distance margin around activation of 10mm. While considered useful, 56% of programs reported at least one instance of disagreement with other measures.
- Direct brain stimulation typically confirmed fMRI findings (74%) when guiding margins, but instances of unpredicted decline were reported by 17% of programs and 54% reported unexpected preservation of function.
- Clinicians using fMRI to guide surgical margins do not typically map known language-critical areas beyond Broca's and Wernicke's.

- Conclusions: This initial data shows many clinical teams are confident using fMRI not only for language lateralization but also to guide surgical margins. Reported cases of unexpected language preservation when fMRI activation is resected, and cases of language decline when it is not, emphasize a critical need for further validation.

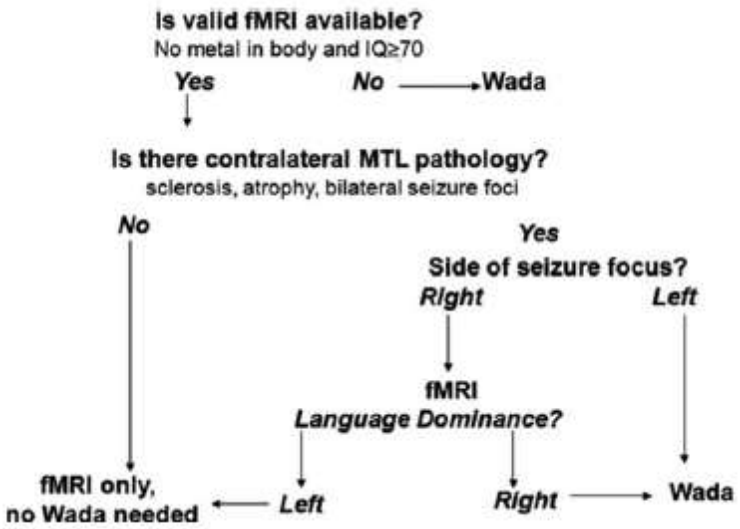

Figure from Swanson, 2015 (cited in Benjamin, 2018)

Guidelines:

Szaflarski, 2017

- American Academy of Neurology practice guideline on use of functional MRI in presurgical epilepsy planning
- https://www.aan.com/Guidelines/home/GetGuidelineContent/840
- Methods: 11 member expert panel
- Results and recommendations:
  - The use of fMRI may be considered an option for lateralizing language functions in place of intracarotid amobarbital procedure (IAP) in patients with medial temporal lobe epilepsy (MTLE; Level C), temporal epilepsy in general (Level C), or extratemporal epilepsy (Level C).
  - For patients with temporal neocortical epilepsy or temporal tumors, the evidence is insufficient (Level U).
  - fMRI may be considered to predict postsurgical language deficits after anterior temporal lobe resection (Level C).
  - The use of fMRI may be considered for lateralizing memory functions in place of IAP in patients with MTLE (Level C) but is of unclear utility in other epilepsy types (Level U).
  - fMRI of verbal memory or language encoding should be considered for predicting verbal memory outcome (Level B). fMRI using nonverbal

memory encoding may be considered for predicting visuospatial memory outcomes (Level C).
    - Presurgical fMRI could be an adequate alternative to IAP memory testing for predicting verbal memory outcome (Level C).
    - Clinicians should carefully advise patients of the risks and benefits of fMRI vs IAP during discussions concerning choice of specific modality in each case.

Coverage policies from others

Aetna, 2018

http://www.aetna.com/cpb/medical/data/700_799/0739.html

Aetna considers functional magnetic resonance imaging (fMRI) medically necessary to identify the eloquent cortex in pre-surgical evaluation of persons with brain tumors (except temporal tumors), epilepsy (except temporal neocortical epilepsy), or vascular malformations.

Aetna considers fMRI experimental and investigational to identify the eloquent cortex in pre-surgical evaluation of persons with temporal neocortical epilepsy or temporal tumors.

Aetna considers fMRI experimental and investigational for the diagnosis, monitoring, prognosis, or surgical management of all other indications, including any of the following conditions/diseases (not an all-inclusive list) because its effectiveness for these indications has not been established

- Alzheimer's disease
- Anxiety disorder
- Anoxic-ischemic brain injury
- Attention-deficit hyperactivity disorder
- Bipolar disorder
- Childhood mal-treatment
- Chronic pain (including fibromyalgia)
- Disorders of consciousness (e.g., locked-in syndrome, minimally conscious state (subacute/chronic; traumatic/non-traumatic), and coma/vegatative state)
- Multiple sclerosis
- Obsessive-compulsive disorder
- Parkinson's disease
- Psychotic depression
- Schizophrenia
- Stroke/stroke rehabilitation
- Trauma (e.g., head injury).

HealthNet, 2018
https://www.healthnet.com/static/general/unprotected/pdfs/national/policies/FunctionalMRI.pdf

Policy/Criteria

I. It is the policy of health plans affiliated with Centene Corporation® that fMRI is **medically necessary** when performed for either A, B, C, or D:

A. Assessment of intracranial neoplasm and other targeted lesions for one of the following:

1. Pre-surgical planning and operative risk assessment, or
2. Assessment of eloquent cortex (e.g. language, sensory motor, visual centers) in relation to tumor or other focal lesions, or
3. Surgical planning (biopsy or resection), or
4. Therapeutic follow-up.

B. Evaluation of preserved eloquent cortex.

C. Assessment of eloquent cortex for epilepsy surgery.

D. Assessment of radiation treatment planning and post-treatment evaluation of eloquent cortex.

II. It is the policy of health plans affiliated with Centene Corporation that fMRI for any indication not listed above is considered **not medically necessary**.

HERC Staff Summary

fMRI is less invasive and less expensive than the current standard of care, the Wada test. fMRI appears likely to have good (but not excellent) concordance with the Wada test for language laterality. There appears to be increasing use of the fMRI as part of presurgical workup and some argue that it can result in avoidance of the Wada test.

Less evidence is available about fMRI versus Wada for memory (although Wada is apparently not very good at this). Less evidence is available in children than adults.

HERC Staff Recommendations:

1. Add the following CPT codes to Line 174 GENERALIZED CONVULSIVE OR PARTIAL EPILEPSY WITHOUT MENTION OF IMPAIRMENT OF CONSCIOUSNESS Treatment: SINGLE FOCAL SURGERY
    a. CPT 70555 *Magnetic resonance imaging, brain, functional MRI; requiring physician or psychologist administration of entire neurofunctional testing*
    b. CPT 96020 *Neurofunctional testing selection and administration during noninvasive imaging functional brain mapping, with test administered entirely by a physician or other qualified health care professional (ie, psychologist), with review of test results and report*
2. Remove the Line 660 entries for cpt codes 70555 and 96020
3. Leave 70554 *Magnetic resonance imaging, brain, functional MRI; including test selection and administration of repetitive body part movement and/or visual stimulation, not requiring physician or psychologist administration* on Line 660, as it is not focused on language and does not involve physician or psychologist involvement
4. Add a new guideline to line 174

    GUIDELINE NOTE XXX FUNCTIONAL MRI FOR PRESURGICAL PLANNING
    Line 174

    fMRI is included on this line only to identify the eloquent cortex during preoperative planning for epilepsy surgery.

REVIEW

Can fMRI safely replace the Wada test for preoperative assessment of language lateralisation? A meta-analysis and systematic review

Prisca R Bauer,[1,2] Johannes B Reitsma,[3] Bernard M Houweling,[4] Cyrille H Ferrier,[1] Nick F Ramsey[1]

▶ Supplementary tables S1 to S3 and supplementary figure S1 are published online only. To view the files please visit the journal online (http://dx.doi.org/10.1136/jnnp-2013-305659).

[1]Department of Neurology and Neurosurgery, Section Brainfunction and Plasticity, Rudolf Magnus Institute of Neuroscience, University Medical Center Utrecht, Utrecht, The Netherlands
[2]Department of Research, SEIN- Epilepsy Institute in the Netherlands Foundation, Heemstede, The Netherlands
[3]Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, The Netherlands
[4]Department of Anesthesiology, Erasmus Medical Center, Rotterdam, The Netherlands

Correspondence to
Professor Nick F Ramsey, Department of Neurology and Neurosurgery, Section Brainfunction and Plasticity, Rudolf Magnus Institute of Neuroscience, University Medical Center Utrecht, HP G.03.124, Heidelberglaan 100, 3584 CX Utrecht, The Netherlands; n.f.ramsey@umcutrecht.nl

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ABSTRACT

Recent studies have shown that fMRI (functional magnetic resonance imaging) may be of value for presurgical assessment of language lateralisation. The aim of this study was to systematically review and analyse the available literature. A systematic electronic search for studies comparing fMRI with Wada testing was conducted in the PubMed database between March 2009 and November 2011. Studies involving unilateral Wada testing, study population consisting exclusively of children younger than 12 years of age or involving five patients or fewer were excluded. 22 studies (504 patients) were included. A random effects meta-analysis was conducted to obtain pooled estimates of the positive and negative predictive values of the fMRI using the Wada test as the reference standard. The impact of several study features on the performance of fMRI was assessed. The results showed that 81% of patients were correctly classified as having left or right language dominance or mixed language representation. Techniques were discordant in 19% of patients. fMRI and Wada test agreed in 94% for typical language lateralisation and in 51% for atypical language lateralisation. Language production or language comprehension tasks and different regions of interest did not yield statistically significant different results. It can be concluded that fMRI is reliable when there is strong left-lateralised language. The Wada test is warranted when fMRI fails to show clear left-lateralisation.

INTRODUCTION

For patients suffering from medically intractable epilepsy or other brain lesions such as tumours or vascular malformations, neurosurgery may be the only available treatment. To minimise the risk of postoperative cognitive deficits, lateralisation of language function has to be assessed accurately prior to surgery. Especially in patients with brain lesions that have existed since early childhood, cognitive functions, such as language function, may have been reorganised.[1 2] In healthy individuals, language function is lateralised to the left hemisphere in 73%–96% of cases.[1 3] In epilepsy patients, however, atypically represented language (bilateral or right-dominant) occurs more often.[1] Language function is localised in Broca's and Wernicke's areas, and adjacent areas in middle temporal, inferior temporal, fusiform and angular gyri and the prefrontal cortex.[4]

The Wada test (intracarotid amobarbital test or intracarotid amobarbital procedure, respectively, IAT or IAP)[5] is considered the gold standard for preoperative assessment of lateralisation of language and memory function.[6] This test consists of an amobarbital injection in the internal carotid artery, which causes functional disruption of the ipsilateral cerebral hemisphere for 3–5 min. Meanwhile, the patient is asked to perform language tasks. If (s)he can do this without problems, language is probably located on the contralateral side. If the patient becomes aphasic, language is considered to be lateralised to the injected hemisphere. There are several drawbacks to this test: (i) it is invasive and in a vascular compromised population angiography has a complication rate of 1.3%–11%, of which about 0.6% are permanent;[7 8] (ii) during and shortly after testing amobarbital may cause somnolence, agitation and confusion, which can be distressing for the patient and which can obscure test results;[9 10] (iii) the tests have to be carried out within 3–5 min because of the duration of the effect of amobarbital; and (iv) it can give unreliable results, possibly due to anatomical variations in the brain vascularisation.[11–14]

In the past 10 years, especially with the emergence of other, non-invasive techniques, the Wada test has increasingly been questioned as a routine examination.[15 16]

Functional MRI (fMRI) is one of the emergent non-invasive techniques that could offer a safe, non-invasive and relatively rapid alternative to the Wada test,[17–19] which offers the possibility to conduct a retest, is less distressing for the patient and costs a third of the Wada test.[17] fMRI cannot always be used, for instance in patients with a pacemaker, with ferromagnetic material (from previous operations) and in patients with severe obesity and macrocephaly. In addition, fMRI can be problematic in young children and in patients who suffer from claustrophobia, who have attention problems or are mentally challenged.[20] In some cases, patients suffer from language deficits prior to the operation, complicating language testing.[21] An optimal fMRI protocol for language testing has not yet been developed, and protocols used both for fMRI and the Wada test differ widely between centres.

fMRI has become an accepted and matured tool for neuroscience. It is increasingly used for neurosurgical planning, although not routinely.[6] Studies

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FULL-LENGTH ORIGINAL RESEARCH

Epilepsia®

Diagnostic accuracy of functional magnetic resonance imaging, Wada test, magnetoencephalography, and functional transcranial Doppler sonography for memory and language outcome after epilepsy surgery: A systematic review

Elisabeth Schmid[1,2,3] | Aljoscha Thomschewski[1,2,3,4] | Alexandra Taylor[1,2] | Georg Zimmermann[1,3,5] | Margarita Kirschner[1] | Teia Kobulashvili[1] | Francesco Brigo[6,7] | Matea Rados[8] | Christoph Helmstaedter[9] | Kees Braun[8] | Eugen Trinka[1,3,4] | on behalf of the E-PILEPSY consortium

[1]Department of Neurology, Christian Doppler Medical Center, Paracelsus Medical University, Salzburg, Austria

[2]Department of Psychology, Paris Lodron University of Salzburg, Salzburg, Austria

[3]Spinal Cord Injury and Tissue Regeneration Center Salzburg, Salzburg, Austria

[4]Center for Cognitive Neuroscience, Salzburg, Austria

[5]Department of Mathematics, Paris Lodron University of Salzburg, Salzburg, Austria

[6]Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy

[7]Department of Neurology, Franz Tappeiner Hospital, Merano, Italy

[8]Department of Child Neurology, University Medical Center, Utrecht, The Netherlands

[9]Department of Epileptology, Medical Center, University of Bonn, Bonn, Germany

Correspondence
Eugen Trinka, Department of Neurology, Christian Doppler Medical Center, Paracelsus Medical University, Salzburg, Austria.
Email: e.trinka@salk.at

Summary

Objective: The European Union–funded E-PILEPSY project was launched to develop guidelines and recommendations for epilepsy surgery. In this systematic review, we aimed to assess the diagnostic accuracy of functional magnetic resonance imaging (fMRI), Wada test, magnetoencephalography (MEG), and functional transcranial Doppler sonography (fTCD) for memory and language decline after surgery.

Methods: The literature search was conducted using PubMed, Embase, and CENTRAL. The diagnostic accuracy was expressed in terms of sensitivity and specificity for postoperative language or memory decline, as determined by pre- and postoperative neuropsychological assessments. If two or more estimates of sensitivity or specificity were extracted from a study, two meta-analyses were conducted, using the maximum ("best case") and the minimum ("worst case") of the extracted estimates, respectively.

Results: Twenty-eight papers were eligible for data extraction and further analysis. All tests for heterogeneity were highly significant, indicating large between-study variability ($P < 0.001$). For memory outcomes, meta-analyses were conducted for Wada tests (n = 17) using both memory and language laterality quotients. In the best case, meta-analyses yielded a sensitivity estimate of 0.79 (95% confidence interval [CI] = 0.67-0.92) and a specificity estimate of 0.65 (95% CI = 0.47-0.83). For the worst case, meta-analyses yielded a sensitivity estimate of 0.65 (95% CI = 0.48-0.82) and a specificity estimate of 0.46 (95% CI = 0.28-0.65). The overall quality of evidence, which was assessed using Grading of Recommendations Assessment, Development, and Evaluation methodology, was rated as very low. Meta-analyses concerning diagnostic accuracy of fMRI, fTCD, and MEG were not feasible due to small numbers of studies (fMRI, n = 4; fTCD,

n = 1; MEG, n = 0). This also applied to studies concerning language outcomes (Wada test, n = 6; fMRI, n = 2; fTCD, n = 1; MEG, n = 0).

Significance: Meta-analyses could only be conducted in a few subgroups for the Wada test with low-quality evidence. Thus, more evidence from high-quality studies and improved data reporting are required. Moreover, the large between-study heterogeneity underlines the necessity for more homogeneous and thus comparable studies in future research.

KEYWORDS

diagnostic accuracy, epilepsy surgery, language, memory, systematic review

1 | INTRODUCTION

In 2014, the European Union funded E-PILEPSY, a pilot network of 28 reference centers for refractory epilepsy and epilepsy surgery (http://www.ucl.ac.uk/www.e-pilepsy.eu). Its overall objectives are to enhance access to epilepsy surgery in Europe and to increase the number of patients cured of drug-resistant epilepsy. In a first step, the current practices in brain imaging and electromagnetic source localization procedures,[1] long-term video-electroencephalographic monitoring,[2] and neuropsychological assessments[3] were evaluated. In a second step, the network aimed to create recommendations and guidelines for surgical evaluation and epilepsy surgery based on the best available evidence.

Epilepsy surgery is an elective procedure considered to be an effective treatment for patients with drug-resistant epilepsy.[4] However, patients may experience postoperative cognitive impairments.[5,6] After temporal lobe resection, which is the most common type of epilepsy surgery,[4] memory and language impairments have been reported.[5,7] The observed memory impairments tend to be material-specific (verbal/visual) depending on language lateralization.[6] After temporal lobe resection involving the speech-dominant hemisphere, verbal memory decline is more consistent and well documented[8] as compared to visual memory loss in the nondominant hemisphere.[8,9] In a systematic review by Sherman et al,[5] an estimated risk of 44% for verbal memory decline after left-sided temporal lobe surgery was reported (vs 20% after right-sided surgery). For visual memory, no difference with regard to side of surgery was found (21% after left-sided surgery vs 23% after right-sided surgery). Furthermore, language impairments have been reported in 34% of patients with left-sided temporal lobe surgery.[5]

To estimate the risk of postoperative memory and language impairments, various methods have been applied to examine the lateralization and localization of language and/or memory functions preoperatively. The intracarotid amobarbital test, or so-called selective Wada test,[10] is still considered the gold standard for assessing language lateralization.[11] However, memory lateralization and its predictive value for postoperative decline are less valid,[12–16] as memory testing during selective Wada test assesses more than mesial temporal lobe functions.[16] Furthermore, aphasia may have a major impact on verbal memory testing during cortical anesthesia of the speech-dominant hemisphere.[17] Thus, the superselective Wada test was developed, in which barbiturate is injected into the posterior cerebral artery[18] or anterior choroidal artery.[19] This enables memory testing while preserving language functions. Noninvasive alternatives conducted in epilepsy centers for presurgical evaluation of language and memory lateralization include functional magnetic resonance imaging (fMRI), magnetoencephalography (MEG), and functional transcranial Doppler sonography (fTCD).[3] The diagnostic accuracy of these methods for postoperative language and memory decline has been the focus of numerous studies. However, most studies only report mean differences in group data or correlations as outcome parameters, thus making it difficult to estimate the individual risk for possible postoperative decline in clinical practice.

Key Points

- Diagnostic accuracy of fMRI, Wada test, MEG, and fTCD was expressed in terms of sensitivity and specificity of each method
- Meta-analyses could be conducted for the Wada test only; overall quality of evidence was rated as very low
- High variability exists regarding protocols, stimuli, neuropsychological tests, and assessment of language and memory functions
- Substantial between-study heterogeneity indicates the need for more comparable studies
- The majority of papers could not be included in the analysis due to insufficient data reporting, thus emphasizing the need for guidelines

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Review

Pre-surgical mapping of eloquent cortex for paediatric epilepsy surgery candidates: Evidence from a review of advanced functional neuroimaging

Sarah Collinge[a], Garreth Prendergast[b], Steven T. Mayers[c], David Marshall[d], Poppy Siddell[e], Elizabeth Neilly[f], Colin D. Ferrie[g], Gayatri Vadlamani[h], Jeremy Macmullen-Price[i], Daniel J. Warren[i], Arshad Zaman[i], Paul Chumas[j], John Goodden[j], Matthew C.H.J. Morrall[e,*]

[a] Birch Hill Hospital, Birch Road, Rochdale, OL12 9QB, UK
[b] Institute of Psychological Sciences, The University of Manchester, Oxford Road, Manchester M13 9PL, UK
[c] Complex Rehabilitation Unit, Walton Centre for Neurology and Neurosurgery, Lower Lane, Fazakerley, Liverpool, L9 7LJ, UK
[d] Department of Clinical Psychology, South West Yorkshire Partnership NHS Foundation Trust, Newton Lodge, Fieldhead Hospital, Ouchthorpe Lane, WF1 3SP, UK
[e] Paediatric Neuropsychology, The Leeds Teaching Hospitals NHS Trust, E Floor, Martin Wing, Leeds General Infirmary, Great George Street, Leeds, LS1 3EX, UK
[f] Health Faculty Team Librarian, Health Sciences Library, University of Leeds, Leeds, LS2 9JT, UK
[g] Oxford Science Editing Limited, John Eccles House, Oxford Science Park, Oxford, OX4 4GP, UK
[h] Paediatric Neurology, The Leeds Teaching Hospitals NHS Trust, Leeds General Infirmary, Great George Street, Leeds, LS1 3EX, UK
[i] MRI, The Leeds Teaching Hospitals NHS Trust, G Floor, Jubilee Wing, Leeds General Infirmary, Great George Street, Leeds, LS1 3EX, UK
[j] Department of Neurosurgery, The Leeds Teaching Hospitals NHS Trust, G Floor, Jubilee Wing, Leeds General Infirmary, Great George Street, Leeds, LS1 3EX, UK

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ABSTRACT

Purpose: A review of all published evidence for mapping eloquent (motor, language and memory) cortex using advanced functional neuroimaging (functional magnetic resonance imaging [fMRI] and magnetoencephalography [MEG]) for paediatric epilepsy surgery candidates has not been conducted previously. Research in this area has predominantly been in adult populations and applicability of these techniques to paediatric populations is less established.

Methods: A review was performed using an advanced systematic search and retrieval of all published papers examining the use of functional neuroimaging for paediatric epilepsy surgery candidates.

Results: Of the 2724 papers retrieved, 34 met the inclusion criteria. Total paediatric participants identified were 353 with an age range of 5 months-19 years. Sample sizes and comparisons with alternative investigations to validate techniques are small and variable paradigms are used. Sensitivity 0.72 (95% CI 0.52–0.86) and specificity 0.60 (95% CI 0.35–0.92) values with a Positive Predictive Value of 74% (95% CI 61–87) and a Negative Predictive Value of 65% (95% CI 52–78) for fMRI language lateralisation with validation, were obtained. Retrieved studies indicate evidence that both fMRI and MEG are able to provide information lateralising and localising motor and language functions.

Conclusions: A striking finding of the review is the paucity of studies (n = 34) focusing on the paediatric epilepsy surgery population. For children, it remains unclear which language and memory paradigms produce optimal activation and how these should be quantified in a statistically robust manner. Consensus needs to be achieved for statistical analyses and the uniformity and yield of language, motor and memory paradigms. Larger scale studies are required to produce patient series data which clinicians may refer to interpret results objectively. If functional imaging techniques are to be the viable alternative for pre-surgical mapping of eloquent cortex for children, paradigms and analyses demonstrating concordance with independent measures must be developed.

* Corresponding author.
E-mail addresses: sarahcollinge@nhs.net (S. Collinge), garreth.prendergast@manchester.ac.uk (G. Prendergast), steven.thomas.mayers@gmail.com (S.T. Mayers), david.marshall@swyt.nhs.uk (D. Marshall), poppysiddell@nhs.net (P. Siddell), e.m.neilly@leeds.ac.uk (E. Neilly), colindferrie@aol.com (C.D. Ferrie), gayatri.vadlamani@nhs.net (G. Vadlamani), jeremy.macmullen-price1@nhs.net (J. Macmullen-Price), danielwarren@nhs.net (D.J. Warren), a.zaman@leeds.ac.uk (A. Zaman), p.chumas@nhs.net (P. Chumas), j.goodden@nhs.net (J. Goodden), m.morrall@nhs.net (M.C.H.J. Morrall).

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RESEARCH ARTICLE

WILEY

Presurgical language fMRI: Clinical practices and patient outcomes in epilepsy surgical planning

Christopher F. A. Benjamin[1] | Alexa X. Li[2] | Hal Blumenfeld[1] | R. Todd Constable[1] | Rafeed Alkawadri[1] | Stephan Bickel[3] | Christoph Helmstaedter[4] | Stefano Meletti[5] | Richard Bronen[1] | Simon K. Warfield[6] | Jurriaan M. Peters[6] | David Reutens[7] | Monika Połczyńska[8] | Dennis D. Spencer[1] | Lawrence J. Hirsch[1]

[1]Yale University School of Medicine, 333 Cedar Ave, New Haven, CT, USA

[2]Quinnipiac University School of Medicine, 370 Bassett Rd, North Haven, CT, USA

[3]Northwell Health, Great Neck, NY, USA

[4]University of Bonn, Regina-Pacis-Weg 3, Bonn, Germany

[5]University of Modena and Reggio Emilia, Via Università, 4, Modena, MO, Italy

[6]Boston Children's Hospital, 360 Longwood Avenue Boston, MA, USA

[7]The University of Queensland, St. Lucia QLD, Australia

[8]University of California Los Angeles, Westwood Plaza, CA, USA

Correspondence
Christopher F. A. Benjamin, 800 Howard Ave, LL, New Haven, CT 06511, USA.
Email: christopher.benjamin@yale.edu

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Abstract

The goal of this study was to document current clinical practice and report patient outcomes in presurgical language functional MRI (fMRI) for epilepsy surgery. Epilepsy surgical programs worldwide were surveyed as to the utility, implementation, and efficacy of language fMRI in the clinic; 82 programs responded. Respondents were predominantly US (61%) academic programs (85%), and evaluated adults (44%), adults and children (40%), or children only (16%). Nearly all (96%) reported using language fMRI. Surprisingly, fMRI is used to guide surgical margins (44% of programs) as well as lateralize language (100%). Sites using fMRI for localization most often use a distance margin around activation of 10mm. While considered useful, 56% of programs reported at least one instance of disagreement with other measures. Direct brain stimulation typically confirmed fMRI findings (74%) when guiding margins, but instances of unpredicted decline were reported by 17% of programs and 54% reported unexpected preservation of function. Programs reporting unexpected decline did not clearly differ from those which did not. Clinicians using fMRI to guide surgical margins do not typically map known language-critical areas beyond Broca's and Wernicke's. This initial data shows many clinical teams are confident using fMRI not only for language lateralization but also to guide surgical margins. Reported cases of unexpected language preservation when fMRI activation is resected, and cases of language decline when it is not, emphasize a critical need for further validation. Comprehensive studies comparing commonly-used fMRI paradigms to predict stimulation mapping and post-surgical language decline remain of high importance.

KEYWORDS
epilepsy, fMRI, language, presurgical

1 | INTRODUCTION

Neurosurgery is an effective and potentially curative treatment for temporal lobe epilepsy (Wiebe, Blume, Girvin, & Eliasziw, 2001). Surgical risk to language and memory can exclude a patient from treatment. As 34%–41% of left temporal patients undergoing focal resections experience a decline in naming (Busch et al., 2016; Sherman et al., 2011), determining the surgical risk to language remains essential.

While the Intracarotid Amobarbital Test ("Wada" testing) has been the gold standard for determining the language dominant hemisphere,

SPECIAL ARTICLE

Practice guideline summary: Use of fMRI in the presurgical evaluation of patients with epilepsy

Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology

Jerzy P. Szaflarski, MD, PhD
David Gloss, MD, MPH&TM
Jeffrey R. Binder, MD
William D. Gaillard, MD
Alexandra J. Golby, MD
Scott K. Holland, PhD
Jeffrey Ojemann, MD
David C. Spencer, MD
Sara J. Swanson, PhD
Jacqueline A. French, MD
William H. Theodore, MD

Correspondence to American Academy of Neurology: guidelines@aan.com

ABSTRACT

Objective: To assess the diagnostic accuracy and prognostic value of functional MRI (fMRI) in determining lateralization and predicting postsurgical language and memory outcomes.

Methods: An 11-member panel evaluated and rated available evidence according to the 2004 American Academy of Neurology process. At least 2 panelists reviewed the full text of 172 articles and selected 37 for data extraction. Case reports, reports with <15 cases, meta-analyses, and editorials were excluded.

Results and recommendations: The use of fMRI may be considered an option for lateralizing language functions in place of intracarotid amobarbital procedure (IAP) in patients with medial temporal lobe epilepsy (MTLE; Level C), temporal epilepsy in general (Level C), or extratemporal epilepsy (Level C). For patients with temporal neocortical epilepsy or temporal tumors, the evidence is insufficient (Level U). fMRI may be considered to predict postsurgical language deficits after anterior temporal lobe resection (Level C). The use of fMRI may be considered for lateralizing memory functions in place of IAP in patients with MTLE (Level C) but is of unclear utility in other epilepsy types (Level U). fMRI of verbal memory or language encoding should be considered for predicting verbal memory outcome (Level B). fMRI using nonverbal memory encoding may be considered for predicting visuospatial memory outcomes (Level C). Presurgical fMRI could be an adequate alternative to IAP memory testing for predicting verbal memory outcome (Level C). Clinicians should carefully advise patients of the risks and benefits of fMRI vs IAP during discussions concerning choice of specific modality in each case. *Neurology*® 2017;88:395–402

GLOSSARY

AAN = American Academy of Neurology; **ATL** = anterior temporal lobe; **fMRI** = functional MRI; **IAP** = intracarotid amobarbital procedure; **LI** = laterality index; **MTL** = medial temporal lobe; **MTLE** = medial temporal lobe epilepsy; **ROI** = region of interest; **TLE** = temporal lobe epilepsy.

This article summarizes an American Academy of Neurology (AAN) guideline on use of functional MRI (fMRI) for presurgical mapping in epilepsy. Additional information is provided in the complete guideline, available as a data supplement at Neurology.org. Appendices e-1 through e-5, available in the complete guideline, tables e-1 and e-2, and references e1–e16, cited here, are available at Neurology.org.

The choice of performing intracarotid amobarbital procedure (IAP) or fMRI for presurgical language and memory assessment depends on multiple factors that need to be taken into account when selecting the study. fMRI is properly described as an image acquisition technique that has come to mean imaging brain activity. fMRI results may depend on, for example, scanner strength, analysis methods, type of task contrast used, patient compliance and cooperation with the tasks, or medications administered at the time of the procedure; neither selection of fMRI tasks nor data processing methods have been universally standardized.[1–4] Nonetheless, standard practices are beginning to emerge.[5] The IAP language or memory testing is also not standardized; the reviewed studies vary with regard to the procedure used for comparison. IAP may

Supplemental data at Neurology.org

From the Department of Neurology (J.P.S.), University of Alabama at Birmingham; Department of Neurology (D.G.), Charleston Area Medical Center, WV; Department of Neurology (J.R.B., S.J.S.), Medical College of Wisconsin, Milwaukee; Children's National Medical Center (W.D.G.), George Washington University, Washington, DC; Departments of Neurosurgery and Radiology (A.J.G.), Brigham and Women's Hospital, Boston, MA; Cincinnati Children's Hospital Research Foundation (S.K.H.), OH; Department of Neurosurgery (J.O.), Seattle Children's Hospital, WA; Department of Neurology (D.C.S.), Oregon Health & Science University, Portland; Department of Neurology (J.A.F.), New York University, New York; and Clinical Epilepsy Section (W.H.T.), National Institute of Neurological Disorders and Stroke, NIH, Bethesda, MD.

Approved by the Guideline Development, Dissemination, and Implementation Subcommittee on February 29, 2016; by the Practice Committee on March 10, 2016; and by the AAN Institute Board of Directors on October 18, 2016.

This guideline was endorsed by the American College of Radiology on September 14, 2016, and by the American Epilepsy Society on December 14, 2016.

Go to Neurology.org for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.

Injections for Plantar Fasciitis

Question: Should procedure codes for injections into the plantar fascia be paired with plantar fasciitis?

Question source: Hearings Division

Issue: Plantar fasciitis (ICD-10 M72.2 Plantar fascial fibromatosis) is currently on line 537 LESION OF PLANTAR NERVE; PLANTAR FASCIAL FIBROMATOSIS, and does not pair with the procedure code for injections into the plantar fascia (CPT 20550 Injection(s); single tendon sheath, or ligament, aponeurosis (eg, plantar "fascia")). CPT 20550 appears on multiple funded lines. There was a recent case that went to the Hearings Division regarding the pairing of these codes. No previous review of this topic was found in old minutes.

Various treatments involving injections into the plantar fascia are currently utilized in practice. The most common injection is corticosteroids, but platelet rich plasma and dehydrated amniotic membrane are also injected in some practices.

Evidence

1) **David 2017**, Cochrane review of corticosteroid injections for plantar heel pain https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD009348.pub2/epdf/full
    a. N=39 studies (2492 patients)
        i. Most studies were small (median=59 patients)
        ii. Follow up ranged from 1 month to 2 years
        iii. With one exception, trials were assessed at high risk of bias in one or more domains, mostly relating to lack of blinding,
    b. N=8 trials (724 patients)) compared steroid injection versus placebo or no treatment.
        i. Steroid injection may lead to lower heel pain visual analogue scores (VAS) (0 to 100; higher scores = worse pain) in the short-term (< 1 month) (MD -6.38, 95% CI -11.13 to - 1.64; 350 participants; 5 studies; I^2 = 65%; low quality evidence). Based on a minimal clinically significant difference (MCID) of 8 for average heel pain, the 95% CI includes a marginal clinical benefit. This potential benefit was diminished when data were restricted to three placebo-controlled trials. Steroid injection made no difference to average heel pain in the medium-term (1 to 6 months follow-up) (MD -3.47, 95% CI -8.43 to 1.48; 382 participants; 6 studies; I^2 = 40%; low quality evidence). There was very low quality evidence for no effect on function in the medium-term and for an absence of serious adverse events (219 participants, 4 studies). No studies reported on other adverse events, such as post-injection pain, and on return to previous activity.
    c. The available evidence for other comparisons was rated as very low quality. We are therefore very uncertain of the estimates for the relative effects on people with heel pain of steroids compared with other interventions (tibial nerve block, orthoses, oral NSAIDs, intensive PT, laser therapy, radiation therapy, locally injectable NSAID, platelet-rick plasma injections, botulinum toxin injections, cryopreserved human amniotic membrane injection)
    d. We are also uncertain about the estimates from trials testing different techniques of local steroid injection: ultrasonography-guided versus palpation-guided (5 trials); and scintigraphy-guided versus palpation-guided (1 trial).
    e. An exploratory analysis involving pooling data from 21 trials reporting on adverse events revealed two ruptures of plantar fascia (reported in 1 trial) and three injection site

infections (reported in 2 trials) in 699 participants allocated to steroid injection study arms. Five trials reported a total of 27 participants with less serious short-term adverse events in the 699 participants allocated steroid injection study arms.

f. Authors' conclusions We found low quality evidence that local steroid injections compared with placebo or no treatment may slightly reduce heel pain up to one month but not subsequently. The available evidence for other outcomes of this comparison was very low quality. Where available, the evidence from comparisons of steroid injections with other interventions used to treat heel pain and of different methods of guiding the injection was also very low quality. Although serious adverse events relating to steroid injection were rare, these were under-reported and a higher risk cannot be ruled out.

Expert guidelines

1) **American College of Foot and Ankle Surgeons 2018**: Clinical Consensus Statement Diagnosis and Treatment of Adult Acquired Infracalcaneal Heel Pain
    a. The panel determined that the following statements are appropriate
        i. Corticosteroid injections are safe and effective in the treatment of plantar fasciitis.
            1. In a recent Cochrane review and meta-analysis of 3 RCTs, David et al concluded that local steroid injections compared with placebo or no treatment might slightly reduce heel pain for ≤1 month but not subsequently. The panel was of the same opinion and admitted to using injectable steroids for the acute relief of symptoms, recognizing that these are not disease modifying and have little lasting effect beyond the first 4 weeks.
    b. The panel determined that the following statements were uncertain—neither appropriate nor inappropriate.
        i. Other injection techniques (e.g., amniotic tissue, platelet-rich plasma, botulinum toxin, needling, and prolotherapy) are safe and effective in the treatment of plantar fasciitis.
            1. Although other injection techniques are emerging for the treatment of plantar fasciitis, they have been supported only by low quality studies consisting of case series, retrospective comparative studies, or small trials, lacking long-term follow-up data. Rather than speculate on the value of these injection therapies, the panel thought that further investigation is needed to assess how these will compare with the more conventional treatment protocols.

Injections for Plantar Fasciitis

HERC staff summary:
Based on low quality evidence, corticosteroid injections for plantar fasciitis have a non-clinically significant impact on short term (<1 month) pain, but not on function. There are limited adverse events reports. Other injections (amniotic tissue, platelet-rich plasma, botulinum toxin, etc.) have very low quality of evidence which does not allow determination of their effectiveness and are not recommended by experts.

HERC staff recommendation:

1) Add CPT 20550 (Injection(s); single tendon sheath, or ligament, aponeurosis (eg, plantar "fascia")) to line 537 LESION OF PLANTAR NERVE; PLANTAR FASCIAL FIBROMATOSIS, with the coding specification below
    a. "CPT 20550 only appears on this line for corticosteroid injections."
    b. The treatment is appropriate to the condition, but has limited evidence of effectiveness

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ACFAS Clinical Consensus Statement

American College of Foot and Ankle Surgeons Clinical Consensus Statement: Diagnosis and Treatment of Adult Acquired Infracalcaneal Heel Pain

Harry P. Schneider, DPM, FACFAS [1,2,3], John M. Baca, DPM, AACFAS [4], Brian B. Carpenter, DPM, FACFAS [5,6], Paul D. Dayton, DPM, MS, FACFAS [7,8], Adam E. Fleischer, DPM, MPH, FACFAS [9,10], Brett D. Sachs, DPM, FACFAS [11,12]

[1]*Chairperson, Heel Pain Clinical Consensus Statement, Chicago, IL*
[2]*Assistant Professor of Surgery, Harvard Medical School, Cambridge, MA*
[3]*Residency Program Director, Cambridge Health Alliance, Cambridge, MA*
[4]*Private Practice, Dallas Podiatry Works, Dallas, TX*
[5]*Professor, Department of Orthopedics, The University of North Texas Health Science Center, Fort Worth, TX*
[6]*Private Practice, Paradise, TX*
[7]*Assistant Professor, College of Podiatric Medicine and Surgery, Des Moines, IA*
[8]*Residency Program Director, UnityPoint Health, Fort Dodge, IA*
[9]*Associate Professor, Dr. William M. Scholl College of Podiatric Medicine at Rosalind Franklin University of Medicine and Science, North Chicago, IL*
[10]*Director of Research, Weil Foot and Ankle Institute, Chicago, IL*
[11]*Private Practice, Rocky Mountain Foot & Ankle Center, Wheat Ridge, CO*
[12]*Faculty, Highlands-Presbyterian/St. Luke's Podiatric Medicine and Surgery Residency Program, Denver, CO*

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ABSTRACT

Adult acquired inferior calcaneal heel pain is a common pathology seen in a foot and ankle practice. A literature review and expert panel discussion of the most common findings and treatment options are presented. Various diagnostic and treatment modalities are available to the practitioner. It is prudent to combine appropriate history and physical examination findings with patient-specific treatment modalities for optimum success. We present the most common diagnostic tools and treatment options, followed by a discussion of the appropriateness of each based on the published data and experience of the expert panel.

Executive Summary

The following document represents the findings of the adult acquired infracalcaneal heel pain consensus panel sponsored by the American College of Foot and Ankle Surgeons. The 6-member panel used a modified Delphi method to reach a clinical consensus regarding the diagnostic and treatment methods based on the best available evidence in the literature, combined with clinical experience and best patient practice.

The panel determined that the following statements are appropriate:

1. Plantar fasciitis is diagnosed, in most cases, by the history and physical examination findings alone.
2. Routine use of radiographs is not necessary for the diagnosis of nontraumatic plantar fasciitis.
3. The presence of a calcaneal spur will not generally alter the treatment course.
4. Advanced imaging, such as magnetic resonance imaging and ultrasonography, is not necessary for the diagnosis or guidance of treatment of nontraumatic plantar fasciitis.
5. In most cases, infracalcaneal heel pain is a soft tissue-based disorder and calcaneal spurring is most likely not a causative factor.
6. Appropriate treatment of plantar fasciitis requires sufficient understanding of the patient's chronicity of symptoms.
7. Biomechanical support is safe and effective in the treatment of plantar fasciitis.

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Conflict of Interest: Revance Therapeutics sponsored A. Fleischer's research on botulinum toxin injection for plantar fasciitis.

Address correspondence to: Harry P. Schneider, DPM, FACFAS, Clinical Consensus Statements, American College of Foot and Ankle Surgeons, 8725 West Higgins Road, Suite 555, Chicago, IL 60631-2724.

E-mail address: hschneider@cha.harvard.edu (H. Schneider).

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Radiofrequency Ablation for Knee Osteoarthritis

Question: Should radiofrequency ablation be paired with knee osteoarthritis on the Prioritized List?

Question source: coverage guidance nomination process, manufacturer

Issue: Radiofrequency ablation (RFA) does not currently pair with knee osteoarthritis. Avanos (the manufacturer of a cooled RFA system) nominated this topic for a coverage guidance. However, a Washington HTA report was just published on this topic, and therefore a full coverage guidance review was not felt to be necessary. Radiofrequency ablation of the knee (CPT 64640 Destruction by neurolytic agent; other peripheral nerve or branch) currently does not pair with any condition on the Prioritized List.

When an individual exhibits knee pain, the pain signals can be generated from the peripheral nerves. Innervating the knee, including several branches of the genicular nerve, an ablative procedure that can include radiofrequency ablation, cryoneurolysis and chemical neurolysis of the genicular nerves, may be performed to restore function and alleviate knee pain as an alternative therapy. Surgical treatment may not be an option for patients with multiple comorbidities; these ablative procedures have been proposed as an alternative for the treatment of chronic pain.

Peripheral nerve ablation, using chemical, surgical, or thermal ablation techniques, destroys sensory nerve tissues that transmit pain signals from the affected area back to the brain. Three types of RFA have been developed. Conventional thermal RFA is a minimally invasive procedure that uses heat and coagulation necrosis to damage or destroy nerve tissue. Pulsed RF treatment uses short bursts of RF current and generate lower tissue temperatures compared to continuous current conventional RFA. Cooled RF devices apply more energy at the desired location, but use water cooling to prevent as much heat from diffusing beyond the target area. Cryoablation uses a cryogen within a probe casing to deliver very cold temperatures that damage the nerves.

Current Prioritized List status

Radiofrequency ablation of the knee (CPT 64640 Destruction by neurolytic agent; other peripheral nerve or branch) currently does not pair with any condition on the Prioritized List.
Knee osteoarthritis (ICD-10 M17 family) is on lines 356 RHEUMATOID ARTHRITIS, OSTEOARTHRITIS, OSTEOCHONDRITIS DISSECANS, AND ASEPTIC NECROSIS OF BONE Treatment ARTHROPLASTY, RECONSTRUCTION and 461 OSTEOARTHRITIS AND ALLIED DISORDERS Treatment MEDICAL THERAPY, INJECTIONS.

Evidence

1) **WA HTA 2018**, Peripheral nerve ablation for the treatment of limb pain https://www.hca.wa.gov/assets/program/pna-final-report-20181211.pdf
    a. N=5 RCTs of conventional radiofrequency ablation (RFA) for knee pain (N=223 patient included for analysis of function, 150 patients included for analysis of pain)
        i. some improvement in knee function and pain measures, but only 1 followed participants for more than 6 months. Two RCTs using the Oxford Knee Score (OKS) and 2 other RCTs using the total WOMAC found statistically significant improvements at 3 months for the conventional RFA group, which likely meet the MCID threshold. Similarly, 3 RCTs using a VAS pain scale found statistically

significant improvements for the conventional RFA group at 3 months that likely meet the minimally clinically important difference (MCID) threshold.

ii. All 5 studies that evaluated RFA had significant limitations and were rated as having a high risk of bias.

b. N=1 RCT of cooled RFA (cRFA) (N=151 patients)
    i. Cooled RFA improved OKS function measures and NRS pain measures at 6 months compared to an intra-articular steroid injection (IAS). For purposes of the GRADE table, we found very low quality of evidence that cooled RFA11 improved OKS function measures and NRS pain measures at 3 months compared to IAS and likely met the MCID for that scale. This trial was assesses as having a moderate risk of bias
c. N=1 RCT of cryoablation of the genicular nerves (N=180 patients)
    i. We found very low quality of evidence that cryoablation of the genicular nerves improved WOMAC total scores at 3 months compared to a sham procedure and that the difference likely met the MCID threshold. This RCT was assessed as having a high risk of bias.
d. Harms
    i. We found little evidence of serious harms in randomized and nonrandomized studies
e. Guidelines and Payer Policies
    i. No identified clinical practice guideline made a recommendation for the use of these nerve ablation procedures
    ii. Aetna, Cigna and Regence BCBS consider any type of nerve ablation for knee osteoarthritis (or any other diagnosis) to be investigational
f. Ongoing studies
    iii. There are 9 ongoing RCTs of various modalities for peripheral nerve ablation to treat pain in the knee that are expected to be completed between 2018 and 2021.
g. Conclusions
    i. Using the GRADE system, we found very low quality of evidence in favor of peripheral nerve ablation to improve some short-term functional and pain measures for moderate to severe chronic pain from knee osteoarthritis

HERC staff summary

The body of evidence to date on radiofrequency ablation for knee osteoarthritis consists of only a few small RCTs at moderate to high risk of bias. The WA HTA concluded that the quality of evidence is very low, but is in favor of peripheral nerve ablation for improving short term function and pain. Further research is ongoing for this technology. Other therapies for knee osteoarthritis, including injections, medications, and surgeries, are currently paired with this diagnosis. RFA is not currently included in expert treatment guidelines and is not currently covered by major insurers.

HERC staff recommendation:

1) Add radiofrequency ablation (standard, cooled or cryoablation) for knee arthritis to line 660 CONDITIONS FOR WHICH CERTAIN INTERVENTIONS ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS/Guideline Note 173
    a. Insufficient evidence of effectiveness
    b. Consider reassessing after additional RCTs are published

GUIDELINE NOTE 173, INTERVENTIONS THAT ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS FOR CERTAIN CONDITIONS

Line 660

The following Interventions are prioritized on Line 660 CONDITIONS FOR WHICH CERTAIN INTERVENTIONS ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS:

Procedure Code	**Intervention Description**	**Rationale**	**Last Review**
64640	Destruction by neurolytic agent; other peripheral nerve or branch	Insufficient evidence of effectiveness	May, 2019 (knee osteoarthritis)

Certification for Lymphedema Providers

Question: Should lymphedema therapy be covered if done by non-LANA certified therapists?

Question sources: several CCOs and providers; coverage guidance nomination process

Issue: Several CCOs are having difficulty contracting with LANA certified therapists. They have therapists in their networks who are certified by other bodies and are requesting consideration of a change to the lymphedema guideline to allow other certification. Specifically, Chickly and Vodder have been proposed as other certifying bodies to consider. One CCO nominated this topic for a coverage guidance. Independently, several providers have contacted HERC staff requesting that the types of certification accepted for lymphedema therapy by OHP be expanded.

When lymphedema was moved to a prioritization above the funding line in 2007, a guideline was written restricting therapists to LANA certified therapists, due to concerns that when this type of therapy is done incorrectly, it can be harmful. This decision was discussed again in 2009, based on a health care network concern for lack of LANA certified therapists in rural areas. At that time, the HSC decided to continue the requirement due to the need to provide some quality control for this type of therapy.

From Leslie Reagan, certified lymphedema therapist in The Dalles

> The North American Lymphedema Education Association (NALEA) is specifically organized around training standards for lymphedema therapists. NALEA is currently an alliance of the four lymphedema therapy certification schools responsible for training the majority of Certified Lymphedema Therapists (CLTs) in North America according to standards set forth by the Lymphology Association of North America (LANA). NALEA member schools share the unified goal of setting and maintaining the highest standards of lymphedema education in North America. The current NALEA member schools are:
>
> Academy of Lymphatic Studies
> Dr. Vodder School International
> Klose Training and Consulting
> Norton School of Lymphatic Therapy
>
> If a therapist is LANA certified, they have paid an additional fee to take a comprehensive examination after completing 100 hours in clinic directly treating lymphedema. One other requirement to sit for the exam is to have done 180 hours of training by one of the 4 schools above. LANA certification is not required by any other state at this time for a CLT to practice.

From MODA

> We have recently noted that due to our access limitations in Eastern Oregon, currently in addition to LANA certified providers, our medical directors are allowing Vodder and Chickly lymphedema therapists.

Current Prioritized List status
Line 421 LYMPHEDEMA

GUIDELINE NOTE 43, LYMPHEDEMA

Line 421

Lymphedema treatments are included on this line when medically appropriate. These services are to be provided by a licensed practitioner who is certified by one of the accepted lymphedema training certifying organizations or a graduate of one of the National Lymphedema Network accepted training courses within the past two years. The only accepted certifying organization at this time is LANA (Lymphology Association of North America; http://www.clt-lana.org). Treatments for lymphedema are not subject to the visit number restrictions found in Guideline Note 6 REHABILITATIVE AND HABILITATIVE THERAPIES.

It is the intent of the HERC that compression dressings/garments and other medical equipment needed for the treatment of lymphedema be covered even in the absence of ulcers or other complications.

Evidence

1) **AHRQ 2010**, systematic review on treatment of secondary lymphedema https://www.ncbi.nlm.nih.gov/books/NBK285652/pdf/Bookshelf_NBK285652.pdf
    a. 17 of 36 reviewed studies on treatment did not provide detail regarding who provided the lymphedema therapy; 19 studies reported that the provider was a physiotherapist (no certification or training specified)

Expert guidelines

1) **NCCN 2019** Survivorship guidelines
    a. Assessment for lymphedema and treatment of lymphedema should be done by a "certified lymphedema therapist (if available)"
    b. The footnote to this entry reads: "Certified lymphedema therapists can be located using the following resource: https://www.clt-lana.org/search/therapists/"

Other payer certification of therapist policies

No payer policies were identified which limited lymphedema therapists by type of certification.

HERC staff summary

There is no published evidence regarding differences in outcomes in lymphedema therapy based on the provider certification type. No other insurer restricts lymphedema therapy to LANA certification. NCCN appears to recommend that therapy be done by a LANA certified therapist, if available.

HERC staff recommendation:

1) Modify GN 43 to remove the restriction to LANA certification only

GUIDELINE NOTE 43, LYMPHEDEMA

Line 421

Lymphedema treatments are included on this line when medically appropriate. These services are to be provided by a licensed practitioner who is certified by one of the accepted lymphedema training certifying organizations or a graduate of one of the National Lymphedema Network or North American Lymphedema Education Association (NALEA) accepted training courses within the past two years. The preferred ~~The only accepted~~ certifying organization at this time is LANA (Lymphology Association of North America; http://www.clt-lana.org), and services should be provided by a LANA certified therapist if available. Treatments for lymphedema are not subject to the visit number restrictions found in Guideline Note 6 REHABILITATIVE AND HABILITATIVE THERAPIES.

It is the intent of the HERC that compression dressings/garments and other medical equipment needed for the treatment of lymphedema be covered even in the absence of ulcers or other complications.

Preventive Lymphedema Therapy for High Risk Cancer Patients

Question: Should preventive lymphedema therapy be added to the breast cancer line for prophylactic treatment of women who have undergone breast cancer surgery or other high-risk surgeries?

Question source: Leslie Reagan, certified lymphedema therapist in The Dalles

Issue: Women who undergo breast cancer surgery, particularly with axillary lymph node dissection, are at high risk of developing lymphedema in their arm. One year after breast surgery, 10-20% of women who had axillary dissection have lymphedema, while fewer than 5% of women with sentinel node biopsy have lymphedema (Komen Foundation 2019). Per NCCN, surgery for other types of cancer, such as melanoma and pelvic organ cancers, can result in lymphedema.

From Ms. Reagan:

> My name is Leslie Reagan and I have been an occupational therapist at MCMC in The Dalles for 14 years. Twelve of those years have been devoted to treating women with breast cancer as a Certified Lymphedema therapist. Early in this practice, I would receive women in the clinic who had underwent breast cancer treatment and then subsequently developed edema in an arm. They would present like "deer in the headlights" as they had no idea what was going on with their limb, and often times bounced from clinician to clinician in the community to get answers as to what was occurring. When then got to me they experienced relief with answers and a tried and true method for treatment and management. Often times the question arose, "Why didn't anyone warn me about this? Is there any way this could have been avoided?" Treatment was intense and time-consuming, requiring 4-5 days/week in the clinic for up to a month or more, per the standards set by lymphedema education programs. I found that not only did they present with edema, but also with soft tissue restrictions of the shoulder and chest accompanied by back, shoulder and neck pain from postural changes. Many had lymphatic cording, or Axillary Web Syndrome, which restricts shoulder AROM and is painful.
>
> In 2015, the breast team at Celilo Cancer Center put together our statistics of those women identified as high risk for developing lymphedema, and who received evaluation and education for lymphedema prior to ever developing symptoms, typically between the time of her surgery and before radiation began, and those who did not. The physicians at Celilo are very forward thinking and believe that in this situation, it pays to be proactive vs reactive when it comes to lymphedema education and treatment.
>
> Our physicians at Celilo in The Dalles, and at Providence Hood River, identify those women who are having musculoskeletal issues post-surgically or who are at higher risk for developing lymphedema (those with an AND + radiation) and they receive an automatic referral for evaluation and education. This is our established continuum of care in the gorge. Today, I see far fewer women in later stages of lymphedema as detection and risk reduction has improved immensely due to our practice.
>
> Up until recently, these women were very well-covered for their therapies with [CCO]. The last two women referred were denied for all CPT codes based on their diagnosis of breast cancer from the physician. Per our insurance authorizer in clinic, "The denial letter itself says "Therapy is not a covered service for breast cancer under the Oregon Health Plan". When I checked the referral dx codes on the line finder while confirming benefits, neither were defined when paired with 97140 or any other CPT. I became LANA certified in 2013 in order to treat women under OHP, as it was otherwise a denied service without.

In summation, we are working as a gorge-wide team to provide the best possible information and care to our breast cancer patients. We are looking at it from both a quality of life as well as a cost-effective standpoint. Seeing women for 4-8 visits to address current and potential future issues, giving them peace of mind to move on with their survivorship, is far more efficacious and worthwhile than having to intensely treat a woman for 16-25 visits for a life-long condition that could be easily identified and managed early. Also, if you need examples of patients who have been covered by [CCO] or OHP in the past, please let me know and I can forward you on names. Please consider allowing breast cancer as a qualifying, above-line diagnosis for therapy treatments.

Evidence

1) **Rafn 2019**, pilot RCT of prospective surveillance and targeted physiotherapy (PSTP) compared to education (EDU) for prevention of lymphedema post breast cancer surgery
    a. N=21 for PSTP, 20 for EDU
        i. Patients included if they had lumpectomy or mastectomy
        ii. More patients in the PSTP group had axillary node dissection (33% vs 25%) and axillary radiation (76% to 60%)
    b. Assessed 12 months postsurgery
    c. Results: At 12 months, 18 (49%) participants (10 PSTP and 8 EDU) had arm morbidity, with EDU participants presenting more complex arm morbidity compared to PSTP participants.
    d. Conclusion**:** Prospective surveillance and targeted physiotherapy is feasible and may lower the complexity of arm morbidity after surgery for breast cancer. While underpowered to establish efficacy, the findings provide guidance for development of future definitive trials.

Expert guidelines

1) **NCCN 2019**, Survivorship
    a. Recommends assessing for symptoms and signs of lymphedema at every follow up visit and referral to lymphedema therapy when clinical concern for assessment and treatment
    b. Recommends lymphedema education for survivors at risk for development
2) **McLaughlin 2018**, American Society of Breast Surgeons guidelines for prevention and treatment of lymphedema
    a. Breast cancer patients at risk for lymphedema after axillary lymph node dissection and axillary radiation should undergo mindful surveillance including baseline and follow-up interstitial fluid quantification, tissue assessments, limb girth measurements, morbidity profiling (considering iatrogenic risk factors), and assessment of previous orthopedic injuries/surgeries, which may increase lymphedema risk
    b. Does not mention preventive lymphedema therapy visits for high risk patients
    c. Recommends patients diagnosed with lymphedema be treated by a trained lymphedema professional

HERC staff summary

The evidence base for preventive visits to a lymphedema specialist is minimal. Expert groups recommend surveillance for lymphedema at follow up visits, and referral to a lymphedema specialist if lymphedema is suspected or diagnosed. The model of preventive visits to reduce the risk of lymphedema in high risk patients (specifically breast cancer survivors who have undergone axillary lymph node dissection and axillary radiation) is attractive, and recommended by the American Society of Breast Surgeons. This model may be considered by the CCOs as a pilot project to evaluate its cost effectiveness.

HERC staff recommendation:

1) Make no change to the current coverage of lymphedema and the current limitation to lymphedema therapy to those patients with diagnosed lymphedema.

Article

CLINICAL REHABILITATION

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Prospective surveillance and targeted physiotherapy for arm morbidity after breast cancer surgery: a pilot randomized controlled trial

Bolette S Rafn[1], Stanley Hung[1], Alison M Hoens[1], Margaret L McNeely[2], Chiara A Singh[3], Winkle Kwan[4], Carol Dingee[5], Elaine C McKevitt[5], Urve Kuusk[5], Jinsi Pao[5], Nancy Van Laeken[5], Charlie H Goldsmith[6,7] and Kristin L Campbell[1]

Abstract

Objective: To evaluate prospective surveillance and targeted physiotherapy (PSTP) compared to education (EDU) on the prevalence of arm morbidity and describe the associated program cost.
Design: Pilot randomized single-blinded controlled trial.
Setting: Urban with assessments and treatment delivered in hospitals.
Participants: Women scheduled for breast cancer surgery.
Interventions: Participants were randomly assigned (1:1) to PSTP ($n=21$) or EDU ($n=20$) and assessed presurgery and 12 months postsurgery. All participants received usual care, namely, preoperative education and provision of an education booklet with postsurgical exercises. The PSTP group was monitored for arm morbidity every three months and referred for physiotherapy if arm morbidity was identified. The EDU group received three education sessions on nutrition, stress and fatigue management.
Main outcome measures: Arm morbidity was based on changes in the surgical arm(s) from presurgery in four domains: (1) shoulder range of motion, (2) strength, (3) volume, and (4) upper body function. Complex arm morbidity indicated ≥2 domains impaired. Second, the cost of the PSTP program was described.
Results: At 12 months, 18 (49%) participants (10 PSTP and 8 EDU) had arm morbidity, with EDU participants presenting more complex arm morbidity compared to PSTP participants. PSTP participants

[1]Department of Physical Therapy, The University of British Columbia, Vancouver, BC, Canada
[2]Department of Physical Therapy, University of Alberta, Edmonton, AB, Canada
[3]Fraser Health Authority, Surrey, BC, Canada
[4]Fraser Valley Centre, BC Cancer Agency, Vancouver, BC, Canada
[5]Department of Surgery, The University of British Columbia, Vancouver, BC, Canada
[6]Faculty of Health Sciences, Simon Fraser University, Burnaby, BC, Canada
[7]Department of Occupational Science & Occupational Therapy, The University of British Columbia, Vancouver, BC, Canada

Corresponding author:
Kristin L Campbell, Department of Physical Therapy, The University of British Columbia, Friedman Building 212, 2177 Wesbrook Mall, Vancouver, BC V6T 1Z3, Canada.
Email: kristin.campbell@ubc.ca

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ORIGINAL ARTICLE – BREAST ONCOLOGY

Considerations for Clinicians in the Diagnosis, Prevention, and Treatment of Breast Cancer-Related Lymphedema, Recommendations from an Expert Panel: Part 2: Preventive and Therapeutic Options

Sarah A. McLaughlin, MD[1], Sarah M. DeSnyder, MD[2], Suzanne Klimberg, MD, PhD[3], Michael Alatriste, LMT, CLT[4], Francesco Boccardo, MD, PhD, FACS[5], Mark L. Smith, MD, FACS[6,7], Alicia C. Staley, MBA, MS, BS[8], Paul T. R. Thiruchelvam, BSc, MD, PhD, FRCS[9], Nancy A. Hutchison, MD, CLT-LANA[10], Jane Mendez, MD[11], Fiona MacNeill, FRCS, MD, FEBS[12], Frank Vicini, MD, FACR, FABS[13], Stanley G. Rockson, MD[14,15], and Sheldon M. Feldman, MD, FACS[16]

[1]Department of Surgery, Mayo Clinic, Jacksonville, FL; [2]Department of Breast Surgical Oncology, The University of Texas MD AndersonCancer Center, Houston, TX; [3]Department of Breast and Surgical Oncology, Winthrop P. Rockefeller Cancer Institute, Little Rock, AR; [4]Lymphedema Alliance of New York, New York, NY; [5]Department of Surgery, Unit of Lymphatic Surgery - S. Martino University Hospital, University of Genoa, Genoa, Italy; [6]Department of Surgery, Northwell Health, Lake Success, NY; [7]Reconstructive Oncology, Northwell Health Cancer Institute, Lake Success, NY; [8]Akari Health, Boston, MA; [9]Imperial College Healthcare, London, UK; [10]Courage Kenny Rehabilitation Institute of AllinaHealth, Minneapolis, MN; [11]Miami Cancer Institute, Miami, FL; [12]Association of Breast Surgery Great Britain and Ireland, Royal College of Surgeons of England, London, UK; [13]Radiation Oncology, UCLA School of Medicine, Los Angeles, CA; [14]Center for Lymphatic and Venous Disorders, Stanford University School of Medicine, Stanford, CA; [15]Lymphatic Research and Biology, Falk Cardiovascular Research Center, Stanford, CA; [16]Division of Breast Surgery and Breast Surgical Oncology, Montefiore Medical Center, The University Hospital for the Albert Einstein College of Medicine, Montefiore Einstein Center for Cancer Care, New York, NY

The American Society of Breast Surgeons (ASBrS) recognizes lymphedema as a significant side effect of breast cancer treatment. Therefore, the ASBrS convened an international, multidisciplinary expert panel to review current data and guidelines on all aspects of lymphedema diagnosis and management to acknowledge the gravity of this public health issue facing breast cancer survivors. The Panel sought to collate clear and meaningful recommendations for providers regarding lymphedema diagnosis, treatment, and prevention. Diagnosis, education, and future directions were discussed in Part 1. Part 2 focuses on prevention and treatment.

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S. A. McLaughlin, MD
e-mail: Mclaughlin.sarah@mayo.edu

RISK-REDUCING BEHAVIORS

Given the study disagreements concerning risk factors and definitions of breast cancer-related lymphedema (BCRL), it is not surprising that clinicians have difficulty accurately predicting who will experience the development of BCRL. To prevent lymphedema, clinicians continue to recommend risk-reducing behaviors (RRB) that have largely been supported only by pathophysiology principles and expert clinical experience. Clinicians apply RRBs and patients adopt them without differentiation between at-risk and affected individuals, with most patients adopting four to five RRBs after axillary surgery.[1,2] Avoidance of venipuncture, injection, or blood pressure in the ipsilateral arm and use of compression sleeves for air travel are the

Pneumatic Compression Devices for Lymphedema Therapy

Question: Should pneumatic compression devices be included as a treatment for lymphedema?

Question source: Coverage guidance nomination process

Issue:
Coverage of pneumatic compression devices was nominated for the coverage guidance process. However, a recent high quality review has been completed and it was felt that there was no need to put this topic through the entire coverage guidance process.

Current Prioritized List status:

HCPCS code	**Code description**	**Current placement**
E0650	Pneumatic compressor, non-segmental home model	Never reviewed
E0651	Pneumatic compressor, segmental home model without calibrated gradient pressure	Never reviewed
E0652	Pneumatic compressor, segmental home model with calibrated gradient pressure	Never reviewed
E0655	Non-segmental pneumatic appliance for use with pneumatic compressor, half arm	Never reviewed
E0656	Segmental pneumatic appliance for use with pneumatic compressor, trunk	Never reviewed
E0657	Segmental pneumatic appliance for use with pneumatic compressor, chest	Never reviewed
E0660	Non-segmental pneumatic appliance for use with pneumatic compressor, full leg	Never reviewed
E0665	Non-segmental pneumatic appliance for use with pneumatic compressor, full arm	Never reviewed
E0666	Non-segmental pneumatic appliance for use with pneumatic compressor, half leg	Never reviewed
E0667	Segmental pneumatic appliance for use with pneumatic compressor, full leg	Never reviewed
E0668	Segmental pneumatic appliance for use with pneumatic compressor, full arm	Never reviewed
E0669	Segmental pneumatic appliance for use with pneumatic compressor, half leg	Never reviewed
E0670	Segmental pneumatic appliance for use with pneumatic compressor, integrated, 2 full legs and trunk	Never reviewed
E0671	Segmental gradient pressure pneumatic appliance, full leg	Never reviewed
E0672	Segmental gradient pressure pneumatic appliance, full arm	Never reviewed
E0673	Segmental gradient pressure pneumatic appliance, half leg	Never reviewed
E0676	Intermittent limb compression device (includes all accessories), not otherwise specified	Never reviewed

Evidence

1) **CADTH 2017**, evidence review of pneumatic compression devices for lymphedema
    a. N=6 studies
        i. One systematic review and meta-analysis (SR), three RCTs and two guidelines
    b. The findings from the SR and two RCTs showed that the combination of decongestive lymphatic therapy (DLT) and intermittent pneumatic compression (IPC) had no significant difference in the volume reduction compared to DLT alone.
    c. The SR found that there were no significant differences in pain and paresthesia between DLT plus IPC group and DLT alone group. Patients in the DLT alone group felt a greater reduction of heaviness than those in the DLT plus IPC group.
    d. The SR found that there were no significant differences in joint mobility between DLT plus IPC group and DLT alone group
    e. There were no statistically significant differences between SLD plus IPC and MLD plus bandaging in quality of life
    f. No adverse events were reported. Theoretical adverse effects of IPC include the recurrence of edema due to residual proteins remaining in the interstitial space, and potential lymphatic structure damage due to high pressure application.
    g. Conclusions: The evidence from the included SR and RCTs suggested that intermittent pneumatic compression (IPC) may not provide additional benefits when used in combination with the routine management of lymphedema. On the other hand, there is some evidence that IPC with higher pressure may reduce lymphedema effectively. The clinical effectiveness and safety of IPC operating at high pressure remain to be determined. Despite the lack of clinical effectiveness of IPC in reducing lymphedema as noted in the 2011 guideline, the 2014 guidelines recommended the short term use of IPC in combination with a lymphedema treatment program for reducing breast cancer-related lymphedema, irrespective to the number of chambers and cycle time. Given the low quality of evidence, the findings should be interpreted with caution. Multi-center trials of high quality with uniform criteria, larger sample sizes, standard treatment protocols and outcome measures, and a new generation of pump devices are needed for future research.
2) **AHRQ 2010,** technology review on treatment of secondary lymphedema https://www.ncbi.nlm.nih.gov/books/NBK285652/pdf/Bookshelf_NBK285652.pdf
    a. N=9 studies on pneumatic compression devices compared to other treatment modalities
        i. IPC found to be superior to massage in 3 studies, inferior to laser therapy in 1 study, and equivalent to manual lymphatic drainage with or without bandaging (2 studies), elastic sleeve (1 study) and skin care (1 study)
    b. Conclusion: No evidence found on whether pneumatic compression devices were effective at maintaining the reduction in lymphedema compared to other treatment modalities (bandaging, manual lymphatic drainage, exercise, etc.)

Other Payer policies

Aetna 2018:

1) Considers pneumatic compression devices to be experimental for treatment of upper extremity lymphedema. No specific comment is made regarding lower extremity lymphedema.
2) Only covers pneumatic compression devices for
    a. the treatment of chronic venous insufficiency of the legs of members who have venous stasis ulcers that have failed to heal after a 6-month trial of conservative therapy directed by the treating physician.
    b. to stimulate circulation and reduce the chances of deep venous thromboses for members who are bedridden due to trauma, orthopedic surgery, neurosurgery or other circumstances preventing ambulation

Medicare, 2002

Indications and Limitations of Coverage

Pneumatic devices are covered for the treatment of lymphedema or for the treatment of chronic venous insufficiency with venous stasis ulcers.

Pneumatic compression devices are covered only when prescribed by a physician and when they are used with appropriate physician oversight, i.e., physician evaluation of the patient's condition to determine medical necessity of the device, assuring suitable instruction in the operation of the machine, a treatment plan defining the pressure to be used and the frequency and duration of use, and ongoing monitoring of use and response to treatment.

The determination by the physician of the medical necessity of a pneumatic compression device must include:

1. The patient's diagnosis and prognosis;
2. Symptoms and objective findings, including measurements which establish the severity of the condition;
3. The reason the device is required, including the treatments which have been tried and failed; and
4. The clinical response to an initial treatment with the device.

The clinical response includes the change in pre-treatment measurements, ability to tolerate the treatment session and parameters, and ability of the patient (or caregiver) to apply the device for continued use in the home.

The only time that a segmented, calibrated gradient pneumatic compression device (HCPCs code E0652) would be covered is when the individual has unique characteristics that prevent them from receiving satisfactory pneumatic compression treatment using a nonsegmented device in conjunction with a segmented appliance or a segmented compression device without manual control of pressure in each chamber.

HERC staff summary

The evidence for the use of pneumatic compression devices for treatment of lymphedema is of low quality. The limited evidence base suggests that intermittent pneumatic compression (IPC) may not provide additional benefits when used in combination with the routine management of lymphedema.

HERC staff recommendation

1) Make no change in the current non-coverage of pneumatic compression devices for lymphedema therapy
    a. Add HCPCS E0650-E0673 and E0676 to line 660/GN173

GUIDELINE NOTE 173, INTERVENTIONS THAT ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS FOR CERTAIN CONDITIONS

Line 660

The following Interventions are prioritized on Line 660 CONDITIONS FOR WHICH CERTAIN INTERVENTIONS ARE UNPROVEN, HAVE NO CLINICALLY IMPORTANT BENEFIT OR HAVE HARMS THAT OUTWEIGH BENEFITS:

Procedure Code	Intervention Description	Rationale	Last Review
E0650-E0673 and E0676	Pneumatic compressor Segmental pneumatic appliance for use with pneumatic compressor	Insufficient evidence of effectiveness	May, 2019

CADTH

CADTH RAPID RESPONSE REPORT:
SUMMARY WITH CRITICAL APPRAISAL

Intermittent Pneumatic Compression Devices for the Management of Lymphedema: A Review of Clinical Effectiveness and Guidelines

Service Line:	Rapid Response Service
Version:	1.0
Publication Date:	May 12, 2017
Report Length:	22 Pages

Summary of Evidence

Quantity of Research Available

A total of 143 citations were identified in the literature search. Following screening of titles and abstracts, 123 citations were excluded and 20 potentially relevant reports from the electronic search were retrieved for full-text review. Eight potentially relevant publications were retrieved from the grey literature search. Of these potentially relevant articles, 22 publications were excluded for various reasons, while six publications, including one SR and MA, three RCTs and two guidelines, met the inclusion criteria and were included in this report. Appendix 1 describes the PRISMA flowchart of the study selection.

Summary of Study Characteristics

The characteristics of the SR and MA,[8] RCTs[9-11] and guidelines[12,13] are summarized below and presented in Appendix 2.

SR and MA

Study Design

The SR[8] included seven RCTs involving the use of ICP pump for treatment of breast cancer-related lymphedema with a total population of 287 patients.

Country of Origin

The SR[14] was conducted by authors from China and was published in 2014.

Population

The overall population of the included studies was patients with a prior history of treatment of breast cancer and lymphedema. The latter was defined as an absolute increase in arm volume of at least 10% or 2 cm between the affected and unaffected arms.

Interventions and Comparators

The interventions included a combination of decongestive lymphatic therapy (DLT) and IPC or IPC alone. The comparators were DLT alone or manual lymphatic drainage or control. The pressure used in the IPC pump ranged from 40 to 60 mmHg, and the IPC treatment duration per session varied between 0.5 and 2.0 hours.

Outcomes

The clinical outcomes included the percentage of edema reduction, and subjective symptoms, such as heaviness, pain and tension, and joint mobility.

Treatment and Follow-up Period

The treatment period ranged from two to 15 weeks, and the follow-up period ranged from two weeks to three months.

Data Analysis and Synthesis

Of the included seven RCTs, three RCTs with 126 patients were available for meta-analysis on the percentage of volume reduction. The findings of the remaining RCTs were synthesized narratively.

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Intermittent Pneumatic Compression Devices

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Policy

Aetna considers full-leg or half-leg pneumatic compression devices for home use medically necessary durable medical equipment (DME) for the treatment of chronic venous insufficiency of the legs of members who have venous stasis ulcers that have failed to heal after a 6-month trial of conservative therapy directed by the treating physician. The trial of conservative therapy must include a compression bandage system or compression garment, appropriate dressings for the wound, exercise, and elevation of the limb.

When a pneumatic compression device is determined to be medically necessary, a non-segmented device or segmented device without manual control of the pressure in each chamber is generally considered adequate to meet the clinical needs of the member. A segmented device with manual control of the pressure in each chamber is considered medically necessary only if there is clear documentation of medical necessity in the individual case. A segmented device with manual control of the pressure in each chamber is considered medically necessary only when there is documentation that the individual has unique characteristics that prevent satisfactory pneumatic compression treatment using a non-segmented device with a segmented appliance/sleeve or a segmented device without manual control of the pressure in each chamber.

Aetna considers intermittent pneumatic compression devices of the lower extremities medically necessary DME to stimulate circulation and reduce the chances of deep venous thromboses for members who are bedridden due to trauma, orthopedic surgery, neurosurgery or other circumstances preventing ambulation. Note: the presence of a cast or splint, the use of an assistive device (e.g., walker, crutches), or non-weightbearing status alone due to injury or surgery are not considered "bedridden" for the purpose of this policy.

Aetna considers intermittent pneumatic compression devices experimental and investigational for the following (not an all-inclusive list) because there is inadequate evidence of their effectiveness for these indications:

- Enhancement of Achilles tendon rupture healing
- Enhancement of fracture and soft-tissue healing
- Management of edema following femoro-popliteal bypass surgery
- Prophylaxis of venous thromboembolism in neurosurgery
- Rehabilitation for distal radial fractures
- Treatment of critical limb ischemia
- Treatment of peripheral arterial occlusive disease/arterial insufficiency
- Treatment of restless legs syndrome
- Treatment of sensory impairment in the upper limb following stroke
- Treatment of upper extremity lymphedema following surgery
- Treatment of upper extremity vascular ulcers

Aetna considers a single patient use intermittent pneumatic compression device (e.g., the VenaPro Vascular Therapy System) not medically necessary.

Aetna considers intermittent pneumatic trunk compression for the prevention of thrombosis following orthopedic surgery experimental and investigational because its effectiveness has not been established.

Note: For persons with a medically necessary inflatable compression garment (e.g., Flowtron Compression Garment, Jobst Pneumatic Compressor), a pump needed to inflate the compression garment is considered medically necessary.

See also CPB 0069 - Lymphedema for Aetna's policy on pneumatic compression devices for arm lymphedema and CPB 0482 - Compression Garments for the Legs.

Background

Gradient elastic stockings, such as those made by Jobst, Sigvaris, Juzzo, or Medi, are generally viewed as the principle means of preventing complications of chronic venous insufficiency. Intermittent pneumatic compression devices compress the leg and/or foot and ankle and act as a pump to improve circulation in the lower extremities. Pneumatic compression devices consist of an inflatable garment for the leg and an electrical pneumatic pump that fills the garment with compressed air. The garment is intermittently inflated and deflated with cycle times and pressures that vary between devices.

Intermittent pneumatic compression (IPC) boots are generally accepted as a method for preventing deep venous thromboses (DVT) and complications of venous stasis in persons after trauma, orthopedic surgery, neurosurgery, or who for other reasons are unable to walk.

Use of the IPC device has expanded to ambulatory persons who suffer from chronic venous insufficiency (CVI) of the legs and consequent edema, stasis dermatitis, ulcerations, and cellulitis. CVI of the legs is caused by abnormalities of the venous wall and valves, leading to obstruction or reflux of blood flow in the veins.

A systemic review of the literature concluded that the effectiveness of the addition of IPC in treatment of venous leg ulcers is unknown. The systemic review identified 3 small, randomized controlled trials (RCTs) of IPC; all of these trials were different in design. Upon pooling of the results, using a random effects model, the reviewers found no difference in healing rates. The review concluded that “[t]hree small [randomized controlled trials] found no evidence of a significant effect on healing with intermittent pneumatic compression in conjunction with compression bandages.”

There is no evidence that IPC devices are superior to gradient compression stockings in preventing complications of chronic venous disease. Compliance with gradient compression stockings has been shown to be essential to their effectiveness; the stockings do not work unless they are worn. There are no studies, however, that have demonstrated that compliance with IPC devices is significantly greater than compliance with gradient compression stockings.

The A-V Impulse System Foot Pump and the KCI Plexipulse are brands of IPC boots on the market; others include those manufactured by Jobst, Chattanooga, Kendal, and Nutech.

The Canadian Coordinating Office of Health Technology Assessment (2004) concluded that “EPC [external pneumatic compression] reduces the risk of DVT for patients who cannot walk due to trauma, joint surgery or neurosurgery. There is still limited evidence, however, supporting the effect of EPC on the healing of venous ulcers and other disorders resulting from chronic VI [venous insufficiency]”.

Current evidence supporting the use of pneumatic compression devices in peripheral arterial disease is limited to small pilot studies with short-term follow up. In a pilot study (n = 30), Ramaswami et al (2005) examined the usefulness of rapid, high-pressure, intermittent pneumatic calf and foot compression (IPCFC) in patients with stable intermittent

claudication. These investigators concluded that "IPCFC improves walking distance in patients with stable intermittent claudication. The combination of IPCFC with other treatment such as risk-factor modification and daily exercise may prove useful in patients with peripheral arterial occlusive disease. It may be a useful first line of therapy in patients with disabling claudication who are unfit for major reconstructive surgery. Improved walking on long-term follow-up and experience from different centers may establish a role for this treatment modality in the future".

Kakkos et al (2005) compared the effect of unsupervised exercise, supervised exercise and IPCFC on the claudication distance, lower limb arterial hemodynamics and quality of life of patients with intermittent claudication (n = 34). These researchers concluded that IPCFC achieved improvement in walking distance comparable with supervised exercise. Long-term results in a larger number of patients will provide valuable information on the optimal treatment modality of intermittent claudication.

Khanna et al (2008) stated that current methods of fracture care use various adjuncts to try and decrease time to fracture union, improve fracture union rates and enhance functional recovery; and one such modality is IPC. These researchers performed a literature review on this approach. A total of 16 studies on the use of IPC in fracture and soft-tissue healing were identified. These studies demonstrated that IPC facilitates both fracture and soft-tissue healing with rapid functional recovery. The authors concluded that IPC appears to be an effective modality to enhance fracture and soft-tissue healing. Moreover, they noted that the number of subjects in human studies is small, and adequately powered RCTs are needed to produce stronger clinically relevant evidence.

In a prospective, randomized, double-blinded, sham-controlled trial, Lettieri and Eliasson (2009) evaluated the effectiveness of pneumatic compression devices (PCDs) as a non-pharmacologic treatment for restless legs syndrome (RLS). Subjects wore a therapeutic or sham device prior to the usual onset of symptoms for a minimum of 1 hour daily. Measures of severity of illness, quality of life, daytime sleepiness, and fatigue were compared at baseline and after 1 month of therapy. A total of 35 subjects were enrolled. Groups were similar at baseline. Therapeutic PCDs significantly improved all measured variables more than shams. Restless legs severity score improved from 14.1 +/- 3.9 to 8.4 +/- 3.4 ($p = 0.006$) and Johns Hopkins restless legs scale improved from 2.2 +/- 0.5 to 1.2 +/- 0.7 ($p = 0.01$). All quality of life domains improved more with therapeutic than sham devices (social function 14 % versus 1 %, respectively; $p = 0.03$; daytime function 21 % versus 6 %, respectively, $p = 0.02$; sleep quality 16 % versus 8 %, respectively, $p = 0.05$; emotional well-being 17 % versus 10 %, respectively, $p = 0.15$). Both Epworth sleepiness scale (6.5 +/- 4.0 versus 11.3 +/- 3.9, respectively, $p = 0.04$) and fatigue (4.1 +/- 2.1 versus 6.9 +/- 2.0, respectively, $p = 0.01$) improved more with therapeutic devices than sham devices. Complete relief occurred in 1/3 of subjects using therapeutic and in no subjects using sham devices. The authors concluded that PCDs resulted in clinically significant improvements in symptoms of RLS in comparison to the use of sham devices and may be an effective adjunctive or alternative therapy for RLS. Moreover, the authors stated that before PCD therapy is ready for more wide-spread use, it will be important to see validating studies in various populations of RLS patients.

In a prospective, randomized trial, te Slaa et al (2011) examined the effects of IPC for the treatment and prevention of post-reconstructive edema following femoro-popliteal bypass surgery. Patients were assigned to one of two groups. All patients suffered from peripheral arterial disease, and all were subjected to autologous femoro-popliteal bypass reconstruction. Patients in group 1 used a compression stocking (CS) above the knee exerting 18 mm Hg (class I) on the leg post-operatively for 1 week (day and night). Patients in group 2 used IPC on the foot post-operatively at night for 1 week. The lower leg circumference was measured pre-operatively and at 5 post-operative time points. A multi-variate analysis was done using a mixed model analysis of variance. A total of 57 patients were analyzed (n = 28 for CS; n = 29 for IPC). Indications for operation were severe claudication (CS 13; IPC 13), rest pain (10/5), or tissue loss (7/11). Re-vascularization was performed with either a supra-genicular (CS 13; IPC 10) or an infra-genicular (CS 15; IPC 19) autologous bypass. Leg circumference increased on day 1 (CS/IPC): 0.4 %/2.7 %, day 4 (2.1 %/6.1 %), day 7 (2.5 %/7.9 %), day 14 (4.7 %/7.3 %), and day 90 (1.0 %/3.3 %) from baseline (pre-operative situation). On days 1, 4, and 7 there was a significant difference in leg circumference between the 2 treatment groups. The authors concluded that edema following femoro-popliteal bypass surgery occurs in all patients. For the prevention and treatment of edema following femoro-popliteal bypass surgery, the use of a class I CS proved superior to treatment with IPC. The authors concluded that the use of CS remains the recommended practice following femoro-popliteal bypass surgery.

Pfizenmaier et al (2005) noted that ischemic vascular ulcerations of the upper extremities are an uncommon and

frequently painful condition most often associated with scleroderma and small vessel inflammatory diseases. Digital amputation has been advocated as primary therapy because of the poor outcome with medical care. Intermittent pneumatic compression pump therapy can improve ulcer healing in lower extremity ischemic ulcerations; however, the value of this treatment in upper extremity ischemic ulcerations is not known. This observational pilot study consisted of a consecutive series of 26 patients with 27 upper extremity ischemic vascular ulcers seen at the Mayo Gonda Vascular Center from 1996 to 2003. Inclusion criteria were documented index of ulcer size and follow-up ulcer size and use of the IPC pump as adjunctive wound treatment. Twenty-six of 27 ulcers (96 %) healed with the use of the IPC pump. Mean baseline ulcer size was 1.0 cm2 (SD = 0.3 cm2) and scleroderma was the underlying disease in 65 % (17/26) of cases. Laser Doppler blood flow in the affected digit was 7 flux units (normal greater than 100). The mean ulcer duration before IPC treatment was 31 weeks. The average pump use was 5 hours per day. The mean time to wound healing was 25 weeks. Twenty-five of 26 patients reported an improvement in wound pain with pump use. The authors concluded that intensive IPC pump use is feasible and associated with a high rate of healing in upper extremity ischemic ulcers. Furthermore, they stated that prospective, RCTs of IPC is needed to determine whether IPC treatment improves wound healing compared to standard medical care.

Handoll et al (2006) examined the effects of rehabilitation interventions in adults with conservatively or surgically treated distal radial fractures. These investigators searched the Cochrane Bone, Joint and Muscle Trauma Group Specialised Register (December 2005), the Cochrane Central Register of Controlled Trials (The Cochrane Library Issue 4, 2005), MEDLINE, EMBASE, CINAHL, AMED, PEDro, OTseeker and other databases, conference proceedings and reference lists of articles. No language restrictions were applied. Randomized or quasi-RCTs evaluating rehabilitation as part of the management of fractures of the distal radius sustained by adults. Rehabilitation interventions such as active and passive mobilization exercises, and training for activities of daily living, could be used on their own or in combination, and be applied in various ways by various clinicians. The authors independently selected and reviewed trials. Study authors were contacted for additional information. No data pooling was done. A total of 15 trials, involving 746 mainly female and older patients, were included. Initial treatment was conservative, involving plaster cast immobilization, in all but 27 participants whose fractures were fixed surgically. Though some trials were well-conducted, others were methodologically compromised. For interventions started during immobilization, there was weak evidence of improved hand function for hand therapy in the days after plaster cast removal, with some beneficial effects continuing 1 month later (1 trial). There was weak evidence of improved hand function in the short-term, but not in the longer term (3 months), for early occupational therapy (1 trial), and of a lack of differences in outcome between supervised and unsupervised exercises (1 trial). For interventions started post-immobilization, there was weak evidence of a lack of clinically significant differences in outcome in patients receiving formal rehabilitation therapy (4 trials), passive mobilization (2 trials), ice or pulsed electromagnetic field (1 trial), or whirlpool immersion (1 trial) compared with no intervention. There was weak evidence of a short-term benefit of continuous passive motion (post-external fixation) (1 trial), IPC (1 trial) and ultrasound (1 trial). There was weak evidence of better short-term hand function in participants given physiotherapy than in those given instructions for home exercises by a surgeon (1 trial). The authors concluded that the available evidence from RCTs is insufficient to establish the relative effectiveness of the various interventions used in the rehabilitation of adults with fractures of the distal radius.

In a preliminary study, Cambier et al (2003) evaluated the effectiveness of IPC in treating sensory impairments in the hemiplegic upper limb in stroke patients. A total of 23 stroke patients were enrolled in this RCT that compared the application of IPC with a passive treatment strategy. The experimental group (n = 11) received standard physiotherapy combined with IPC treatment (10 cycles of 3 mins with a peak of 40 mmHg) for their hemiplegic upper limb. The control group (n = 12) received supplementary to their conventional physiotherapy a placebo treatment, namely sham short-wave therapy on the hemiplegic shoulder for 30 mins. Sensory impairments were clinically assessed at 3 occasions over a period of 4 weeks using the Nottingham Sensory Assessment scale. Both groups improved in somato-sensation over time, but the experimental group improved more than the control group (p = 0.036) or 81.1% improvement versus 30.9 %. The authors concluded that the use of IPC in the rehabilitation of stroke patients may be of clinical importance for the restoration of sensory function. Drawbacks of this study included small sample size and short follow-up period.

Doyle et al (2010) examined the effects of interventions that target upper limb sensory impairment after stroke. These investigators searched the Cochrane Stroke Group Trials Register (last searched October 8, 2009), the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library 2009, Issue 1), MEDLINE (1966 to January 2009),

EMBASE (1980 to January 2009), and 6 further electronic databases to January 2009. They also hand-searched relevant journals, contacted authors in the field, searched doctoral dissertation databases, checked reference lists, and completed citation tracking. Randomized controlled trials and controlled trials comparing interventions for sensory impairment after stroke with no treatment, conventional treatment, attention placebo or with other interventions for sensory impairment were included in this analysis. Two review authors selected studies, assessed quality and extracted data. They analyzed study data using mean differences and odds ratios as appropriate. The primary outcome was sensory function; and secondary outcomes included upper limb function, activities of daily living, impact of stroke and quality of life as well as adverse events. These researchers included 13 studies, with a total 467 participants, testing a range of different interventions. Outcome measures included 36 measures of sensory impairment and 13 measures of upper limb function. All but 2 studies had unclear or high-risk of bias. While there is insufficient evidence to reach conclusions about the effects of interventions included in this review, 3 studies provided preliminary evidence for the effects of some specific interventions, including mirror therapy for improving detection of light touch, pressure and temperature pain; a thermal stimulation intervention for improving rate of recovery of sensation; and IPC intervention for improving tactile and kinesthetic sensation. These researchers could not perform meta-analysis due to a high-degree of clinical heterogeneity in both interventions and outcomes. The authors concluded that there is insufficient evidence to support or refute the effectiveness of the described interventions in improving sensory impairment, upper limb function, or participants' functional status and participation. Moreover, they stated that there is a need for more well-designed, better-reported studies of sensory rehabilitation.

The American College of Chest Physicians' evidence-based clinical practice guidelines on "Antithrombotic and thrombolytic therapy for ischemic stroke" (Lansberg et al, 2012) provided recommendations on the use of anti-thrombotic therapy in patients with stroke or transient ischemic attack (TIA). These investigators generated treatment recommendations (Grade 1) and suggestions (Grade 2) based on high (A), moderate (B), and low (C) quality evidence. In patients with acute ischemic stroke, these researchers recommended IV recombinant tissue plasminogen activator (r-tPA) if treatment can be initiated within 3 hrs (Grade 1A) or 4.5 hrs (Grade 2C) of symptom onset; these investigators suggested intra-arterial r-tPA in patients ineligible for IV tPA if treatment can be initiated within 6 hrs (Grade 2C); they suggested against the use of mechanical thrombectomy (Grade 2C) although carefully selected patients may choose this intervention; and they recommended early aspirin therapy at a dose of 160 to 325 mg (Grade 1A). In patients with acute stroke and restricted mobility, the authors suggested the use of prophylactic-dose heparin or IPC devices (Grade 2B) and suggested against the use of elastic compression stockings (Grade 2B). In patients with a history of non-cardioembolic ischemic stroke or TIA, they recommended long-term treatment with aspirin (75 to 100 mg once-daily), clopidogrel (75 mg once-daily), aspirin/extended release dipyridamole (25 mg/200 mg bid), or cilostazol (100 mg bid) over no anti-platelet therapy (Grade 1A), oral anti-coagulants (Grade 1B), the combination of clopidogrel plus aspirin (Grade 1B), or triflusal (Grade 2B). Of the recommended anti-platelet regimens, the authors suggested clopidogrel or aspirin/extended-release dipyridamole over aspirin (Grade 2B) or cilostazol (Grade 2C). In patients with a history of stroke or TIA and atrial fibrillation, they recommended oral anti-coagulation over no anti-thrombotic therapy, aspirin, and combination therapy with aspirin and clopidogrel (Grade 1B).

Zhao and colleagues (2012) noted that total hip replacement (THR) is an effective treatment for reducing pain and improving function and quality of life in patients with hip disorders. While this operation is very successful, DVT and pulmonary embolism (PE) are significant complications after THR. Different types of IPC devices have been used for thrombosis prophylaxis in patients following THR. Available devices differ in compression garments, location of air bladders, patterns of pump pressure cycles, compression profiles, cycle-length, duration of inflation time and deflation time, or cycling mode such as automatic or constant cycling devices. Despite the widely accepted use of IPC for the treatment of arterial and venous diseases, the relative effectiveness of different types of IPC systems as prophylaxis against thrombosis after THR is still unclear. In a Cochrane review, these investigators evaluated the comparative safety and effectiveness of different IPC devices with respect to the prevention of venous thromboembolism in patients after THR. The Cochrane Peripheral Vascular Diseases Group Trials Search Coordinator searched the Specialized Register (May 2012), CENTRAL (2012, Issue 4), MEDLINE (April Week 3 2012) and EMBASE (Week 17 2012). Clinical trial databases were searched for details of ongoing and unpublished studies. Reference lists of obtained articles were also screened. There were no limits imposed on language or publication status. Randomized and quasi-RCTs were eligible for inclusion. Two review authors independently selected trials, assessed trials for eligibility and methodological quality, and extracted data. Disagreement was resolved by discussion or, if necessary, referred to a third review author. Only 1 quasi-RCT with 121 study participants comparing 2 types of IPC devices met the inclusion

criteria. The authors found no cases of symptomatic DVT or PE in either the calf-thigh compression group or the plantar compression group during the first 3 weeks after the THR. The calf-thigh pneumatic compression was more effective than plantar compression for reducing thigh swelling during the early post-operative stage. The strength of the evidence in this review was weak as only 1 trial was included and it was classified as having a high-risk of bias. The authors concluded that there is a lack of evidence from RCTs to make an informed choice of IPC device for preventing venous thromboembolism (VTE) following THR. They stated that more research is needed, ideally a multi-center, properly designed RCT including a sufficient number of participants. Clinically relevant outcomes such as mortality, imaging-diagnosed asymptomatic VTE and major complications must be considered.

Dennis et al (2013) evaluated the effectiveness of IPC to reduce the risk of DVT in patients who have had a stroke. The CLOTS 3 trial is a multi-center parallel group randomized trial assessing IPC in immobile patients (i.e., who cannot walk to the toilet without the help of another person) with acute stroke. These researchers enrolled patients from day 0 to day 3 of admission and allocated them via a central randomization system (ratio 1:1) to receive either IPC or no IPC. A technician who was masked to treatment allocation did a compression duplex ultrasound (CDU) of both legs at 7 to 10 days and, wherever practical, at 25 to 30 days after enrolment. Care-givers and patients were not masked to treatment assignment. Patients were followed up for 6 months to determine survival and later symptomatic VTE. The primary outcome was a DVT in the proximal veins detected on a screening CDU or any symptomatic DVT in the proximal veins, confirmed on imaging, within 30 days of randomization. Patients were analyzed according to their treatment allocation. Between December 8, 2008, and September 6, 2012, a total of 2,876 patients were enrolled in 94 centers in the United Kingdom. The included patients were broadly representative of immobile stroke patients admitted to hospital and had a median age of 76 years (IQR 67 to 84). The primary outcome occurred in 122 (8.5 %) of 1,438 patients allocated IPC and 174 (12.1 %) of 1,438 patients allocated no IPC; an absolute reduction in risk of 3.6 % (95 % confidence interval [CI]: 1.4 to 5.8). Excluding the 323 patients who died before any primary outcome and 41 without any screening CDU, the adjusted odds ratio (OR) for the comparison of 122 of 1,267 patients versus 174 of 1,245 patients was 0.65 (95 % CI: 0.51 to 0.84; p = 0·001). Deaths in the treatment period occurred in 156 (11 %) patients allocated IPC and 189 (13 %) patients allocated no IPC died within the 30 days of treatment period (p = 0.057); skin breaks on the legs were reported in 44 (3 %) patients allocated IPC and in 20 (1 %) patients allocated no IPC (p = 0.002); falls with injury were reported in 33 (2 %) patients in the IPC group and in 24 (2 %) patients in the no-IPC group (p = 0.221). the authors concluded that IPC is an effective method of reducing the risk of DVT and possibly improving survival in a wide variety of patients who are immobile after stroke.

It is interesting to note that an UpToDate review on “Prevention of venous thromboembolic disease in medical patients” (Pai and Douketis, 2014) states that “Data on the efficacy and safety of IPCs are limited. However, one large randomized trial in patients with stroke suggested that IPCs reduce the incidence of VTE [Dennis et al, 2013]. A multicenter, randomized trial of 2,876 immobile patients with acute stroke (CLOTS 3) reported that, compared to no device, IPC use was associated with a lower rate of VTE at 30 days (12 versus 8.5 percent; absolute risk reduction 3.6 percent; 95% CI 1.4 to 5.8) without altering mortality (13 versus 11 percent). While use of low molecular weight heparin was similar in both groups (32 versus 30 percent), more patients in the IPC group wore compression stockings (15 versus 6 percent) which may have biased results in favor of IPC use”.

Ye et al. (2018) examined various definitions of immobility used in recent pharmacological thromboprophylaxis clinical trials. PubMed and relevant references from articles/reviews from 2008 to 2016 were searched. RCTs and other clinical studies involving adult hospitalized medical patients in acute care hospital settings that used the term immobility were selected. Two investigators independently abstracted data in duplicate, and accuracy was checked by a third investigator. Twenty-one clinical studies were included. There was heterogeneity among individual VTE risk factors, with respect to the definition of immobility in medical inpatients in these trials. Thirteen studies utilized objective criteria to define ‘‘immobility’’ including duration (12 studies) and distance or time walked (6 studies). In contrast, 7 studies focused principally on subjective definitions (ie, describing the nature of immobility rather than specifying its quantitative measurement). Three RCTs vaguely defined the level of patient’s immobility after hospitalization. The authors concluded that despite the well-known effectiveness of pharmacological thromboprophylaxis for the prevention of VTE in acutely ill medical patients, there is no current consensus on how to define immobility. The heterogeneous nature of definitions of immobility has led to uncertainty about the importance of immobility in VTE risk assessment models. Although clinical studies have incorporated varying definitions of immobility into their inclusion criteria, immobility as a specific VTE risk factor has not been clearly defined.

Kwak et al. (2017) conducted a retrospective comparative study to evaluate intermittent pneumatic compression (IPC) for the prevention of VTE after total hip arthroplasty. A total of 379 adult patients were included of which 233 patients were in the intervention group and 146 patients in the control group. All patients took low-dose aspirin for 6 weeks after surgery. IPC was applied to both legs just after surgery and maintained all day until discharge. When a symptom or a sign suspicious of VTE, such as swelling or redness of the foot and ankle, Homans' sign, and dyspnea was detected, computed tomography (CT) angiogram or duplex ultrasonogram was performed. For both groups, patients were excluded if they were younger than 17 years, taking anticoagulant stronger than aspirin for any reason, had history of previous VTE, could not take aspirin for any reason, and were followed up for less than 3 months after surgery. Both calves were compressed all day long except when patients were out of bed. All patients started active leg muscle contraction exercise when recovered from anesthesia and started crutch walking as soon as possible. Patients were discharged when they could walk with a walker or crutches. Until 3 months after surgery, symptomatic VTE occurred in three patients in the IPC group and in 6 patients in the control group. The incidence of VTE was much lower in the IPC group (1.3%) than in the control group (4.1%), but the difference was not statistically significant. Complications associated with the application of IPC were not detected in any patient. Patients affected by VTE were older and hospitalized longer than the unaffected patients. The incidence of VTE in the IPC group was less than 30% of that in the control group. The authors concluded that IPC might be an effective and safe method for the prevention of postoperative VTE. Limitations include retrospective study with a relatively small number of cases and only the patients with suspicious symptoms or signs were examined by CT or US.

Critical Limb Ischemia:

In a systematic review, Abu Dabrh and associates (2015) synthesized the existing evidence about various non-revascularization-based therapies used to treat patients with severe or critical limb ischemia (CLI) who are not candidates for surgical revascularization. These investigators searched multiple databases through November 2014 for RCTs and non-randomized studies comparing the effect of medical therapies (prostaglandin E1 and angiogenic growth factors) and devices (pumps and spinal cord stimulators). They reported ORs and 95 % Cis of the outcomes of interest pooling data across studies using the random effects model. These researchers included 19 studies that enrolled 2,779 patients; none of the non-revascularization-based treatments was associated with a significant effect on mortality. Intermittent pneumatic compression (OR, 0.14; 95 % CI: 0.04 to 0.55) and spinal cord stimulators (OR, 0.53; 95 % CI: 0.36 to 0.79) were associated with reduced risk of amputation. A priori established subgroup analyses (combined versus single therapy; randomized versus non-randomized) were not statistically significant. The authors concluded that very low-quality evidence, mainly due to imprecision and increased risk of bias, suggested that IPC and spinal cord stimulators may reduce the risk of amputations; and evidence supporting other medical therapies is insufficient.

Moran and colleagues (2015) stated that IPC is designed to aid wound healing and limb salvage for patients with CLI who are not candidates for revascularisation. These researchers conducted a systematic review of the literature to identify and critically appraise the evidence supporting its use in this population. A search was conducted in Embase, MEDLINE and clinical trial registries up to the end of March 2013. No date or language restrictions were applied. Quality assessment was performed by 2 investigators independently. Quality was assessed using the Cochrane risk of bias tool and the NICE case-series assessment tool. Two controlled before-and-after (CBA) studies and 6 case series were identified. One retrospective CBA study involving compression of the calf reported improved limb salvage and wound healing (OR 7.00, 95 % CI: 1.82 to 26.89, $p < 0.01$). One prospective CBA study involving sequential compression of the foot and calf reported statistically significant improvements in claudication distances and SF-36 quality of life scores. No difference in all-cause mortality was found. Complications included pain associated with compression, as well as skin abrasion and contact rash as a result of the cuff rubbing against the skin. All studies had a high risk of bias. The authors concluded that the limited available results suggested that IPC may be associated with improved limb salvage, wound healing and pain management. However, they stated that in the absence of additional well-designed analytical studies examining the effect of IPC in CLI, this treatment remains unproven.

Enhancement of Achilles Tendon Rupture Healing:

Abdul Alim and colleagues (2017) noted that adjuvant IPC during leg immobilization following Achilles tendon rupture (ATR) has been shown to reduce the risk of DVT. These researchers examined if IPC can also promote tendon healing.

A total of 150 patients with surgical repair of acute ATR were post-operatively leg-immobilized and prospectively randomized. Patients were allocated for 2 weeks of either adjuvant IPC treatment (n = 74) or treatment-as-usual (n = 74) in a plaster cast without IPC. The IPC group received 6 hours daily bilateral calf IPC applied under an orthosis on the injured side. At 2 weeks post-operatively, tendon healing was assessed using micro-dialysis followed by enzymatic quantification of tendon callus production, procollagen type I (PINP) and type III (PIIINP) N-terminal propeptide, and total protein content. A total of 14 IPC and 19 cast patients (control group) consented to undergo micro-dialysis. During weeks 3 to 6, all subjects were leg-immobilized in an orthosis without IPC. At 3 and 12 months, patient-reported outcome was assessed using reliable questionnaires (ATRS and EQ-5D). At 12 months, functional outcome was measured using the validated heel-rise test. At 2 weeks post-rupture, the IPC-treated patients exhibited 69 % higher levels of PINP in the ruptured Achilles tendon (AT) compared to the control group (p = 0.001). Interestingly, the IPC-treated contralateral, intact AT also demonstrated 49 % higher concentrations of PINP compared to the non-treated intact AT of the plaster cast group (p = 0.002). There were no adverse events (AEs) observed associated with IPC. At 3 and 12 months, no significant (n.s.) differences between the 2 treatments were observed using patient-reported and functional outcome measures. The authors concluded that patients in post-operative lower limb immobilization after ATR demonstrated a significantly enhanced early healing response when using adjuvant calf IPC for 2 weeks. They noted that that IPC in addition to exert a prophylactic effect against DVT also may be a viable and effective treatment to prevent immobilization-induced impairments on the healing process. Moreover, they stated that further studies should examine if prolonged IPC usage during the whole immobilization time could shorten the time to recovery and optimize final outcome.

The authors stated that a potential drawback of this study was that they could not conclude the exact time length that the enhanced healing response associated with adjuvant IPC therapy will persist. The observations of equal patient-reported and functional outcome measures between the 2 groups at 3 and 12 months post-operatively demonstrated that the 2 weeks IPC intervention did not improve outcome measures from 3 months onwards. However, after the end of the IPC intervention at week 2, both treatment groups received immobilization in an orthosis until 6 weeks post-operatively when immobilization was ended. This suggested that the healing stimulatory effects of the IPC therapy did not persist after cessation of treatment when continued immobilization was applied. This conclusion needs additional studies where the IPC therapy should be applied during the whole time of post-operative lower limb immobilization. By applying IPC treatment during 6 weeks the therapy would impact both the proliferative as well as the regenerative healing phases during immobilization, which could conceivably affect also the patient-reported and functional outcome measures as well as lead to earlier return to activity. These researches stated that whether mechanical compression therapy should be administered as an out-patient treatment for leg-immobilized patients is, with the present and another published study in mind, a matter of both preventing the development of DVT as well as of counteracting the impaired healing associated with immobilization. As for yet, no cost-benefit analysis has been performed, yet the therapy is highly accepted by the patients. They stated that further investigation of the health economics of IPC intervention ought to be conducted to permit an informed decision on implementation at a population level.

Prophylaxis of Venous Thromboembolism in Neurosurgery:

Chibbaro et al (2018) noted that the incidence of VT in neurosurgical practice is astonishingly high, representing a major cause of morbidity and mortality. Prophylaxis strategies include elastic stockings, low-molecular-weight heparin (LMWH), and IPC devices. These investigators evaluated the safety and efficacy of 2 different VT prophylaxis protocols implemented in a European neurosurgical center. All patients admitted for neurosurgical intervention between 2012 and 2016 were stratified as low-, moderate-, and high-risk of VT and received a combination of elastic stockings and LMWH. The protocol was modified in 2014 with the inclusion of peri-operative IPC devices for all patients and only in the high-risk group also post-operatively. At time of post-hoc analysis, data obtained from patients included in this study before 2014 (Protocol A, 3,169 patients) were compared with those obtained after the introduction of IPC (Protocol B, 3,818 patients). Among patients assigned to protocol A, 73 (2.3 %) developed DVT and 28 (0.9 %) developed PE, 9 of which were fatal (0.3 %). Among patients assigned to protocol B, 32 developed DVT (0.8 %) and 7 (0.18 %) developed PE, with 2 eventually resulting in the death of the patient. A post-hoc analysis confirmed that the use of pre-operative LMWH was not associated with a statistically significant greater risk of post-operative bleeding. The authors concluded that this study, despite its limitations of the non-randomized design, appeared to suggest that peri-operative IPC devices are a non-negligible support in the prophylaxis of clinically symptomatic DVT and PE.

Treatment of Upper Extremity Lymphedema Following Surgery:

Moseley et al (2007) noted that secondary arm lymphedema is a chronic and distressing condition which affects a significant number of women who undergo breast cancer treatment. A number of health professional and patient instigated conservative therapies have been developed to help with this condition, but their comparative benefits are not clearly known. This systematic review undertook a broad investigation of commonly instigated conservative therapies for secondary arm lymphedema including; complex physical therapy, manual lymphatic drainage, pneumatic pumps, oral pharmaceuticals, low level laser therapy, compression bandaging and garments, limb exercises and limb elevation. It was found that the more intensive and health professional based therapies, such as complex physical therapy, manual lymphatic drainage, pneumatic pump and laser therapy generally yielded the greater volume reductions, while self-instigated therapies such as compression garment wear, exercises and limb elevation yielded smaller reductions. The authors concluded that all conservative therapies produced improvements in subjective arm symptoms and quality of life issues, where these were measured. Moreover, they stated that despite the identified benefits, there is still the need for large scale, high level clinical trials in this area.

The Canadian Agency for Drugs and Technologies in Health (CADTH)'s guidelines on "Intermittent pneumatic compression devices for the management of lymphedema" (Tran and Argaez, 2017) stated that "There is no cure for lymphedema. The complex decongestive therapy (CDT) is a multimodal therapy, which is recognized as a conservative management of lymphedema and consists of compression therapy (i.e., multilayer bandaging), manual lymphatic drainage (MLD), exercise and skin care. Intermittent pneumatic compression (IPC) can be used in the treatment of lymphedema as an adjunct to CDT, particularly in patients with compromised mobility or physical exercise. Although lymphedema reduces after application, the use of IPC remains controversial due to its adverse effects, including the recurrence of edema due to residual proteins remaining in the interstitial space, and potential lymphatic structure damage due to high pressure application". The guideline also noted that the Japan Lymphedema Study Group "recommended" that "Currently, there is no evidence that IPC decreases the circumferential diameter of limbs with lymphedema (Recommendation grade: D)".

Table: CPT Codes / HCPCS Codes / ICD-10 Codes

Code	Code Description

Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by "+":

Other CPT codes related to the CPB:

29581	Application of multi-layer compression system; leg (below knee), including ankle and foot
29582	thigh and leg, including ankle and foot, when performed

HCPCS codes covered if selection criteria are met:

A4600	Sleeve for intermittent limb compression device, replacement only, each
E0650	Pneumatic compressor; non-segmental home model
E0651	Pneumatic compressor, segmental home model without calibrated gradient pressure
E0652	Pneumatic compressor, segmental home model with calibrated gradient pressure
E0655	Non-segmental pneumatic appliance for use with pneumatic compressor, half arm
E0656	Segmental pneumatic appliance for use with pneumatic compressor, trunk
E0657	Segmental pneumatic appliance for use with pneumatic compressor, chest
E0660	Non-segmental pneumatic appliance for use with pneumatic compressor; full leg
E0665	Non-segmental pneumatic appliance for use with pneumatic compressor, full arm

E0666	Non-segmental pneumatic appliance for use with pneumatic compressor, half leg
E0667	Segmental pneumatic appliance for use with pneumatic compressor, full leg
E0668	Segmental pneumatic appliance for use with pneumatic compressor, full arm
E0669	Segmental pneumatic appliance for use with pneumatic compressor, half leg
E0670	Segmental pneumatic appliance for use with pneumatic compressor, integrated, 2 full legs and trunk
E0671	Segmental gradient pressure pneumatic appliance; full leg
E0672	Segmental gradient pressure pneumatic appliance, full arm
E0673	Segmental gradient pressure pneumatic appliance, half leg
E0675	Pneumatic compression device, high pressure, rapid inflation/deflation cycle, for arterial insufficiency (unilateral or bilateral system)
E0676	Intermittent limb compression device (includes all accessories), not otherwise specified [not covered for single patient use pneumatic compression device]

HCPCS codes not covered for indications listed in the CPB:

E0675	Pneumatic compression device, high pressure, rapid inflation/deflation cycle, for arterial insufficiency (unilateral or bilateral system)

Other HCPCS codes related to the CPB:

A6530 - A6549	Gradient compression stockings

ICD-10 codes covered if selection criteria are met:

I83.001 - I83.229	Varicose veins of lower extremities
I87.311 - I87.319	Chronic venous hypertension (idiopathic) with ulcer
I87.331 - I87.339	Chronic venous hypertension (idiopathic) with ulcer and inflammation
Z74.01	Bed confinement status [covered for members who are bedridden due to trauma, orthopedic surgery, neurosurgery or other circumstances preventing ambulation]

ICD-10 codes not covered for indications listed in the CPB:

G25.81	Restless leg syndrome
I69.098, I69.198, I69.298, I69.398, I69.898, I69.998	Other sequelae of cerebrovascular disease
I70.201 - I70.799	Atherosclerosis
I73.00 - I73.9, I77.70 - I77.79, I79.1 - I79.8	Other peripheral vascular disease
I74.2 - I74.4	Embolism and thrombosis of arteries of the extremities
I99.8	Other disorder of circulatory system[critical limb ischemia]
M62.20 - M62.28	Other disorder of circulatory system[critical limb ischemia]
S52.501A - S52.509A	Unspecified [closed] fracture of the lower end of radius [Dupuytren's fracture]
S86.001A - S86.019S	Injury of Achilles tendon
T79.6xxA - T79.6xxS	Traumatic ischemia of muscle
Z86.73	Personal history of transient ischemic attack (TIA), and cerebral infarction without residual

deficits

The above policy is based on the following references:

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Policy History

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- Review History
- Definitions

Additional Information

- Clinical Policy Bulletin Notes