FACULTY OF MEDICINE AND HEALTH SCIENCES

MATERNAL AND NEONATAL MAGNESEMIA AFTER NEUROPROTECTION

MASTERTHESIS IN MEDICINE

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ABSTRACT

1.1 ENGLISH

Introduction Antenatal magnesium sulphate ($MgSO_4$) has shown to minimize the risk of cerebral palsy in preterm infants. This practice is now widely recommended for women with imminent risk of delivery at less than 32' weeks of gestation.

Objective The aim of this study was to evaluate the influence of antenatal $MgSO_4$ on neonatal serum magnesium (sMg) during the first 15 days of life.

Materials and Methods A retrospective single center study, conducted on neonates (less than 32 weeks' gestation) born in the Ghent University Hospital between January 2012 and December 2015. Comparative analysis between three groups: no antenatal $MgSO_4$ exposure, exposure for neuroprotective intent (NP) and exposure for prevention of eclampsia (PE).

Results The study population consisted out of 307 mothers and 362 neonates. 60 mothers received $MgSO_4$ solely as a neuroprotective agent, 57 were exposed for (pre)-eclampsia.
The median total $MgSO_4$ dose received for NP was 10.02g vs. 62.62g for PE. From day 0 to 3 the neonatal sMg was significantly higher in the neuroprotective group compared to the control group (respectively p <0.001, <0.001, <0.001, 0.007). Furthermore, the PE group had significantly higher levels than the controls from day 0 to 4 (respectively p <0.001, <0.001, <0.001, <0.001, 0.012). Between days 0 and 3 the magnesemia in the NP group was significantly lower compared to the PE group (p <0.001, <0.001, <0.001, 0.002 respectively). None of the neonates receiving magnesium in NP dosage had sMg levels exceeding 2.25 mmol/L, a known boundary for increased neonatal mortality.
During the first 7 days of life the neonatal magnesemia had a statistically significant association with the total maternal $MgSO_4$ dose, irrespective of maternal BMI and neonatal serum creatinine (NP and PE cohorts combined). This association remained detectable during subgroup analysis for only neuroprotective intent in the first 6 days of life. Furthermore, maternal and neonatal magnesemia were associated during the first 8 days, irrespective of gestational age and total parenteral nutrition. Finally, an association between the total maternal $MgSO_4$ dose and maternal magnesemia was detected, whilst correcting for serum creatinine. No subgroup analyses were possible due to limited data.

Conclusion The total $MgSO_4$ dose was associated with neonatal serum magnesium concentrations. This association remained detectable during subgroup analyses for primary intent neuroprotection. Furthermore maternal magnesemia was associated with the total maternal $MgSO_4$ dose and with neonatal magnesemia. However, we should be cautious extrapolating these last results to the subgroup of infusion with primary intent neuroprotection, taking into account the non-reaching of a steady state of this subgroup and the under representation in our study.
Antenatal $MgSO_4$ in neuroprotective dosage seems to be safe in the immediate postnatal period. We therefore question if closely monitoring magnesium dosage and maternal or neonatal serum concentrations is in fact clinically relevant in these cases, taking into account physicians do not extent infusion time beyond protocol.

1.2 NEDERLANDS

Inleiding Prenataal magnesiumsulfaat ($MgSO_4$) heeft een gekend neuroprotectief effect bij vroeggeboorte. Op heden wordt dit gebruik wereldwijd aangeraden bij dreigende vroeggeboorte op minder dan 32 weken zwangerschapsduur.

Doelstelling Het doel van deze studie is om de relatie tussen antenataal $MgSO_4$ en de neonatale magnesiëmie te evalueren gedurende de eerste 15 dagen postnataal.

Methodologie Het gaat om een retrospectieve monocentrische studie, uitgevoerd op neonaten (<32 weken zwangerschapsduur) geboren in het Universitair ziekenhuis Gent tussen januari 2012 en december 2015. Er werd een vergelijkende analyse tussen 3 groepen uitgevoerd: geen prenatale $MgSO_4$ blootstelling, blootstelling voor neuroprotectie (NP), blootstelling voor (pre)-eclampsie (PE).

Resultaten De studiepopulatie bestond uit 307 vrouwen en 362 neonaten. 60 vrouwen kregen $MgSO_4$ met als primair doeleind neuroprotectie, 57 werden blootgesteld in het kader van (pre)-eclampsie. De mediane totaal $MgSO_4$ dosis voor neuroprotectie bedroeg 10.02g versus 62.62g voor (pre)-eclampsie. De neonatale magnesiëmie in de neuroprotectieve groep was statistisch gezien significant hoger dan die van de controlegroep tijdens de eerste 4 levensdagen (dag 0 – 3 respectievelijk p <0.001, <0.001, <0.001, 0.007). Vergeleken met de controles was de magnesiëmie significant hoger in de (pre)-eclampsie groep gedurende de eerste 5 levensdagen (dag 0 – 4 respectievelijk p <0.001, <0.001, <0.001, <0.001, 0.012). Bovendien was de magnesiëmie na neuroprotectieve blootstelling significant lager gedurende de eerste 4 levensdagen dan na blootstelling voor (pre)-eclampsie (dag 0 – 3 respectievelijk p <0.001, <0.001,

<0.001, 0.002). Na neuroprotectieve blootstelling overschreed geen enkele neonatale magnesiëmie 2.25 mmol/L, gelinkt aan hogere neonatale mortaliteit.
De totaal $MgSO_4$ dosis en neonatale magnesiëmie waren statistisch gezien significant geassocieerd tijdens de eerste 7 levensdagen, onafhankelijk van materneel BMI en neonataal creatinine (NP en PE cohorten gezamenlijk). Deze associatie bleef tijdens subgroep analyse voor alleen neuroprotectie detecteerbaar op de eerste 6 levensdagen. Verder werd een associatie tussen materneel en neonataal serum magnesium vastgesteld tijdens de eerste 8 levensdagen, onafhankelijk van zwangerschapsduur en totale parenterale nutritie. Tot slot, was de totaal $MgSO_4$ dosis geassocieerd met het materneel serum magnesium, onafhankelijk van serum creatinine. Subgroep analyses waren niet mogelijk wegens gebrek aan data.

Conclusie Er is een associatie tussen de totale $MgSO_4$ dosis en neonatale magnesiëmie. Deze associatie bleef detecteerbaar tijdens subgroep analyse voor alleen neuroprotectie. Verder bleek de maternale magnesiëmie geassocieerd met totale $MgSO_4$ dosis en met de neonatale magnesiëmie. We zijn echter terughoudend om deze laatste resultaten te extrapoleren naar de subgroep met primaire intentie neuroprotectie, rekening houdend met het niet bereiken van een steady state en de onder representatie in onze studie.
In deze studie bleek antenatale $MgSO_4$ toediening in neuroprotectieve dosis veilig in de directe postnatale periode. We stellen daarom in vraag of het van dichtbij monitoren van magnesium dosages en maternele of neonatale magnesium concentraties klinisch relevant is in deze gevallen, onder voorbehoud dat infusies niet langer dan voorgeschreven worden gecontinueerd.

LIST OF ABBREVIATIONS

CP	Cerebral palsy
$MgSO_4$	Magnesium sulphate
RCT	Randomized controlled trial
Mg	Magnesium
TPN	Total parenteral nutrition
COS	Center for developmental disorders
NP	Antenatal $MgSO_4$ with primary indication neuroprotection
PE	Antenatal $MgSO_4$ with primary indication (pre)-eclampsia
GEE	Generalized estimating equations
ICSI	Intracytoplasmic sperm injection
IVF	In vitro fertilization
IUI	Intrauterine insemination
PPROM	Premature prelabour rupture of membranes
NS	Not significant
IUGR	Intrauterine growth restriction
BMI	Body mass index

INTRODUCTION

Worldwide, approximately 10% of children are born preterm (1,2), ranging from 5% in several European countries to 18% in some African countries. WHO defines preterm birth as any birth before 37 completed weeks of gestation (3). Preterm birth can be further subdivided according to gestational age: moderate or late preterm (≥ 32 - < 37 weeks), very preterm (≥ 28 - < 32 weeks), extremely preterm (< 28 weeks). Although the vast majority of preterm births occur after 32 completed weeks of gestation, nearly 1/10 is born very or extremely preterm (2). According to STATBEL (Belgian statistical office), in 2015, 8.1% (n = 9.724) of the children born alive in Belgium were born preterm, of which 13.2% (n = 1,284) very or extremely preterm.

Infants born preterm, have a higher risk of dying in early life compared to those born at term (4,5). Improvements in neonatal-perinatal medicine have led to a higher survival rate of preterm born children. Although this is a remarkable success, the long-term neurodevelopmental deficits in survivors are increasingly recognized (6,7). Preterm birth is a major risk factor for cerebral palsy (CP), blindness, deafness, lower educational attainment and deficits in cognitive functioning (4, 7). Furthermore, individuals born preterm have higher rates of schizophrenia, autistic spectrum disorders and attention deficit/hyperactivity disorders (8).

Cerebral palsy describes a group of permanent disorders in the development of movement and posture, causing activity limitation, that are attributed to non-progressive disturbances occurring in the developing fetal or infant brain (9). The prevalence remains fairly static at 2-3 per 1000 births (10,11). The gestational age is inversely correlated with the risk of developing CP (11,12).

Due to the low efficiency of current preventive measures for preterm birth, effective therapies to reduce the risk of neurological impairments for preterm survivors are paramount. The mechanisms leading to brain injuries related to preterm birth are numerous and many risk factors may be present before, during and after birth. Since these brain injuries have multifactorial causes, no single neuroprotective intervention is known to prevent them. However, neuroprotective strategies can be adopted to reduce the risks. One of these interventions is antenatal administration of magnesium sulphate ($MgSO_4$) (13).

The association between antenatal $MgSO_4$ exposure and a reduced risk of cerebral palsy was first reported in 1995 (14). Encouraged by this article, several randomized controlled trials were organized, which will be discussed further (15-17). As several meta-analyses confirmed the neuroprotective effect (18-21), widespread use of antenatal $MgSO_4$ infusion for neuroprotection in

women at imminent risk of very preterm birth is nowadays recommended. Current guidelines at the Ghent University Hospital recommend the use of $MgSO_4$ for neuroprotective intent when birth is imminent between 24-26 and 32 weeks of gestation *(Dreigende vroeggeboorte – 24/10/2014 – document number: 2798)*.

MAGNESIUM AS NEUROPROTECTION: THE EVIDENCE

Randomized controlled trials

The association between antenatal exposure to magnesium sulphate and a reduction in the risk of cerebral palsy was first suggested by a case-control study published in 1995 (14). Five randomized controlled trials were organized in the 1990s and 2000s to determine whether antenatal $MgSO_4$ prevents adverse outcomes such as pediatric death and cerebral palsy.

In 2002, the so-called Magnesium and Neurologic Endpoints Trial (MagNET) was published. It ran from 1995 to 1997 in Chicago and enrolled a total of 149 women in preterm labour between 25 and 34 weeks' gestation. The trial contained two treatment arms depending on cervical dilatation; a tocolytic arm (4g loading dose, 2-3 g/h maintenance $MgSO_4$ or other tocolytic) and a neuroprotective arm (4g loading dose $MgSO_4$ without further infusion or placebo) (16). The study stopped prematurely due to a statistically significant higher overall pediatric mortality rate after tocolytic $MgSO_4$ exposure. In conclusion, the MagNET trial did not support the hypothesis of neuroprotective effect, it even showed a trend towards worse health outcomes (22).

A larger RCT was published in 2003, the Australian collaborative Trial of Magnesium Sulphate (ACTOMgSO4). A total of 1062 women (weeks' gestation <30) were enrolled in Australia and New Zealand from 1996 until the year 2000. They either received $MgSO_4$ (4g loading dose, 1g/hour maintenance, for maximum 24 hours) or a placebo.
In the $MgSO_4$ cohort, rates of total pediatric mortality over 2 years (RR 0.83; CI 95% 0.64 – 1.09), cerebral palsy (6.8% vs 8.2%; RR 0.83; CI 95% 0.54 – 1.27) and combined death or cerebral palsy at age 2 years (RR 0.83; CI 95% 0.66 – 1.03) were all lower. However, none of the differences were statistically significant. There was a significant reduction of children with substantial motor dysfunction in the magnesium sulphate group (3.4% vs 6.6%; RR 0.51; CI 95% 0.29 – 0.91) and in the combined outcome of death or substantial motor dysfunction (RR 0.75; CI 95% 0.59 – 0.96). This trial gave some reassurance surrounding the concern of pediatric mortality since mortality was lower in the magnesium group (13.8%) compared to the placebo group (17.1%) (23).

The third trial, PREMAG, was published in 2006. From July 1997 until July 2003, 573 women with a gestational age lower than 33 weeks were enrolled in France. They either received 4g of $MgSO_4$ by infusion or a saline (placebo) infusion. The primary outcomes before hospital discharge were all lower for the $MgSO_4$ group compared to placebo but the differences were not statistically significant; total mortality (OR 0.79; CI 95% 0.44 – 1.44), rate of severe white-matter injury (OR 0.78; CI 95% 0.47 – 1.31) and combined outcome (OR 0.86; CI 95% 0.55 – 1.34) (17).

The BEAM trial was published in 2008. A total of 2241 women at risk for delivery between 24 and 31 weeks of gestation were enrolled in the United States from December 1997 through May 2004. $MgSO_4$ was administered intravenously in a 6g bolus followed by a maintenance dose of 2g per hour for 12 hours. The primary composite outcome (death by 1 year or moderate or severe CP at or beyond 2 years of corrected age) was lower in the $MgSO_4$ group (11.3% to 11.7%; RR 0.97; CI 95% 0.77 – 1.23) but not statistically significant. Magnesium sulphate administration was associated with significant decreased risk of severe or moderate CP (1.9% vs 3.5%; RR 0.55; CI 95% 0.32 – 0.95). This trial confirmed the neuroprotective effect of $MgSO_4$ (15).

A large international trial with the aim to evaluate the impact of antenatal $MgSO_4$ in the prevention of eclampsia included 10.141 women between July 1998 and November 2001. The women were randomly allocated to receive either $MgSO_4$ (4g loading dose, 1g/h maintenance for 24h) or placebo (24). A pediatric follow-up study showed no differences in pediatric neurological outcomes or mortality at 18 months (25).

Evidence concerning the neuroprotective effect of magnesium (Mg) was not compelling enough to recommend widespread use. More so, none of the randomized controlled trials showed a statically significant effect on the composite outcome of death and CP. More evidence was needed, hence several meta-analyses were conducted (26).

Meta-analyses

The 5 previously mentioned randomized controlled trials have been the subject of 4 meta-analyses and 1 individual participant data meta-analysis with consistent findings.

Antenatal $MgSO_4$ infusion, given to women at risk for preterm labour, was associated with a statistically significant reduction in cerebral palsy (all severities included). The relative risk ranged from 0.61 to 0.70 and the number needed to treat to prevent one case of cerebral palsy ranged

between 41 and 74 (table 1). None of the meta-analyses showed an overall significant decrease in the composite outcome death or cerebral palsy (18-21, 27).

	Pediatric mortality[a]	Cerebral palsy[a]	Death or cerebral palsy[a]	Number needed to treat to avoid 1 CP[b]
Doyle et al.	1.04 (0.92–1.17)	0.68 (0.54–0.87)	0.94 (0.78–1.12)	63 (43–155)
Conde-Agudelo and Romero	1.01 (0.89–1.14)	0.69 (0.55–0.88)	1.01 (0.89–1.14)	74 (41–373)
Costantine et al.	1.01 (0.89–1.14)	0.7 (0.55–0.89)	0.92 (0.83–1.03)	Before 30 WG: 46 (26–187) Between 32 and 34 WG: 56 (34–164)
Zeng et al.	0.92 (0.77–1.11)	0.61 (0.42–0.89) (moderate to severe CP)	N/A	N/A
Crowther et al. (IPD meta-analysis)	1.03 (0.91–1.17)	0.68 (0.54–0.87)	0.86 (0.75–0.99)	46 (CI not shown)

[a]*Relative risk (95% CI).*
[b]*Number needed to treat (95% CI).*
CP, cerebral palsy; CI, confidence interval; IPD, individual participant data.

Table 1. Main outcomes of the meta-analyses (13).

However, when only studies for neuroprotective intent were included, prenatal $MgSO_4$ administration does show a significant reduction in the combined outcome of death or cerebral palsy (19,20,27). Higher rates of minor maternal side effects were detected in the $MgSO_4$ group (i.a. nausea, vomiting, sweating, flushing), but no significant association between $MgSO_4$ and major maternal complications was established (i.a. death, cardiac or respiratory arrest) (18,20,21,27). $MgSO_4$ treatment had no impact on the risk of total pediatric mortality (18-21,27) or neonatal morbidity (i.a., respiratory distress syndrome, low apgar score, convulsions, hypotonia, chronic lung disease) (18,20,25,27).

The neuroprotective benefit varied little by gestational age, cause of prematurity, total received dose or whether maintenance dose was used (27). This supports the use of the smallest effective dose (4g loading dose, 1g/h maintenance), as high doses may be associated with more adverse effects (13,27). The evidence was compelling enough for the WHO to advice the widespread use of antenatal magnesium sulphate for fetal neuroprotection in 2014 (27,28).

Long-term outcomes

Following the introduction of neuroprotection with $MgSO_4$ in clinical practice, monitoring of the long-term effects was mandatory.

Cohorts of the ACTOMgSO4 and PREMAG trials were followed throughout their school-age years. From the ACTOMgSO4 trial, 669 children were assessed at the mean age of 8.4±1.0 years. Antenatal $MgSO_4$ had no impact on neurological, cognitive, behavioural, growth or functional outcomes (29).

For the PREMAG trial 431 children were assessed) by a parentally completed questionnaire at a mean age of 11 years (range 7 – 14). The rates of at least one motor or cognitive impairment (including CP), behavioural disorder, and death were lower in the $MgSO_4$ group; however, not statistically significant.

The lack of statistical significant benefits at school age in these 2 trials does not negate the proven effect of $MgSO_4$ based on the collective evidence from all RCT's. Additional studies with larger cohorts are needed (30).

Possible mechanisms of action

In the central nervous system, magnesium is a non-competitive blocker of the N-methyl-D-aspartate glutamate receptor and modulates calcium influx. In that way magnesium prevents excitotoxic calcium induced brain injury and may reduce activation of apoptosis (31). In addition, it inhibits ischemia-induced glutamate release, again reducing excitotoxity (32). Magnesium also has anti-inflammatory properties. It reduces oxidative stress and reduces the production of pro-inflammatory cytokines interleukin-6 and tumor necrosis factor-α (33,34).

NEONATAL MAGNESEMIA

Meta-analyses showed no adverse effect of antenatal $MgSO_4$ for neuroprotective intent on pediatric mortality, nonetheless concerns were raised. In literature several studies suggest increased neonatal morbidity and mortality beyond certain neonatal serum magnesium (sMg) levels (35-37). Hence, it is indispensable to know the normal neonatal sMg concentrations and how they are influenced by antenatal $MgSO_4$ infusion.

Normal neonatal serum magnesium

Mg Reference values in adults are well defined (0.75 mmol/L; 95% CI 0.45 – 1.05) (38). In contrast, reference values in infants are more difficult to pinpoint due to the limited amount of studies evaluating concentrations in healthy term and preterm infants without antenatal magnesium exposure. For preterm neonates, some data is available from control groups in studies evaluating the effect of antenatal magnesium for tocolysis, pre-eclampsia or neuroprotection. A meta-analysis by Rigo et al. established a mean estimated umbilical cord magnesium concentration at birth of 0.76 mmol/L (n= 2766; 95% CI 0.52 – 0.99). Furthermore, the analyses revealed a mean sMg estimate of 0.88 mmol/L (n= 993; 95% CI 0.46 – 1.30) during the first week of life. This suggests that infants without antenatal magnesium exposure have increasing sMg levels during the first week of life. Afterwards the level decreases to normal adult levels (39).

Noon et al. examined serum magnesium in extreme low birth weight infants. Mean sMg ranged from 0.9 to 1.1 mmol/L over the first 7 days. There was a rise in sMg during the first week of life. Magnesium then stabilized towards the end of the week and remained relatively unchanged thereafter for the first month. Hypermagnesemia was uncommon and generally associated with acute kidney insufficiency (40).

Neonatal sMg after antenatal $MgSO_4$ exposure

Retrospectively, Basu et al. compared neonatal magnesium levels in very preterm infants with or without exposure to neuroprotection within the first 24 hours of life (6g loading dose, 2g/h maintenance). Statistically significant different mean sMg concentrations were detected (1.75 ± 0.5 vs 1.10 ± 0.3 mmol/L respectively; $p \leq .001$). The exposed neonates were stratified into four groups according to sMg, results are shown in table 2 (35).

Table 2**. Neonatal serum magnesium during first day of life**

Basu et al.				
sMg (mmol/L)	**<1.25**	**≥1.25 - <1.75**	**≥1.75 - <2.25**	**≥2.25**
N (total = 289)	60 (20.8%)	86 (29.8 %)	84 (29.1%)	59 (20.4%)
Mean sMg (mmol/L)	1.05 ± 0.1	1.45 ± 0.15	2 ± 0.15	2.45 ± 0.5
Garcia et al.				
sMg (mmol/L)	**<1.03**	**≥1.03 - <1.44**		**≥1.44**
N (total = 62)	27 (43.5 %)	29 (46.8 %)		6 (9.7%)
Mean sMg (mmol/L)	0.94 ± 0.08	1.15 ± 0.08		1.56 ± 0.08

Garcia et al. likewise confirmed significantly higher sMg levels in neonates exposed to antenatal magnesium for neuroprotective intent (4g loading dose, 1 g/h maintenance). The mean concentration was 1.10 mmol/L ± 0.21 during the first day of life in exposed infants compared to 0.79 ± 0.08 mmol/L in those not exposed. On the second day, mean sMg was 1.07 ± 0.14 mmol/L after neuroprotection versus 0.96 ± 0.16 mmol/L in the non-exposed group. Even neonates only receiving the loading bolus due to the imminence of delivery, had significant higher sMg levels than non-exposed neonates (41).

Lastly, a meta-analysis by Rigo et al. containing six studies with term and preterm infants, revealed a mean magnesium concentration at birth of 1.29 mmol/L (95% CI 0.50 - 2.08) in umbilical cord blood in exposed neonates for neuroprotection, pregnancy induced hypertension or pre-eclampsia. The mean sMg in exposed neonates at 24 hours was 1.46 mmol/L (95% CI 0.634 – 2.28) (39).

We conclude that serum magnesium levels in neonates exposed to antenatal $sMgO_4$ are higher compared to non-exposed children in the early stages of life. This seems to be true for term and preterm born children.

Postpartum factors contributing to neonatal sMg

After birth many factors influence neonatal sMg concentrations including postnatal magnesium intake, renal function, gestational age at birth and birth weight. Parenteral nutrition, given in the majority of very and extremely preterm infants, is one form of postnatal magnesium supplementation (39). Postnatal magnesium can also be administered as treatment for pulmonary hypertension (42). The neonatal renal function plays a key role in the rapidly changing sMg levels during the first days of life. In preterm neonates renal immaturity is observed at birth, causing a quick rise in sMg. The renal function improves progressively during the first weeks of life (43).

Elevated neonatal sMg post $MgSO_4$ exposure and short-term neonatal outcome

Magnesium is a smooth muscle relaxant (44), which in high concentrations can be toxic for the mother. For example, the patellar reflex disappears if sMg reaches 4.0 mmol/L due to non-competitive antagonism of calcium ions at the neuromuscular junction. The fetal-neonatal effects of prenatal magnesium are less clear (45,46). Early case reports suggested that antenatal magnesium exposure might induce neuromuscular blockade in the infants manifesting as respiratory depression, hypotonia and hyporeflexia (47). Subsequently small series failed to demonstrate this deleterious effect, primary indication pre-eclampsia (4g loading dose, 1g/h maintenance infusion) (48). However, Abbassi-Ghanavati et al. suggested a relationship between neonatal complications (hypotonia, low Apgar scores …) and increased maternal sMg (46).

The MagNET trial evaluated the relationship between the extent of magnesium exposure, measured by the umbilical cord serum ionized Mg at delivery, and adverse health outcomes (neonatal intraventricular hemorrhage, periventricular leucomalacia, death and cerebral palsy). Children with adverse health outcomes had a median umbilical cord Mg level of 0.685 mmol/L, which was 25% higher compared to those without any adverse outcomes (0.55 mmol/L). These differences were statically significant (n = 82, p = 0.03) (16). However, the ionized magnesium concentration is poorly related to the total Mg content and more related to acidosis (39,49).

This was confirmed by a retrospective study by Basu et al. (loading dose 6g, followed by 2g/h maintenance). However, when the exposed neonates were stratified into four groups according to neonatal sMg (table 2), the following was observed: preterm neonates born with a sMg of ≥ 2.25 mmol/L during the first 24 hours of life had an increased mortality rate, whilst correcting for their

gestational age, birth weight or other comorbidities, in comparison to neonates with a sMg of less than 1.25 mmol/L. The difference was not significant between the group of ≥2.25 mmol/L and neonates from groups ≥1.25 to <1.75 mmol/L and ≥1.75 to <2.25 mmol/L. The exposed neonates had higher incidences of prematurity retinopathy, presence of patent ductus arteriosus, greater time to reach full feeds and an increased length of stay. These findings were no longer significant when corrected for gestational age and birth weight. No differences in any other early morbidities were found (35).

Garcia et al. (loading dose 4g, maintenance 1g/h, GA <32 weeks) showed higher incidences of neonatal resuscitation, surfactant doses, bronchopulmonary dysplasia and retinopathy of prematurity in infants exposed to magnesium for neuroprotective intent. However, none of these differences were statistically significant. Furthermore, a trend towards more adverse outcomes with increasing sMg was seen, again statistically insignificant (41). Coinciding Johnson et al. did not demonstrate an association between the cord blood Mg concentration and the need for neonatal resuscitation when exposed to antenatal $MgSO_4$ for neuroprotective intent (50).

Lastly a study by Morag et al. (loading dose 5g, maintenance 2g/h) did not reveal an increased risk of early neonatal morbidities among infants whose sMg exceeded 1.44 mmol/L compared to those with lower concentrations (51).

Elevated neonatal sMg post $MgSO_4$ exposure and long-term neonatal outcome

Morag et al. also examined long-term outcome. The neurodevelopmental assessment (Griffiths Mental Development Scales) took place at a mean corrected age of 6 months (range 3 – 12) and was available for 79 out of 145 children. Although developmental scores were within norms in both groups, infants with elevated sMg (> 1.44 mmol/L) scored significantly lower on locomotor and personal-social subscales compared to those with lower concentrations, even after correction for known risk factors of adverse neurodevelopmental outcomes (51).

Total maternal $MgSO_4$ dose – maternal sMg – neonatal sMg

As demonstrated above, maternal $MgSO_4$ administration influences neonatal sMg. Hence, to keep neonatal sMg at safe and effective levels it's key to gain insight in the relationship between $MgSO_4$ dosage, maternal sMg and neonatal sMg.

Few studies investigated this relationship for $MgSO_4$ solely used as neuroprotection. A retrospective study by Borja et al., excluding pre-eclamptic women, documented a correlation between the total maternal magnesium dose at 24 and 48 hours of infusion and neonatal sMg (Pearson's correlation; r = 0.55 (p < .001) and r = 0.35 (p < .001) respectively). No correlation

between maternal and neonatal sMg was found, nor between maternal sMg and the total maternal dose. However the majority of mothers delivered within 24 hours after the initiation of infusion. Therefore a steady state in maternal sMg was never reached, possibly explaining the lack of correlation (52). A prospective cohort study, by Garcia et al. (GA < 32w, (pre)-eclampsia included), likewise established a significant linear correlation between the total maternal dose and neonatal sMg during the first 24 hours of life ($r^2 = 0.379$; $p < .001$) (41).

OPTIMAL THERAPEUTIC MATERNAL MAGNESIUM EXPOSURE

Randomized controlled trials evaluating magnesium as neuroprotection all used different dosing regimens. Therefore, there is a lack of consensus with regard to dosing, duration of infusion and safety.

Optimal magnesium dosage

A cohort analysis by McPherson et al. evaluated the association between the duration of infusion, and therefore cumulative dose, with death or CP. The composite outcome (death or CP) occurred in 11.7% of women receiving magnesium less than 12 hours, in 10.3% of those who received 12-18 hours of infusion and in 8.8% of women who received it for more than 18 hours. The declining trend in risk of composite outcome was not significantly different amongst groups (< 12 hours as reference), neither for the risk of CP or death alone. The duration of the neuroprotective infusion was not associated with the risk of any other neonatal morbidity or maternal adverse drug events. Hence, the optimal treatment duration for neuroprotection remained unknown (36).

Another study using a pharmacokinetic model on the BEAM cohort simulated that 64g (95%CI 30 – 98g) was the total administered magnesium dose associated with the lowest probability of delivering an infant with cerebral palsy. Their model suggested a higher risk reduction of CP with increasing total doses of $MgSO_4$. They argued that the only trial not detecting a significant neuroprotective effect was the one using the lowest dosing (PREMAG: only 4g loading dose (53).

The individual participant data meta-analysis by Crowther et al. showed no obvious linear trends between higher $MgSO_4$ dosing and any of the major outcomes (CP or death, CP, death, death or major neurosensory disability). Nor was there a difference in treatment effects whether maintenance therapy was given or not. They suggested, with maternal side effects increasing with higher total doses, at a clinical level it might be best to minimize the dose of magnesium to a 4 g bolus loading dose with or without maintenance dose of 1 g/hour (27).

Timing of $MgSO_4$ administration

Research into the association of time from last exposure to magnesium and CP showed that exposure more proximal to delivery (< 12 hours) is associated with lower risk of CP compared to exposure longer than 12 hours before (2.3% vs 4.4%; OR 0.41; 95% CI 0.18 – 0.91). No difference in the outcomes (composite outcome of moderate or severe CP and death, moderate or severe CP) was shown. This could imply a need of retreatment if delivery does not occur after initial administration (54). However, no obvious linear trend for any major outcome was seen when categorizing according to time between the start of infusion and birth (27).

Maternal magnesium concentration: the target

Recent meta-analysis, including data of 2395 mothers, estimated the mean sMg in healthy pregnant women without any magnesium supplementation, around 0.74 mmol/l (95% CI; 0.43 – 1.04) at the time of delivery. The range for non-pregnant healthy adults, including men, is 0.75-0.95 mmol/L (39).

Using a pharmacokinetic model that predicts maternal sMg, based on a prescribed dose of $MgSO_4$ administered over a specific duration of time, the optimal maternal sMg to prevent CP was estimated. They determined that the sMg in women who did not receive magnesium was 0.74 mmol/L, coinciding with the previous cited study. Furthermore simulation showed that a maternal sMg of 1.69 mmol/l (95% CI 1.52 – 1.81) was associated with the lowest probability of delivering an infant with CP (53). This concentration could be achieved after 5.5 hours of infusion in average weight women (4g bolus, maintenance 2g/h) (55).

COST-EFFECTIVENESS

The lifetime cost of CP was estimated at 800 000 euros for women and 860 000 euro for men in Denmark (56). Another economic evaluation showed that the cost of preventing one case of cerebral palsy with magnesium would be 10 291 dollar (9 050 €) (18). Several studies evaluating the cost-effectiveness of neuroprotective magnesium for all women at risk of preterm birth with less than 32 weeks' of gestation, concluded that it is a dominant (i.e. cost-effective) strategy. This means that it is less costly and more effective compared to alternatives of no treatment (57, 58).

AIM OF THIS MASTERTHESIS

Antenatal $MgSO_4$ administration for neuroprotection has recently been introduced into clinical practice. Previous research established higher neonatal sMg after exposure. We aim to describe the evolution of neonatal sMg during the first 15 days of life, whether neonatal sMg levels differ

according to primary indication for $MgSO_4$, and whether unsafe sMg levels are reached in our population. Furthermore we'll explore the relationship between the total maternal dose and neonatal sMg.

Research questions

Part 1: Descriptive analysis of the database and analysis neonatal/maternal serum magnesium

A. Characteristics of the study population
B. Maternal magnesium sulphate infusion: number of courses and duration
C. Maternal pre-delivery serum magnesium
D. Neonatal serum magnesium during the first 15 days of life
E. Neonatal outcomes

Part 2: Association between neonatal magnesemia – magnesium sulphate dosage - maternal magnesemia

A. Association between the total maternal MgSO4 dose and neonatal magnesemia during the first 15 days of life
B. Association between the prepartal maternal magnesemia and neonatal magnesemia during the first 15 days of life
C. Association between the total maternal $MgSO_4$ dose and prepartal maternal magnesemia

MATERIALS AND METHODS

METHODOLOGY LITERATURE STUDY

To find relevant published literature, two searches in PubMed were conducted 1) ("Neurodevelopmental Disorders"[Mesh] OR "Cerebral Palsy"[Mesh] OR "Motor Skill Disorders"[Mesh] OR "Neurodevelopmental Disorders"[All Fields] OR "cerebral palsy"[All Fields] OR "motor skill disorders"[All Fields] OR ("cerebral"[All Fields] AND "palsy"[All Fields])) AND ("premature birth"[MeSH] OR ("premature"[All Fields] AND "birth"[All Fields]) OR "premature birth"[All Fields] OR ("premature"[All Fields] AND ("parturition"[Mesh] OR "parturition"[All Fields] OR "birth"[All Fields]))) AND ("neuroprotection"[Mesh Terms] OR "neuroprotection"[All Fields] OR "magnesium sulphate"[Mesh] OR "magnesium sulphate"[All Fields]) and 2) neonatal serum magnesium neuroprotection. The Web of science database was searched for: 'neonatal serum magnesium neuroprotection'. In total 140 articles were identified. Articles were selected based on their language, journal impact factor and relevance to the topic. By using snowball method, 39 articles were added. Two articles were provided by the promotor. Out of a total of 173 articles, 63 were retained (attachment 1: Prisma).

STUDY DESIGN

This dissertation is a retrospective single-institution study at the Ghent University Hospital. The required data was collected from electronic patient files (EPD) and obstetrical files (MOSOS) in the department of obstetrics and gynaecology. The study was approved on 3/05/2017 by the Medical Ethics Committee of Ghent University Hospital with registration number B670201732319.

In 2016 the database on preterm birth was created, using a wide variety of variables (attachment 2: codebook). Mothers in preterm delivery, between 24+0 and 31+6 weeks' gestation, in Ghent University Hospital from January 2012 until December 2015 were included in the study. Patients with major congenital disorders with influence on neonatal parameters, intra-uterine death at admission and neonates born in other hospitals were excluded. Because of low numbers, triplets were excluded.

Additional data was collected for this dissertation: maternal serum magnesium (mmol/L) closest to delivery (with exclusion of values more than 24 hours before), maternal creatinine (mg/dl), neonatal sMg (day 0 - 14), sodium (Na), chloride (Cl), calcium (Ca), phosphorous (P), urea and creatinine

(for pragmatic reasons, if multiple blood draws were available, the first lab result of the day reporting neonatal sMg was used), days of TPN administration and postnatal neonatal magnesium administration.

Women receiving $MgSO_4$ were identified together with their primary indication for administration: prevention of eclampsia or neuroprotection. Our study cohort only contains very and extremely preterm deliveries. Patients receiving $MgSO_4$ with pre-eclampsia as primary indication therefore belong by definition also to the neuroprotective group.

The treatment protocol for preterm labour in Ghent University Hospital can be found in attachment 3. The protocol prescribes a loading dose of 4 grams $MgSO_4$ administered over 15-20 minutes, followed by a maintenance dose of 1-1.5 g/h. $MgSO_4$ for neuroprotection is to be stopped after 24 hours if delivery has not yet occurred and is no longer considered imminent. Magnesium is to be restarted when imminent delivery reoccurs. For the prevention of eclampsia, the magnesium infusion is in general continued until delivery and beyond. The start date and –time of infusion was collected, as well as the duration. Based on the duration and concentration, the total maternal dose (g) was calculated. If multiple courses were given, the total maternal dose was the summation of all courses. Mothers with an infusion interruption longer than 4 hours were excluded.

In our center, very and extremely preterm born infants often receive total parenteral nutrition (TPN). The protocol (attachment 4) prescribes an increasing dosage during the first 5 days of life; 80, 100, 120,140, 160 ml/kg/24h respectively. Parenteral nutrition consists out of a combination of glucose, amino acid and lipid solution; of which the glucose solution contains magnesium (0.20 mmol/100ml). The sMg reference value in our center is: 0.7 - 1.05 mmol/L, without discrimination in age.

Follow up by the center for developmental disorders (COS) is indicated for preterm infants born before 2015 with a gestational age of less than 30 weeks and/or a birth weight lower than 1250 grams and for neonates born in 2015 with a gestational age below 32 weeks and/or a birth weight less than 1500 grams. Four follow-ups are scheduled, on the 4^{th} month, the 10^{th}, at 2 years and lastly at the age of 4 years.

STATISTICAL ANALYSIS

Data analysis was performed using the statistical software package SPSS (version 25.0).

Part 1

Parametric continuous variables were presented as mean values with a standard deviation and analyzed with one-way analysis of variance. Non-parametric continuous variables were reported as median values with an interquartile range and analyzed with the Kruskal Wallis test. Frequencies of categorical variables are reported and the Chi-square, or if necessary Fisher's exact, test is used. Differences between the three groups in which our population was divided were explored: controls (no antenatal magnesium), NP (Antenatal $MgSO_4$ with primary indication neuroprotection) and PE (Antenatal $MgSO_4$ with primary indication (pre)-eclampsia). In our population 18.3% were twins. Generalized estimating equations (GEE) were used to take the non-independency of twins into account. In case of multiple testing, the Bonferroni correction was applied.

Part 2

Generalized linear models (using GEE) were constructed to determine the magnitude of the association between the total antenatal $MgSO_4$ dosage, maternal magnesemia and the neonatal sMg from day 0 to 14.

Candidate covariates associated with the variability in neonatal serum magnesium were identified in literature. Consequently, a stepwise selection process was used with the alpha-to-enter and alpha-to-remove set at 0.05. The association, between the following maternal and neonatal covariates/factors and neonatal sMg, was explored on days 0, 7 and 14: maternal serum creatinine, neonatal serum creatinine, gestational age at delivery, birth weight, pregestational body mass index (BMI), postnatal magnesium administration through total parenteral nutrition (TPN) and the presence of pre-eclampsia. Each variable found to be significantly associated with neonatal sMg in one of the models (days 0, 7 or 14) was included in the final model. Both maternal pre-delivery creatinine and neonatal creatinine on day 0 were available in our dataset. The association between these variables was studied ($r^2 = 0.901$; $p < 0.001$). Several associations will be explored during the first 15 days of life. The neonatal serum creatinine is known for all 15 days in contrast to only one maternal pre-delivery creatinine value. Therefore, in order to be more consistent we prefer using the neonatal serum creatinine in our model over maternal serum creatinine on day 0.

The association between total antenatal $MgSO_4$ dosage and neonatal magnesemia was graphically explored. As the data did not follow a normal distribution, a log transformation was performed on the dependent variable and independent variable total antenatal $MgSO_4$ (non-log transformed graphs consultable in attachment 5). To investigate the association between maternal and neonatal magnesemia, no log transformation was needed. Finally, the association between total antenatal $MgSO_4$ dosage and pre-partal maternal magnesemia was examined, again a log transformation was performed. The result, after back transforming mean logarithmic values to the original scale, is the geometric mean.

STUDENT'S CONTRIBUTION

The student completed the previously designed preterm database of Celien Van Poeck and Dr. I Dehaene together with another dissertation student Florien Casteels. Statistical analyses was performed by the student, guided by 'Cel Biostatistics' of the faculty of Medical and Health sciences, Ghent University. Writing was performed by the student, guided by Prof. Dr. K. Roelens, Dr. I. Dehaene and Dr. K. De Coen.

RESULTS

PART 1: DESCRIPTIVE ANALYSIS OF THE DATABASE AND MATERNAL/NEONATAL SERUM MAGNESIUM

Characteristics of the study population

The study population contained 307 mothers. We divided the cohort into 3 groups: mothers who did not receive magnesium (controls), mothers receiving $MgSO_4$ for neuroprotection (NP) and mothers who received magnesium for prevention of eclampsia (PE). Respectively 190, 60 and 57 women were categorized into these groups.

In our cohort 86% of the patients were transferred from another hospital. Maternal demographics are provided in table 3. Most women were Caucasian (80.1%) and obtained a secondary degree or higher. The mean maternal age was a little over 30 years (30.3 ± 5.3 years). The majority had a normal BMI before pregnancy (57%), however more than one third was overweight. In our study cohort nearly 60% was primipara and approximately 80% of pregnancies were spontaneously conceived. The vast majority of parous women did not have any history of preterm birth. Nearly 78% of mothers never smoked while 16.3% smoked during the whole pregnancy. Alcohol or drug abuse was minimal.

Pre-pregnancy and pre-delivery BMI were significantly different between the three groups. A trend towards higher pre-pregnancy BMI was seen in the PE group compared to the others. Before delivery 56.3% of pre-eclamptic women with known BMI were classified as obese compared to respectively 13.4 and 23.8% in the control and NP group. None of the other maternal demographics in table 3 showed statistically significant differences.

Table 3. **Maternal demographics**[a]

	All mothers (307)	Control (190)	NP (60)	PE (57)	*p*-value
Maternal age (years)					.702[b]
- **Mean (± SD)**	30.3 (5.3)	30.4 (5.2)	29.8 (6.0)	30.4 (4.9)	
- Min – max	16 - 44	16 - 41	16 - 43	17 - 44	
BMI pre-pregnancy					.009[c]
- **Underweight (<18.5)**	18 (5.9)	8 (4.2)	6 (10.0)	4 (7.0)	
- Normal (18.5 – 24.9)	175 (57.0)	120 (63.2)	33 (55.0)	22 (38.6)	
- Overweight (25 – 29.9)	74 (24.1)	45 (23.7)	12 (20.0)	17 (29.8)	

- Obesity (>30)	40 (13.0)	17 (8.9)	9 (15.0)	14 (24.6)	
BMI before delivery					<.001[c]
- Normal (18.5 – 24.9)	89 (29.0)	67 (35.3)	16 (26.7)	6 (10.5)	
- Overweight (25 – 29.9)	106 (34.5)	75 (39.5)	16 (26.7)	15 (26.3)	
- Obesity (>30)	59 (19.2)	22 (11.6)	10 (16.7)	27 (47.4)	
- Missing	53 (17.3)	26 (13.7)	18 (30.0)	9 (15.8)	
Education					.352[d]
- No education	2 (0.7)	2 (1.1)	0	0	
- Primary	6 (2.0)	6 (3.2)	0	0	
- Secondary	51 (16.6)	34 (17.9)	8 (13.3)	9 (15.8)	
- Bachelor	55 (17.9)	32 (16.8)	11 (18.3)	12 (21.1)	
- Master	43 (14.0)	19 (10.0)	13 (21.7)	11 (19.3)	
- Missing	150 (48.9)	97 (51.1)	28 (46.7)	25 (43.9)	
Race					.203[d]
- Caucasian	246 (80.1)	153 (80.5)	45 (75)	48 (84.2)	
- Black	9 (2.9)	6 (3.2)	1 (1.7)	2 (3.5)	
- Asian	17 (5.5)	10 (5.3)	7 (11.7)	0	
- Other	35 (11.4)	21 (11.1)	7 (11.7)	7 (12.3)	
Parity					.682[c]
- 0	181 (59.0)	107 (56.3)	39 (65.0)	35 (61.4)	
- 1	71 (23.1)	48 (25.3)	10 (16.7)	13 (22.8)	
- ≥2	55 (17.9)	35 (18.4)	11 (18.3)	9 (15.7)	
Fertility treatment					.273[d]
- None	241 (78.5)	150 (78.9)	45 (75.0)	46 (80.7)	
- ICSI/IVF[e]	46 (15.0)	31 (16.3)	9 (15.0)	6 (10.5)	
- Ovulation induction	12 (3.9)	7 (3.7)	2 (3.3)	3 (5.3)	
- Donor egg	2 (0.7)	0	1 (1.7)	1 (1.8)	
- IUI[f]	6 (2.0)	2 (1.1)	3 (5.0)	1 (1.8)	
Previous preterm delivery[g]					.442[d]
- 0	78 (61.9)	53 (63.8)	11 (52.3)	14 (63.6)	
- 1	42 (33.3)	26 (31.3)	8 (38.1)	8 (36.4)	
- >1	6 (4.7)	4 (4.8)	2 (9.5)	0	
Smoking					.319[d]
- Never smoked	239 (77.9)	147 (77.4)	49 (81.7)	43 (75.4)	
- Stopped smoking[h]	18 (5.9)	8 (4.2)	4 (6.7)	6 (10.5)	
- Smoked whole pregnancy	50 (16.3)	35 (18.4)	7 (11.7)	8 (14.0)	
Alcohol use during pregnancy					.995[d]

- None	256 (83.4)	157 (82.6)	50 (83.3)	49 (86.0)	
- Yes	4 (1.3)	3 (1.6)	1 (1.7)	0	
- Missing	47 (15.3)	30 (15.8)	9 (15.0)	8 (14.0)	
Drug use during pregnancy					.801[c]
- None	250 (81.4)	152 (80.0)	49 (81.7)	49 (86.0)	
- Yes[i]	1 (0.3)	1 (0.5)	0	0	
- Missing	56 (18.2)	37 (19.5)	11 (18.3)	8 (14.0)	

[a]Data are represented as n(%) unless otherwise mentioned [b]One-way ANOVA [c]Chi-squared test [d]Fisher's exact test [e]Intracytoplasmic sperm injection and in vitro fertilization [f]Intrauterine insemination [g]Non primipara [h]Stopped smoking before or during pregnancy [i]Cannabis

The Flemish consensus on periviability is not to start active perinatal management before 24 weeks' gestation. Between the gestational age of 24+0 and 25+6w parents are given the chance to choose for obstetrical and neonatal active management after counseling by an obstetrician and neonatologist. Starting from 26 weeks, all children receive active management. In further analyses, we will only take into account cases where active management was undertaken. 15 neonates were excluded and a new total of 295 mothers and 347 neonates was reached (53 twin pregnancies). 59 mothers received antenatal magnesium sulphate as neuroprotection, 57 for prevention of eclampsia and 179 belonged to the control group.

Obstetrical characteristics are presented in table 4. The study population contained 53 (18.0%) twins with 2 interval-deliveries (postponed birth of the second twin). In one twin pregnancy, an intra-uterine death of one member occurred. Premature prelabour rupture of membranes (PPROM) was the most common reason for admission (35.3%), followed by spontaneous preterm labour (32.5%). Approximately one fourth (26.4%) was admitted due to pre-eclampsia or growth restriction and 4.4% presented with placenta praevia. The number of twins did not significantly differ between groups.

Table 4. **Obstetrical characteristics per mother[a]**

	Total (295)	Control (179)	NP (59)	PE (57)
Number of fetuses				
- Singletons	242 (82.0)	143 (79.8)	47 (79.7)	52 (91.2)
- Twins	53 (18.0)	36 (20.1)	12 (20.3)	5 (8.8)
Antenatal treatment				
- Tocolysis	196 (66.4)	136 (76.0)	57 (96.6)	3 (5.3)
- Corticosteroids	276 (93.6)	165 (92.2)	57 (96.6)	54 (94.7)

- Antibiotics[b]	143 (48.5)	96 (53.6)	39 (66.1)	8 (14.0)

[a]Data are represented as n(%) [b] Not GBS or perioperative prophylaxis

As concerns birth characteristics, presented in table 5, the vast majority (77.2%) of our study population was born very preterm, 22.8% was born extremely preterm. Approximately 51% of neonates were male and 56.4% of deliveries were caesarean sections. This rate was significantly higher in the PE group (96.8%) compared to the control (55.6%) and NP group (23.2%). Furthermore the rate of cesareans was significantly lower in the NP group compared to the control subjects. Median birth weight was 1280 grams. The PE cohort had a significantly lower birth weight and higher presence of intrauterine growth restriction compared to the other groups.

Table 5**. Birth characteristics[a]**

	All infants (347)	Control (216)	NP (69)	PE (62)	*p*-value
Gender (males)	178 (51.3)	116 (53.7)	34 (49.3)	28 (45.2)	NS[b]
Gestational age					NS
- Extreme preterm	79 (22.8)	43 (19.9)	22 (31.9)	14 (22.6)	
- Very preterm	268 (77.2)	173 (80.1)	47 (68.1)	48 (77.4)	
Modus partus (1 missing)					≠[c]
- Vaginal birth	151 (43.5)	96 (44.4)	53 (76.8)	2 (3.2)	
- Caesarean	195 (56.2)	120 (55.6)	16 (23.2)	60 (96.8)	
Birth weight (g)					≠[d]
- Median	1280	1363	1250	973	
- IQR	980 - 1540	1081 - 1574	848 - 1627	776 - 1253	
IUGR[e] (1 missing)	42 (12.1)	16 (7.4)	1 (1.4)	25 (40.3)	≠[f]
Meconium (25 missing)	21 (6.1)	13 (6.0)	4 (5.8)	4 (6.5)	NS

[a]Data are represented as n(%) unless otherwise mentioned [b]NS: Not significant [c]C vs NP (p <.001), C vs PE (p <.001), NP vs PE (p <.001) [d]C vs PE (p <.001), NP vs PE (p =.003), C vs NP (NS) [e]IUGR: intrauterine growth restriction [f]C vs PE (p <.001), NP vs PE (p <.001), C vs NP (NS)

None of the lifeborn infants received postnatal magnesium for medical purposes. Table 6 provides the duration that the infants received TPN containing magnesium. Most neonates received TPN longer than 14 days. Only one infant received none due to mortality on the first day of life. Relative frequencies show a longer duration of TPN administration in the PE group, however no statistically significant differences between the three groups were detected.

Table 6**. Total parenteral nutrition in lifeborn infants**

	Control (216)	NP (68)	PE (58)

None	1 (0.5)	0	0
1 - 7 days	14 (6.5)	3 (4.4)	2 (3.4)
8 - 13 days	75 (34.7)	23 (33.8)	11 (19.0)
≥ 14 days	124 (57.4)	37 (54.4)	44 (75.9)
Missing	2 (0.9)	5 (7.4)	1 (1.7)

Maternal magnesium sulphate infusion: number of courses and duration

59 mothers (20%) received $MgSO_4$ primarily for neuroprotective purposes. The number of neuroprotective infusion courses alongside with their duration is presented in table 7. Three women received two courses and one received four (interval-delivery). Although the protocol dictates a maximum of 24 hours of infusion, 11 (18.6%) women's first infusion continued beyond 24 hours.

Table 7. **Courses of neuroprotection**

	Number (n(%))	Duration (minutes)		
		Median	IQR	Min - max
First course	59 (100)	381	133 – 1168	39 - 3023
Second course	4 (6.8)	231	163 – 716	157 – 861
Third course	1 (1.7)	2040		
Fourth course	1 (1.7)	1100		

Table 8 provides us with the total duration of infusion and total dose of administered $MgSO_4$ by primary indication. We were unable to determine the start date of infusion for 1 case belonging the PE cohort. The median total duration of infusion was 3536 minutes (2 days, 10 hours and 56 minutes) in the PE group and 381 minutes (6 hours and 21 minutes) in the NP group. In total a median of 62.62 grams was administered in the PE group vs. 10.02 grams for NP.

Table 8. **Total duration and dose infused $MgSO_4$**

	NP (59)	PE (56)	*p*-value
Total duration (minutes)			<.001
- **Median**	381	3536	
- **IQR**	133 - 1168	1027 - 8529	
- **Min - max**	39 - 5599	15 - 31163	
Total dose (g)			<.001
- **Median**	10.02	62.62	
- **IQR**	5.82 - 24.29	20.84 - 151.25	
- **Min - max**	2.62 - 108.32	3.40 - 523.13	

The infusion for pre-eclampsia lasted significantly longer compared to the infusion for neuroprotection. Furthermore they had a statistically significant higher total $MgSO_4$ dose (table 8). Figure 1 provides the distribution of the total maternal $MgSO_4$ dose by primary indication.

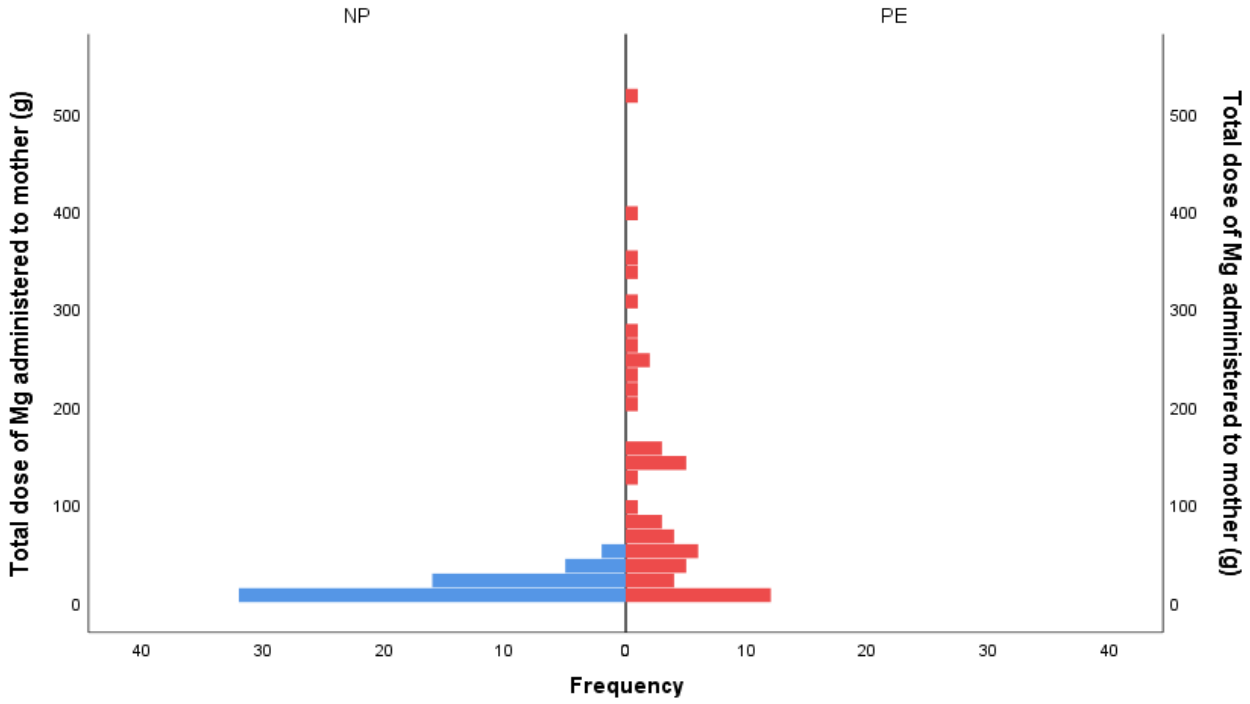


Figure 1. Distribution of the total magnesium dose by primary indication for $MgSO_4$

Maternal pre-delivery serum magnesium

There are a great number of missing maternal pre-delivery sMg values, especially in the control and NP group. Maternal sMg concentrations according to primary indication for $MgSO_4$ are provided in table 9.

Table 9. **Maternal sMg by indication for $MgSO_4$ (mmol/L)**

	Controls (29)	NP (5)	PE (46)
Median	0.78	1.50	1.86
IQR	0.72 – 1.20	0.87 – 1.59	1.34 – 2.48

In literature, the mean maternal sMg concentration at delivery without any $MgSO_4$ supplementation is 0.74 mmol/L (95% CI 0.43 – 1.04) (39). In our study population respectively 24.1% (7), 60% (3) and 84.8% (39) of the mothers had sMg levels above this upper range (>1.04 mmol/L) in the control, NP- and PE-group.

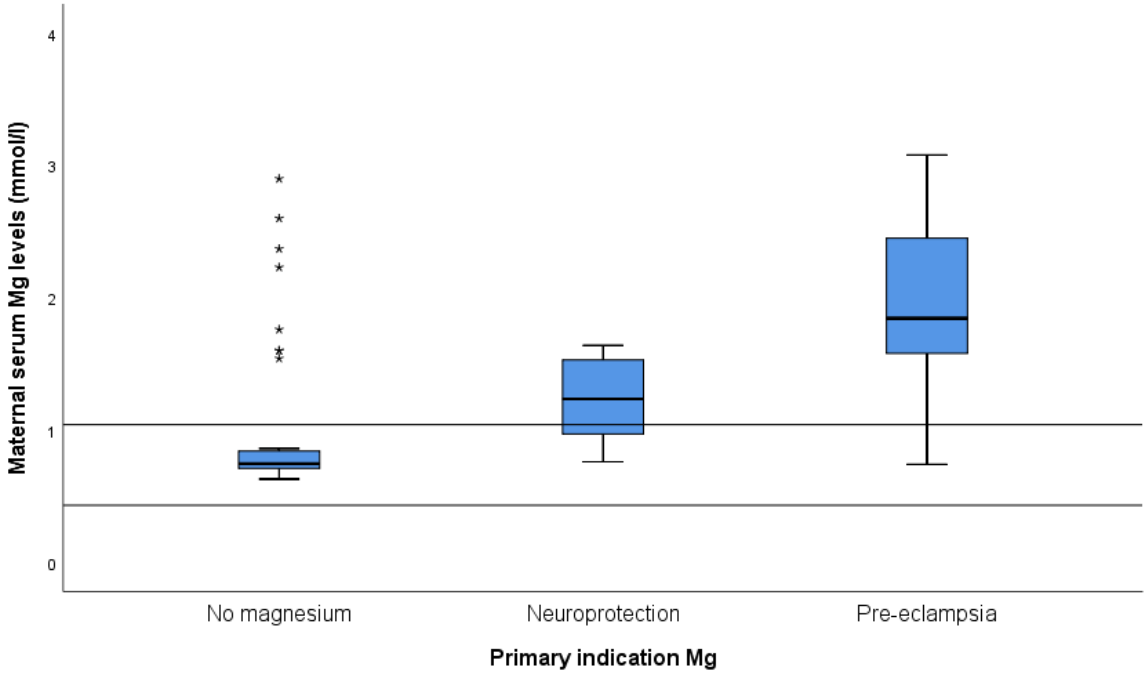


Figure 2. Maternal sMg concentration < 24 hours before delivery by primary indication

Mothers belonging to the PE group had significantly higher pre-delivery sMg concentrations in comparison to the controls (P < 0.001). None of the other groups had significant differences.

Neonatal sMg during the first 15 days of life

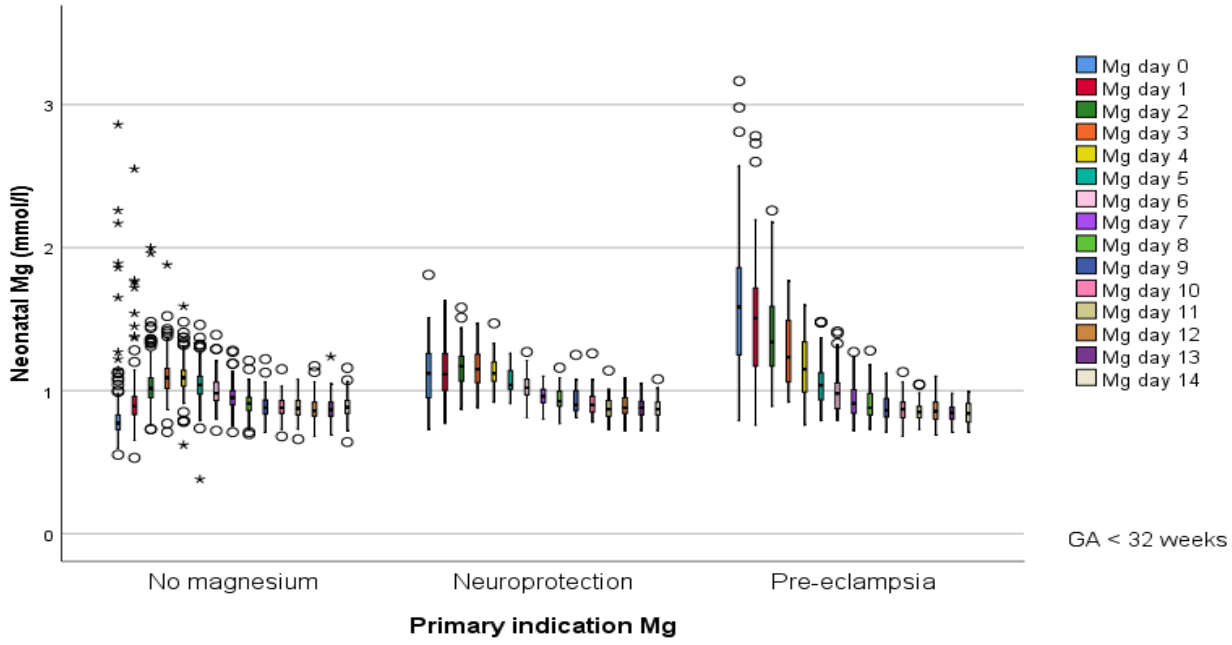


Figure 3. Neonatal sMg during the first 15 days of life according to primary indication for $MgSO_4$

Table 10**. Neonatal magnesemia (mmol/L) day 0-14**

	Day	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
No Mg	N	187	194	200	191	182	169	150	145	124	116	112	104	94	95	98
	Median	0.78	0.90	1.02	1.09	1.09	1.04	0.98	0.95	0.91	0.89	0.88	0.88	0.86	0.87	0.88
	IQR	0.73 - 0.83	0.83 - 0.96	0.95 - 1.09	1.01 - 1.16	1.03 - 1.14	0.97 - 1.10	0.93 - 1.06	0.90 - 1.00	0.86 - 0.96	0.84 - 0.94	0.84 - 0.93	0.83 - 0.94	0.83 - 0.92	0.82 - 0.92	0.84 - 0.93
NP	N	57	62	64	63	60	53	54	39	44	46	37	37	29	40	25
	Median	1.12	1.12	1.17	1.15	1.12	1.04	1.02	0.96	0.93	0.90	0.90	0.88	0.88	0.88	0.87
	IQR	0.95 - 1.26	1.00 - 1.26	1.06 - 1.24	1.05 - 1.26	1.06 - 1.20	1.01 - 1.14	0.97 - 1.08	0.91 - 1.02	0.89 - 1.00	0.86 - 1.00	0.85 - 0.97	0.82 - 0.94	0.84 - 0.96	0.83- 0.93	0.83 - 0.94
PE	N	50	50	53	53	48	52	47	36	38	36	36	29	33	34	25
	Median	1.59	1.51	1.34	1.23	1.15	1.04	0.98	0.91	0.88	0.86	0.87	0.85	0.86	0.85	0.84
	IQR	1.25 - 1.87	1.17 - 1.74	1.17 - 1.60	1.05 - 1.50	0.99 - 1.34	0.93 - 1.13	0.87 - 1.06	0.84 - 1.01	0.83 - 0.98	0.81 - 0.95	0.81 - 0.92	0.81 - 0.90	0.80 - 0.92	0.80 - 0.89	0.78 - 0.92

The evolution in neonatal sMg concentrations during the first 15 days of life is illustrated in figure 3. Table 10 provides the associated median and interquartile range. Neonates without $MgSO_4$ exposure had increasing sMg levels during the first 4 days of life (day 0-3), the median evolved from 0.78 towards 1.09 mmol/l. Levels reached a plateau on the 5th day. From then on they slowly decreased reaching a more or less steady state on day 9. The median between day 9 and 14 ranged between 0.86 and 0.89 mmol/l. In the NP group the median sMg on day 0 was higher: 1.12 mmol/l. The sMg slightly increased towards day 3 (median 1.15 mmol/l). Afterwards, it gradually decreased, reaching a steady state around day 11 at the same level as the control group (median between 0.87 and 0.88 mmol/l). Median neonatal sMg on day 0 was 1.59 mmol/l in the PE group. The magnesemia declined until reaching a more or less steady state on day 11. The median sMg between days 11 and 14 ranged between 0.84 and 0.86 mmol/l.

Neonatal serum magnesium was significantly higher, from day 0 to 3, in the neuroprotective group (p <0.001, <0.001, <0.001, 0.007 respectively) compared to the control group. The PE group had significantly higher levels than the controls from day 0 to 4 (respectively p <0.001, <0.001, <0.001, <0.001, 0.012). Furthermore there were significantly lower levels from day 0 to 3 in the NP group compared to group PE (p = <0.001, <0.001, <0.001, 0.002 respectively).

Neonates were then stratified into three groups according to increasing serum magnesium: 1) group A, <1.05 mmol/l 2) group B, ≥1.05 to < 2.25 mmol/l 3) Group C, ≥2.25 mmol/l. This categorical distribution is illustrated in table 11. A considerable higher amount of infants had hypermagnesemia (groups B and C) during the first days of life in the NP and PE groups. On day 0 for example only 7% of the control cohort had hypermagnesemia compared to 51.5 and 92% in the NP and PE group. The number of neonates having hypermagnesemia slowly decreased in all three groups to nearly none on day 14.

Table 11**. Categorical neonatal magnesemia (mmol/l) day 0 – 14[a]**

	Control			NP			PE		
	A	B	C	A	B	C	A	B	C
Day 0	174 (93.0)	11 (5.9)	2 (1.1)	22 (38.6)	35 (61.4)	/	4 (8.0)	41 (82.0)	5 (10.0)
Day 1	179 (92.3)	14 (7.2)	1 (0.5)	21 (34.4)	40 (65.6)	/	7 (14.0)	40 (80.0)	3 (6.0)
Day 2	126 (66.3)	64 (33.7)	/	15 (23.8)	48 (76.2)	/	6 (11.3)	46 (86.8)	1 (1.9)
Day 3	70 (37.4)	117 (62.6)	/	16 (25.8)	46 (74.2)	/	13 (25.0)	39 (75.0)	/
Day 4	64 (36.6)	111 (63.4)	/	14 (23.7)	45 (76.3)	/	16 (35.6)	29 (64.4)	/
Day 5	100 (62.5)	60 (37.5)	/	30 (58.8)	21 (41.2)	/	30 (61.2)	19 (38.8)	/
Day 6	111 (78.7)	30 (21.3)	/	36 (69.2)	16 (30.8)	/	34 (77.3)	10 (22.7)	/
Day 7	127 (89.4)	15 (10.6)	/	33 (86.8)	5 (13.2)	/	29 (82.9)	6 (17.1)	/
Day 8	120 (96.8)	4 (3.2)	/	40 (93.0)	3 (7.0)	/	31 (81.6)	7 (18.4)	/

Day 9	113 (98.3)	2 (1.7)	/	43 (93.5)	3 (6.5)	/	35 (97.2)	1 (2.8)	/
Day 10	111 (99.1)	1 (0.9)	/	34 (91.9)	3 (8.1)	/	33 (97.1)	1 (2.9)	/
Day 11	103 (99.0)	1 (1.0)	/	36 (97.3)	1 (2.7)	/	29 (100)	/	/
Day 12	91 (97.8)	2 (2.2)	/	16 (94.1)	1 (5.9)	/	32 (97.0)	1 (3.0)	/
Day 13	94 (98.9)	1 (1.1)	/	40 (100)	/	/	34 (100)	/	/
Day 14	84 (97.7)	2 (2.3)	/	24 (96.0)	1 (4.0)	/	25 (100)	/	/

[a]*Data are represented as n (valid percent)*

Neonatal outcomes

Five children were stillborn, four in the PE group and one in the NP group. In addition 20 infants (5.8%) died during the neonatal period. None of the neonatal outcome parameters shown in table 12 were significantly different between the three groups. Follow up by the center of developmental disorders (COS) was indicated in 261 neonates (76.1 %). Data of follow up at 4 months corrected age,10 months corrected age and at 2 and 4 years, were known for respectively 234 (89.7%), 213 (81.6%), 189 (72.4%) and 37 (14.2%) infants. Over the course of 4 years 15 children were diagnosed with cerebral palsy, 14 belonged to the controls and 1 to the pre-eclampsia group.

Table 12. **Outcomes of lifeborn infants[a]**

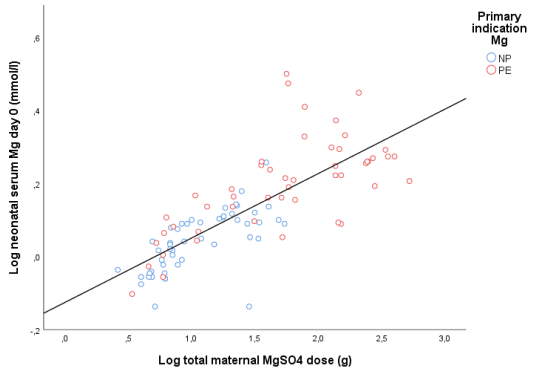
	Total (342)	Control (216)	NP (68)	PE (58)	*p*-value
Neonatal mortality	20 (5.8)	14 (6.5)	4 (5.9)	2 (3.4)	NS
Cerebral palsy	15 (4.4)	14 (6.5)	0	1 (1.7)	≠[b]
Intracerebral haemorrhage (3 missing)	30 (8.8)	18 (8.3)	8 (11.8)	4 (6.9)	NS
Periventricular leucomalacia (3 missing)	64 (18.7)	36 (16.7)	16 (23.5)	12 (20.7)	NS
Respiratory distress syndrome (3 missing)	271 (79.2)	173 (80.1)	56 (82.4)	42 (72.4)	NS
Necrotizing enterocolitis	11 (3.2)	8 (3.7)	1 (1.5)	2 (3.4)	NS

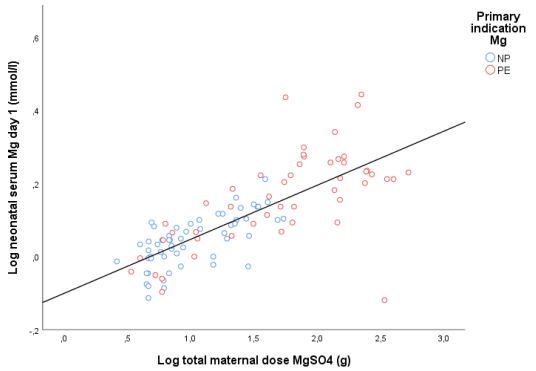
[a]*Data are represented as n(%)* [b]*C vs NP (p <.023), C vs PE (NS), NP vs PE (NS)*

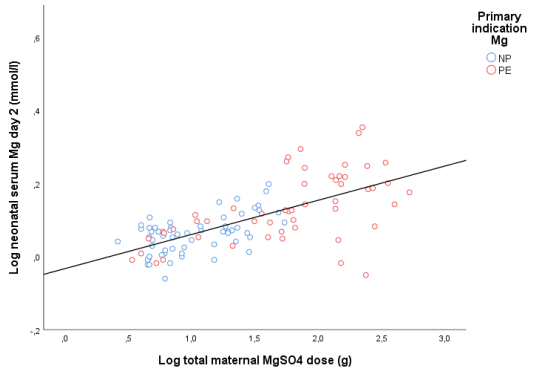
PART 2: ASSOCIATION BETWEEN NEONATAL MAGNESEMIA - MAGNESIUM SULPHATE DOSAGE - MATERNAL MAGNESEMIA

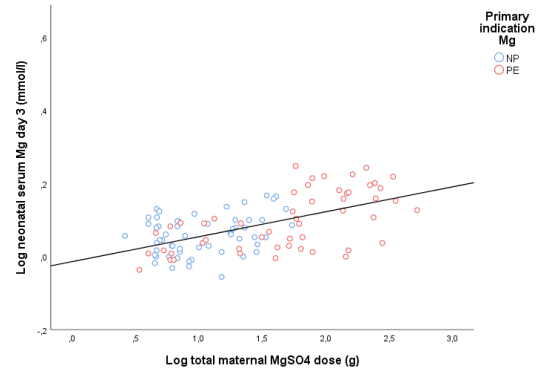
Association between the total maternal MgSO4 dose and neonatal magnesemia during the first 15 days of life

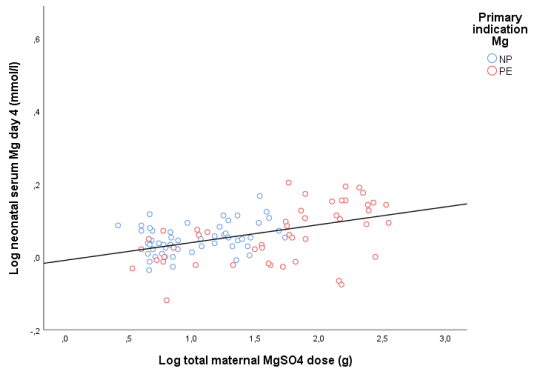
Candidate covariates influencing neonatal sMg were identified through literature search and later on selected by a stepwise process. The final GEE model included following covariates: log total maternal $MgSO_4$ dose (g), neonatal creatinine (mg/dL), pregestational maternal BMI (kg/m^2) and administration of total parenteral nutrition (yes/no). Figures 4-13 demonstrate the association between the total maternal $MgSO_4$ dose and neonatal magnesemia during the first 15 days of life.

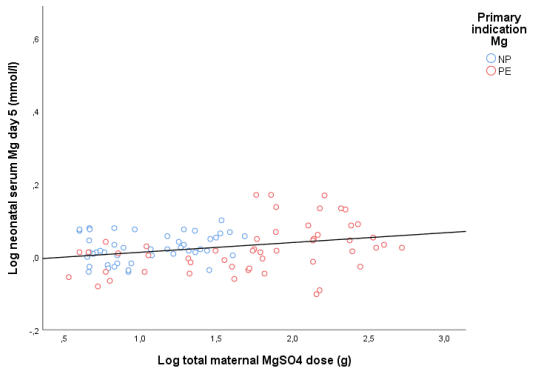


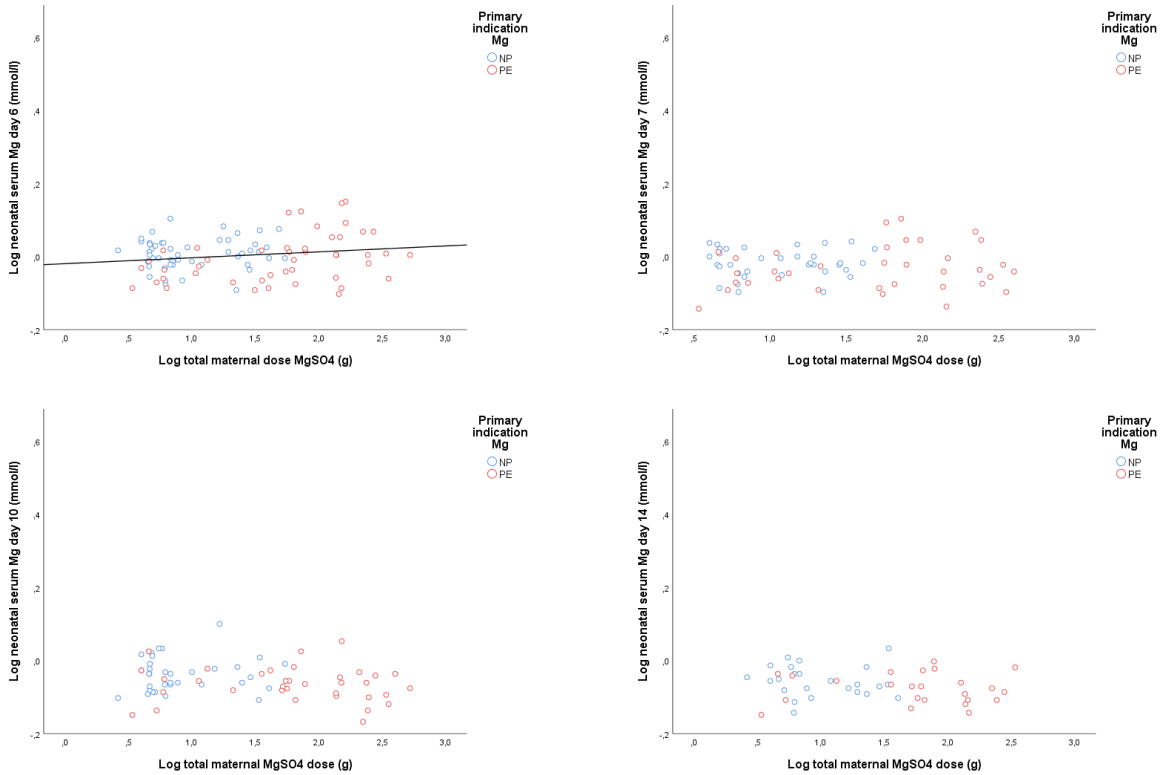












Figures 4-13. Association between total maternal dose $MgSO_4$ and neonatal magnesemia after log transformation (day 0-7, 10, 14)

On the first day of life neonatal magnesemia was associated with the total antenatal $MgSO_4$ dose, irrespective of maternal BMI and neonatal serum creatinine (table 13). A 10-fold increase in the total maternal magnesium dose was associated with an increase in the geometric mean of neonatal magnesemia of 43.2%.

This association remained during the 6 following days (day 1 - 6), irrespective of maternal BMI, neonatal serum creatinine and total parenteral nutrition. A 10-fold increase in the total maternal $MgSO_4$ dose was associated with an increase in the geometric mean neonatal magnesium concentration of respectively 43.2%, 24.5%, 19.1%, 16.1%, 9.4%, 8.1% from day 1 to day 6.

Table 13. **Association between total maternal dose of $MgSO_4$ (g) and neonatal serum magnesium concentration (mmol/l)**

		B (95% CI)		*p*-value	n
		Log transformed[a]	Back transformed		
Day 0	$MgSO_4$ dose	.156 (.132; .181)	1.432 (1.355; 1.517)	<.001	88
	Neonatal Creatinine	.254 (.184; .324)		<.001	
	Maternal BMI	-.005		<.001	

		(-.007; -.002)			
	TPN				
Day 1	$MgSO_4$ dose	.156 (.130; .181)	1.432 (1.349; 1.521)	<.001	92
	Neonatal Creatinine	.188 (.088; .289)		<.001	
	Maternal BMI	-.002 (-.004; 0)		.066	
	TPN				
Day 2	$MgSO_4$ dose	.095 (.070; .119)	1.245 (1.175; 1.315)	<.001	95
	Neonatal Creatinine	.134 (.044; .223)		.003	
	Maternal BMI	-.001 (-.004; .001)		.267	
	TPN				
Day 3	$MgSO_4$ dose	.076 (.054; .099)	1.191 (1.132; 1.256)	<.001	91
	Neonatal Creatinine	.112 (.038; .185)		.003	
	Maternal BMI	- .002 (-.005; 0)		.023	
	TPN	.052 (.027; .076)		<.001	
Day 4	$MgSO_4$ dose	.065 (.045; .085)	1.161 (1.109; 1.216)	<.001	85
	Neonatal Creatinine	.134 (.078; .191)		<.001	
	Maternal BMI	-.002 (-.004; 0)		.016	
	TPN	.013 (-.003; .029)		.117	
Day 5	$MgSO_4$ dose	.039 (.020; .057)	1.094 (1.047; 1.140)	<.001	88
	Neonatal Creatinine	.105 (.040; .171)		.002	
	Maternal BMI	-.002 (-.004; 0)		.102	
	TPN	.054 (.030; .078)		<.001	
Day 6	$MgSO_4$ dose	.034 (.010; .058)	1.081 (1.023; 1.143)	.006	88
	Neonatal Creatinine	.119 (.060; .177)		<.001	

	Maternal BMI	-.002 (-.004; 0)		.064	
	TPN	.059 (.040; .077)		<.001	
Day 7	$MgSO_4$ dose	.022 (0; .044)	1.052 (1; 1.107)	.053	63
	Neonatal Creatinine	.101 (.046; .156)		<.001	
	Maternal BMI	-.001 (-.003, .001)		.0193	
	TPN	.027 (-.006; .061)		.111	
Day 8	$MgSO_4$ dose	.011 (-.009; .030)	1.002 (.979; 1.072)	.278	73
	Neonatal Creatinine	.128 (.082; .173)		<.001	
	Maternal BMI	-.001 (-.003; 0)		.097	
	TPN	.020 (.003; .037)		.018	
Day 9	$MgSO_4$ dose	.009 (-.009; .027)	1.021 (.979; 1.064)	.306	70
	Neonatal Creatinine	.152 (.092; .212)		<.001	
	Maternal BMI	-.001 (-.003; .001)		.241	
	TPN	0 (-.033; .034)		.984	
Day 10	$MgSO_4$ dose	.005 (-.014; .024)	1.012 (.968; 1.057)	.591	67
	Neonatal Creatinine	.156 (.083; .229)		<.001	
	Maternal BMI	-.001 (-.003, .001)		.156	
	TPN	.026 (-.001; .053)		.059	
Day 11	$MgSO_4$ dose	-.007 (-.028; .014)	.984 (.938; 1.033)	.494	57
	Neonatal Creatinine	.061 (.003; .119)		.039	
	Maternal BMI	-.001 (-.003, .001)		.452	
	TPN	.010 (-.021; .041)		.520	
Day 12	$MgSO_4$ dose	.012 (-.013; .037)	1.028 (.971; 1.089)	.351	56

	Neonatal Creatinine	.118 (.019, .217)		.019	
	Maternal BMI	-.002 (-.004; 0)		.017	
	TPN	-.005 (-.037; .028)		.782	
Day 13	$MgSO_4$ dose	-.021 (-.037; -.004)	.953 (.918; .991)	.013	64
	Neonatal Creatinine	.012 (-.039; .063)		.648	
	Maternal BMI	0 (-.002; .003)		.759	
	TPN	-.014 (-.038; .011)		.278	
Day 14	$MgSO_4$ dose	-.001 (-.028; .025)	.998 (.938; 1.059)	.918	45
	Neonatal Creatinine	.107 (-.040; .253)		.153	
	Maternal BMI	-.002 (-.003; 0)		.035	
	TPN	.026 (.002; .050)		.036	

[a]*For neonatal creatinine, maternal BMI and TPN containing non log-transformed data*

During subgroup analyses, mothers solely exposed for neuroprotective intent, the association between neonatal magnesemia and the total antenatal $MgSO_4$ dose remained from the first day of life until the sixth (day 0 - 5) ,irrespective of maternal BMI, TPN and neonatal serum creatinine (table 14). A 10-fold increase in the total maternal $MgSO_4$ dose was associated with an increase in the geometric mean neonatal magnesium concentration of 48.9%, 36.1%, 20.8%, 9.6%, 10.7%, 8.1% for respectively day 0 to 5.

Table 14. **Subgroup analyses: Association between total maternal dose of $MgSO_4$ (g) and neonatal serum magnesium concentration (mmol/l) in cases with neuroprotection as primary intent for $MgSO_4$ administration**

		B (95% CI)		*p*-value	n
		Log transformed[a]	Back transformed		
Day 0	$MgSO_4$ dose	.173 (.122; .224)	1.489 (1.324; 1.575)	<.001	44
	Neonatal Creatinine	-.144 (-.396; .107)		.259	
	Maternal BMI	-.005 (-.008; -.002)		<.001	
	TPN				
Day 1	$MgSO_4$ dose	.134	1.361	<.001	50

		(.093; .175)	(1.239; 1.496)		
	Neonatal Creatinine	.072 (-.060; .203)		.286	
	Maternal BMI	-.001 (-.002; .003)		.710	
	TPN				
Day 2	$MgSO_4$ dose	.082 (.048; .116)	1.208 (1.116; 1.306)	<.001	52
	Neonatal Creatinine	.042 (-.038; .122)		.301	
	Maternal BMI	.002 (0; .004)		.057	
	TPN				
Day 3	$MgSO_4$ dose	.040 (.003; .076)	1.096 (1.007; 1.191)	.032	49
	Neonatal Creatinine	.068 (-.011; .146)		.091	
	Maternal BMI	.001 (-.002; .004)		.520	
	TPN				
Day 4	$MgSO_4$ dose	.044 (.010; .077)	1.107 (1.023; 1.194)	.011	51
	Neonatal Creatinine	.098 (.043; .153)		.001	
	Maternal BMI	0 (-.002; .002)		.942	
	TPN				
Day 5	$MgSO_4$ dose	.034 (.004; .064)	1.081 (1.009; 1.159)	.028	42
	Neonatal Creatinine	.100 (.067; .134)		<.001	
	Maternal BMI	0 (-.002; .001)		.893	
	TPN				
Day 6	$MgSO_4$ dose	.014 (-.013; .041)	1.032 (.971; 1.099)	.206	45
	Neonatal Creatinine	.116 (.052; .181)		<.001	
	Maternal BMI	-.001 (-.003; .001)		.273	
	TPN				
Day 7	$MgSO_4$ dose	.018	1.042	.312	32

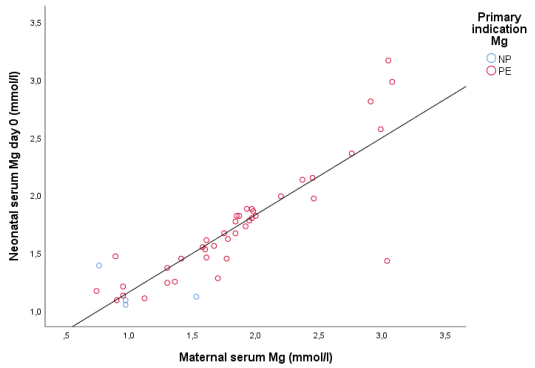
		(-.017; .054)	(.962; 1.132)		
	Neonatal Creatinine	.095 (.045; .145)		<.001	
	Maternal BMI	-.001 (-.003; .001)		.241	
	TPN	.022 (-.012; .056)		.210	
Day 8	$MgSO_4$ dose	.012 (-.018; .042)	1.002 (.959; 1.102)	.427	37
	Neonatal Creatinine	.118 (.064; .173)		<.001	
	Maternal BMI	0 (-.002, .002)		.994	
	TPN	.024 (-.001; .048)		.057	
Day 9	$MgSO_4$ dose	.008 (-.021; .038)	1.018 (.953; 1.091)	.578	38
	Neonatal Creatinine	.133 (.054; .212)		.001	
	Maternal BMI	-.001 (-.003; 0)		.101	
	TPN	-.006 (-.034; .021)		.656	
Day 10	$MgSO_4$ dose	.018 (-.021; .057)	1.042 (.953; 1.140)	.365	33
	Neonatal Creatinine	.127 (.053; .201)		.001	
	Maternal BMI	-.001 (-.004, .002)		.415	
	TPN	.027 (.002; .053)		.032	
Day 11	$MgSO_4$ dose	-.019 (-.055; .018)	0.957 (.881; 1.042)	.319	32
	Neonatal Creatinine	.053 (.002; .108)		.058	
	Maternal BMI	-.002 (-.004, .001)		.167	
	TPN	0 (-.038; .038)		.989	
Day 12	$MgSO_4$ dose	.015 (-.032; .063)	1.035 (.929; 1.156)	.527	25
	Neonatal Creatinine	.114 (-.006, .234)		.062	
	Maternal BMI	-.003 (-.005; -.001)		.006	
	TPN	-.015 (-.049; .019)		.387	

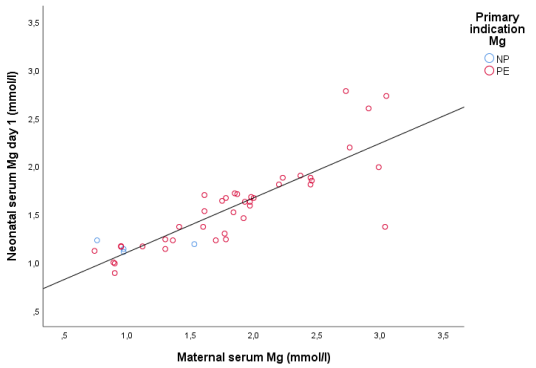
Day 13	$MgSO_4$ dose	0 (-.036; .036)	1 (.920; 1.086)	.992	34
	Neonatal Creatinine	.029 (-.039; .097)		.402	
	Maternal BMI	0 (-.005; .005)		.995	
	TPN	-.013 (-.047; .022)		.463	
Day 14	$MgSO_4$ dose	-.006 (-.050; .037)	.986 (.891; 1.089)	.774	22
	Neonatal Creatinine	.185 (.008; .362)		.040	
	Maternal BMI	-.002 (-.005; 0)		.066	
	TPN	.013 (-.016; .042)		.375	

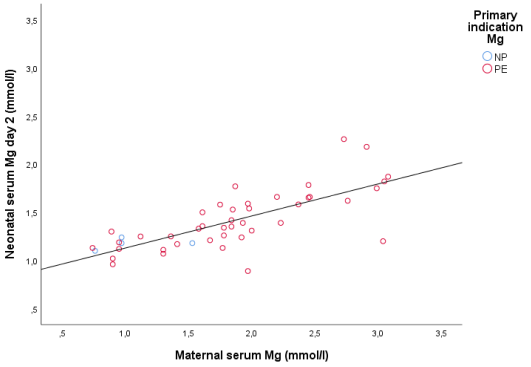
[a]*For neonatal creatinine, maternal BMI and TPN containing non log-transformed data*

Association between the prepartal maternal magnesemia and neonatal magnesemia during the first 15 days of life

Candidate covariates influencing neonatal sMg were selected through literature search and a stepwise selection process. The final GEE model included following covariates: maternal magnesemia (mmol/l), gestational age and total parenteral nutrition (yes/no). The association between prepartal maternal magnesemia and neonatal magnesemia during the first 15 days of life are shown in figures 14-24. It was possible to establish a significant linear association from the first day of life until the eight (day 7) and on days 12 and 13 whilst correcting for gestational age and TPN (table 15). Due to the limited amount of known pre-delivery maternal sMg concentrations in the neuroprotective group, a subgroup analysis was not possible.



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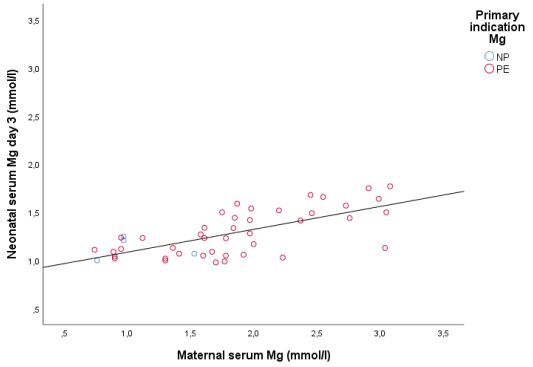
NP
PE
Neonatal serum Mg day 2 (mmol/l)
Maternal serum Mg (mmol/l)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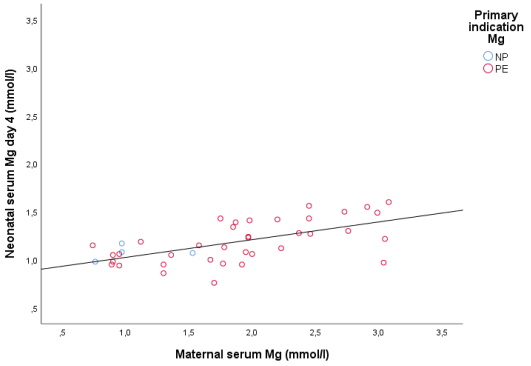
Neonatal serum Mg day 3 (mmol/l)
Maternal serum Mg (mmol/l)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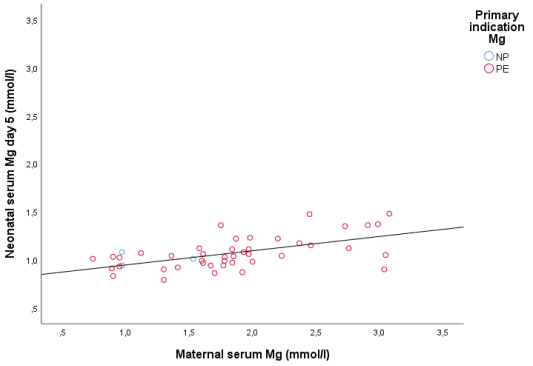
Neonatal serum Mg day 4 (mmol/l)
Maternal serum Mg (mmol/l)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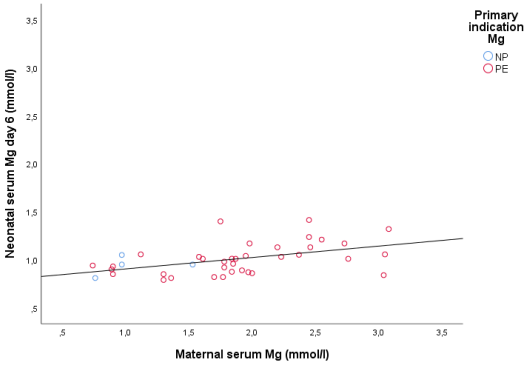
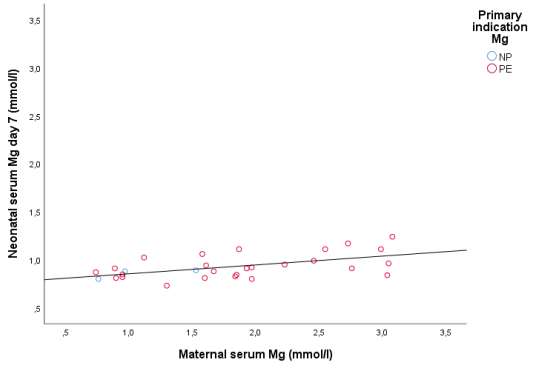
NP
PE
Neonatal serum Mg day 5 (mmol/l)
Maternal serum Mg (mmol/l)


Primary indication Mg
NP
PE
Neonatal serum Mg day 6 (mmol/l)
Maternal serum Mg (mmol/l)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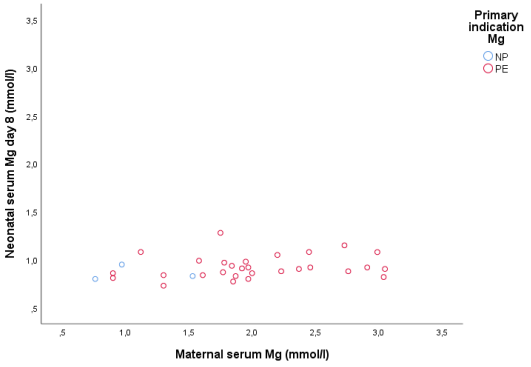
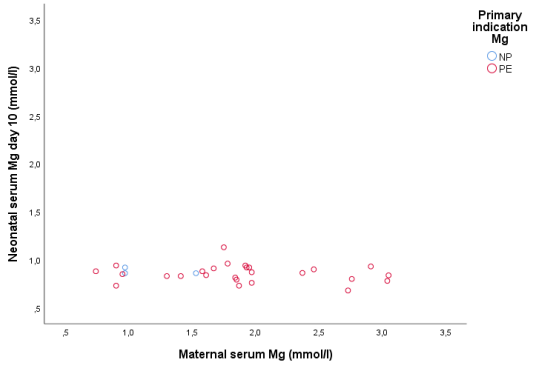
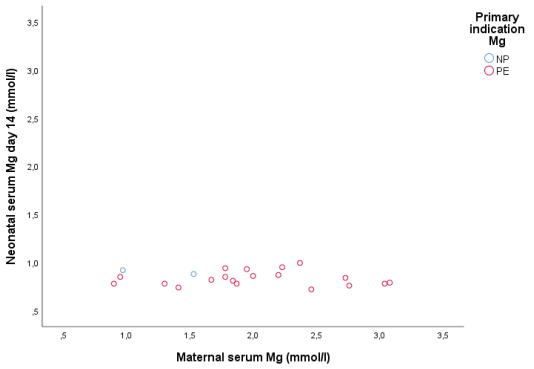
NP
PE
Neonatal serum Mg day 7 (mmol/l)
Maternal serum Mg (mmol/l)


Primary indication Mg
NP
PE
Neonatal serum Mg day 8 (mmol/l)
Maternal serum Mg (mmol/l)


Primary indication Mg
NP
PE
Neonatal serum Mg day 10 (mmol/l)
Maternal serum Mg (mmol/l)



Figures 14-24. Association between maternal and neonatal serum magnesemia (day 0-8, 10, 14).

Table 15. **Association between maternal and neonatal magnesemia (mmol/l)**

		B	95% CI	*p*-value	N
Day 0	sMg	.638	.411; .866	<.001	42
	Gestational age	.004	-.001; .009	.146	
	TPN				
Day 1	sMg	.572	.375; .769	<.001	42
	Gestational age	.004	-.001; .008	.152	
	TPN				
Day 2	sMg	.330	.204; .456	<.001	44
	Gestational age	.002	-.002; .006	.366	
	TPN				
Day 3	sMg	.233	.143; .322	<.001	44
	Gestational age	.001	-.004; .005	.828	
	TPN	-.087	-.176; .002	.056	
Day 4	sMg	.168	.077; .258	<.001	39
	Gestational age	.004	-.001; .009	.130	
	TPN	-.198	-.283; -.114	<.001	
Day 5	sMg	.139	.054; .225	.001	44
	Gestational age	.002	-.002; .005	.384	
	TPN	-.115	-.194; -.036	.004	
Day 6	sMg	.098	.019; .177	.015	39
	Gestational age	.004	0; .009	.047	
	TPN	-.022	-.142; .098	.722	
Day 7	sMg	.088	.021; .156	.010	27
	Gestational age	0	-.004; .004	.935	
	TPN	-.041	-.104; .021	.196	

Day 8	sMg	.003	-.056; .062	.925	30
	Gestational age	.007	.003; .010	<.001	
	TPN	.049	-.010, .107	.102	
Day 9	sMg	.040	-.004; .083	.074	31
	Gestational age	.003	0; .006	.026	
	TPN	.086	.039; .132	<.001	
Day 10	sMg	-.040	-.086; .005	.080	28
	Gestational age	.004	0; .007	.060	
	TPN	-.006	-.094; .082	.892	
Day 11	sMg	-.018	-.051; .016	.303	25
	Gestational age	.004	.001; .007	.004	
	TPN	-.006	-.119; .107	.914	
Day 12	sMg	-.048	-.084; -.011	.010	22
	Gestational age	.007	.004; .010	<.001	
	TPN	-.097	-.184; -.009	.031	
Day 13	sMg	-.044	-.067; -.020	<.001	30
	Gestational age	.004	.002; .006	<.001	
	TPN	.005	-.030, .039	.792	
Day 14	sMg	-.024	-.070; .022	.300	20
	Gestational age	.005	.002; .007	<.001	
	TPN	.091	.190; .163	.013	

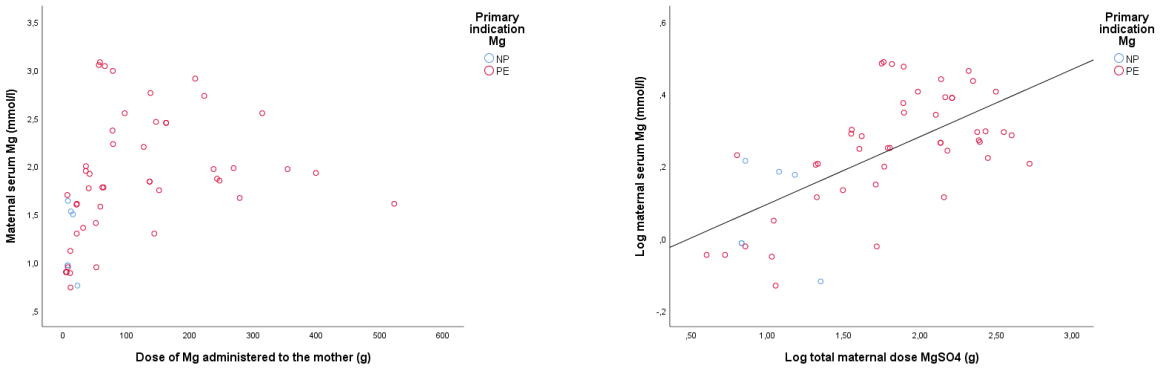
Association between the total maternal $MgSO_4$ dose and prepartal maternal magnesemia

An association was found between the total maternal $MgSO_4$ dose and maternal magnesemia whilst correcting for maternal serum creatinine (n= 53, $p < 0.001$). A 10-fold increase in the total maternal $MgSO_4$ dose was associated with an increase in the geometric mean serum magnesium of 51%.

Table 16. **Association between total maternal $MgSO_4$ dose (g) and maternal magnesemia (mmol/l)**

	B (95% CI)		*p*-value
	Log transformed[a]	Back transformed	
$MgSO_4$ dose	.179 (.128; .230)	1.510 (1.343; 1.698)	<.001
Maternal creatinine	.272 (.187; .358)		<.001

[a]*For maternal creatinine containing non log-transformed data*



Figures 22-23. The association between total maternal $MgSO_4$ dose and maternal magnesemia. LEFT: Non log transformed data. RIGHT: Log transformed data.

DISCUSSION

CHARACTERISTICS OF THE STUDY POPULATION COMPARED TO THE GENERAL POPULATION

No national, nor regional data of other tertiary hospitals was available to compare the demographical characteristics of our study population. Therefore, comparison was made to data of the Study center for Perinatal Epidemiology (SPE, 2017) (59). We must keep in mind that our data concerns more high-risk patients due to being the population of a university hospital.
In Flanders and Brussels combined, 1.7% of pregnancies concerned twins. In our study population approximately 18% were twin pregnancies. As multiple pregnancies are by definition high risk and associated with preterm birth, being a tertiary center could explain our considerably higher rate. Our study population had higher rates of fertility treatment (21.6 vs 7.5%) and a higher mean maternal age (30.7 vs 29.0). Possibly again explained by our status as tertiary center.
In the pre-eclamptic group 24.6% women were obese, considerably more than in the control (15%) and neuroprotective group (8.9%). It is well known that obesity is a risk factor for pre-eclampsia (60).

A little over half our infants (51.3%) were male, similar to the distribution reported by SPE (51.2% male). In the general population 20.9% of deliveries are by caesarean section, our rate was with 56.2% considerably higher. This might be the consequence of several factors. For example, abnormal fetal positions, more common in premature infants, can lead to a caesarean. Furthermore, as a tertiary center we treat high-risk patients such as pre-eclamptic women and women admitted with placenta praevia, both often indications for delivery by caesarean. Pre-eclampsia is caused by a reduced placental perfusion and is associated with IUGR (60). The PE group had a significantly lower mean birth weight and a higher frequency of IUGR compared to the other groups, as expected.

Sixty mothers received $MgSO_4$ solely for neuroprotective purposes in our study population, being only 24% of eligible women. A French single-center study (2011-2012) assessing implementation of $MgSO_4$ infusion for NP found that nearly 70% of eligible women received the treatment. Main reasons for not receiving magnesium are: omission by the medical team, urgent delivery and contra-indication to treatment (61). Our treatment levels were drastically lower. This can partially

be explained as the use of magnesium for neuroprotection was only implemented by the Ghent University Hospital in 2014.

NEONATAL MAGNESEMIA

We charted the natural progression of sMg in our study population of very and extremely preterm infants during the first 15 days of life in three groups according to primary indication for antenatal magnesium administration.

In our control cohort sMg increased during the first 4 days of life (median 0.78 mmol/L to 1.09 mmol/L). It then steadily decreased and stabilized towards day 9 remaining relatively unchanged afterwards. This coincides with previously published data, reporting an increasing sMg during the first week of life (39,40,62). Rigo et al revealed an estimated mean of 0.88 mmol/L (95% CI: 0.46, 1.30) during the first week of life (39). Our median sMg in the control cohort ranged between 0.78 and 1.09 mmol/L during the first week of life.

Antenatal $MgSO_4$ exposure for neuroprotective intent caused significantly higher sMg levels during the first 4 days of life compared to those not exposed. This coincides with findings by Basu et al., Garcia et al. and Rigo et al. (35,39,41). SMg slightly increased during the first 4 days (median 1.12 mmol/L to 1.15 mmol/L). From then on it decreased reaching a steady state on the 12^{th} day at the same level as the control cohort. Our median sMg on days 0 and 1 (1.12 mmol/L) were comparable to the mean sMg determined by Garcia et al. (1.10 mmol/L). However, Basu et al. reported a considerably higher mean sMg: 1.75 mmol/L. More so, approximately 20% of their neonates had sMg higher than 2.25 mmol/L; compared to none in our study population. This is probably the consequence of higher $MgSO_4$ dosage (6g loading dose, 2g/h maintenance compared to 4g loading dose, 1g/h maintenance).

Neonates with antenatal $MgSO_4$ exposure for pre-eclampsia had significantly higher sMg levels than the neuroprotective group during the first 4 days of life, and than controls during the first 5 days. In contrast to the control and NP group, no initial increase in neonatal sMg was seen during the first days of life. The serum magnesium steadily decreased from the first day of life until reaching a steady state on day 11 at an equal level as previous groups. To the best of our knowledge no studies have compared neonatal sMg levels after $MgSO_4$ exposure for pre-eclampsia and neuroprotection.

Few studies correlated neonatal magnesemia and clinical outcomes. Basu et al. observed a significant increase in neonatal mortality during the first 24 hours of life if neonatal sMg exceeded 2.25 mmol/L (35). In our study, none of the neonates receiving NP dosage had levels exceeding

this value. In contrast 5 neonates exceeded it after exposure for pre-eclampsia, none had neonatal mortality. Morag et al. found an association between sMg exceeding 1.44 mmol/L and lower locomotor scores. In our study respectively 2 and 33 neonates had higher levels on day 0 in the NP and PE group, of which none developed CP. Due to the small number of cases no further conclusions could be drawn.

$MGSO_4$ DOSE – MATERNAL MAGNESEMIA - NEONATAL MAGNESEMIA

Neonatal sMg concentrations are associated with the total maternal $MgSO_4$ dose (NP and PE combined) during the first 7 days of life in very and extremely preterm infants, irrespective of maternal BMI and neonatal serum creatinine. During subgroup analyses for only neuroprotective intent this association remained significant during the first 6 days. Furthermore a significant linear association between maternal and neonatal magnesemia during the first 8 days of life was established, irrespective of gestational age and TPN administration. Due to missingness, subgroup analysis was not possible. Finally, the total maternal $MgSO_4$ dose and maternal magnesemia were associated whilst correcting for maternal creatinine. The statistical significant association between the total $MgSO_4$ dose and neonatal sMg on day 12, and between maternal and neonatal sMg on days 12-13 were not ought of clinical significance.

Cruikshank et al. demonstrated a significant correlation between mother's and infant's magnesium concentrations (63). In this study magnesium concentrations were quantified on cord blood whereas we used neonatal blood samples. Their study population contained full-term pre-eclamptic women while our population consisted of women in very and extremely preterm labour with or without pre-eclampsia. Nonetheless we established the same association in our study.

Similarly, a study by Borja et al. describes a correlation between the total neuroprotective infused $MgSO_4$ dose and neonatal sMg concentrations. They were not able to establish a correlation between maternal and neonatal sMg, nor between the total $MgSO_4$ dose and maternal sMg concentrations, in contrast to our findings (52). However, different cohorts were used. Borja et al. excluded (pre)-eclamptic women, while 46 out of the 51 women with known pre-delivery sMg values in our cohort had (pre)-eclampsia. More so, most mothers in the Borja et al. study delivered within 24 hours after infusion initiation, therefore a steady state in maternal sMg was frequently not reached. In our cohort most women were (pre)-eclamptic. Therefore had a long infusion time and did reach that steady state. As we were not able to perform subgroup analyses for the associations total $MgSO_4$ dose – maternal sMg and maternal sMg – neonatal sMg, we can nor confirm nor refute their results.

Garcia et al. detected the same significant linear correlation between the total maternal dose and neonatal sMg during the first 24 hours of life (41). Similarly to our study, infants were delivered before 32 weeks of gestation and (pre)-eclamptic women were included.
Our findings add to these studies by providing information on the duration that the associations remain detectable after delivery. The association between the total maternal $MgSO_4$ dose and neonatal sMg remained detectable during the first 7 days of life. The association between maternal and neonatal sMg was detectable during the first 8 days of life.

CONCLUSION

In this study we documented a relationship between the extent of antenatal magnesium exposure and neonatal serum magnesium levels. These proven associations deliver a possible explanation for the detected differences in neonatal sMg during the first days of life in the neuroprotective and pre-eclamptic group. The PE group received significantly longer infusions and by consequence higher $MgSO_4$ dosages than the NP group. These differences in dosage are a direct consequence of the treatment protocol. $MgSO_4$ infusion for neuroprotection should be interrupted after 24 hours if birth is no longer imminent while it most often is to be continued in case of pre-eclampsia upon delivery and beyond. The median dose of magnesium received by the mothers for neuroprotective intent was 10.02g. None of the neonates receiving magnesium in NP dosage had sMg levels exceeding 2.25 mmol/L, an earlier established boundary for significantly increased neonatal mortality. Therefore antenatal $MgSO_4$ in neuroprotective dosage seems to be safe in the immediate postnatal period, coinciding with the findings of Basu et al (35). Whereas to monitor and predict the neonatal magnesemia in order to keep them in an effective and safe range, Garcia et al. and Borja et al. suggested that total dose of magnesium could be considered a reliable method (41, 52). We are inclined to agree with this statement.
An association between maternal and neonatal sMg levels was found in our study. However we should be cautious extrapolating our results to the subgroup of magnesium infusion with primary intent neuroprotection taking into account the non-reaching of a steady state in this subgroup and the under representation in our study. Whereas to monitor neonatal magnesemia; a blood sample is required to determine maternal sMg, while total dose calculation is non-invasive, easy and fast. None of the neonates receiving $MgSO_4$ for neuroprotection had dangerously elevated serum magnesium levels. We therefore question if closely monitoring magnesium dosage in these cases, as previously recommended (52), is in fact clinically relevant, provided physicians do not extent infusion time beyond protocol.

STRENGTHS AND LIMITATIONS

We recognize the limitations of a retrospective study design. In addition, we had a relatively small sample size from one single center.

The timing of maternal and neonatal blood draws was scattered and non-standardised. Our main limitation was the low number of known maternal pre-delivery sMg levels in the subgroup with neuroprotection as primary intent. Due to this limitation we were not able to do a subgroup analyses on the associations between maternal sMg – neonatal sMg and total $MgSO_4$ dose - maternal sMg. Study results could also be influenced by selection bias for use of antenatal magnesium by obstetricians.

The database contained a large variety of variables, being a major strength. Nonetheless there may still be to date unknown, yet important, covariates influencing the relationship between total maternal $MgSO_4$ dose, maternal and neonatal magnesemia that were unmeasured and unaccounted for. Lastly, in contrast to other studies neonatal sMg levels were known during the first 15 days al life and not only on the first day.

FUTURE RESEARCH

The total $MgSO_4$ dose and range of maternal sMg that is most effective for neuroprotection remains unknown (52). Also the exact total $MgSO_4$ dose and maternal sMg concentration that's safe for children is not known. For example, outcomes of infants with extremely high sMg need further studying since the cohort in present studies were too small (35, 51). Furthermore, more research is needed to evaluate if the association between maternal and neonatal sMg remains after antenatal $MgSO_4$ exposure for solely neuroprotective intent. Lastly, preterm birth not only causes cerebral palsy, it has a major impact on the neurological development in all its facets. Thanks to extensive medical research these neurodevelopmental disabilities, including cognitive impairment, are better known. More research is needed to evaluate the influence of antenatal $MgSO_4$ administration on these various neonatal outcomes.

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ATTACHMENTS

Attachment 1: Prisma

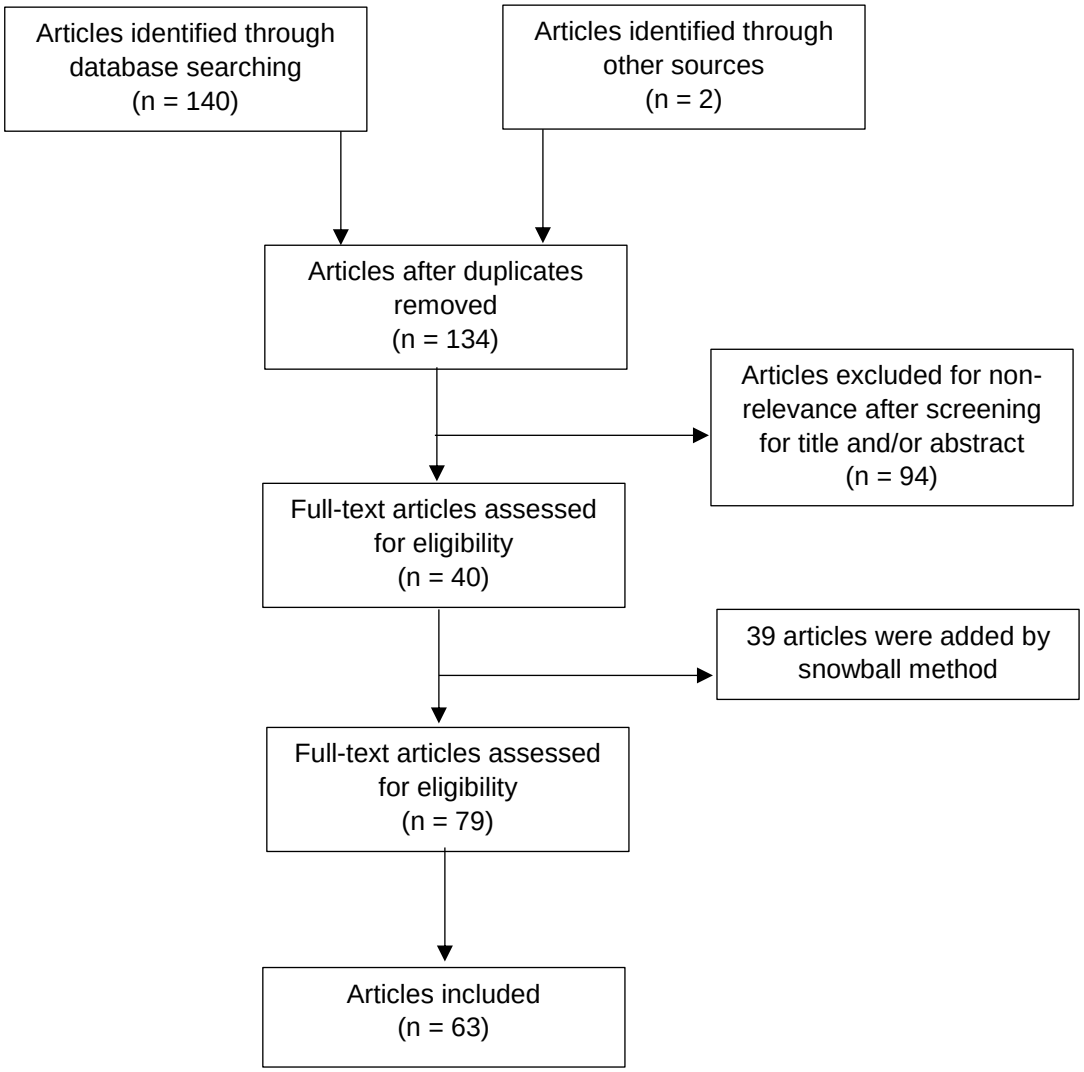
Attachment 2: Codebook

Attachment 3: Preterm birth protocol

Attachment 4: TPN protocol

Attachment 5: Non-Log transformed graphs: association between total maternal $MgSO_4$ dose and neonatal magnesemia (days 0-7, 10, 14).

Prisma


Articles identified through database searching (n = 140)
Articles identified through other sources (n = 2)
Articles after duplicates removed (n = 134)
Articles excluded for non-relevance after screening for title and/or abstract (n = 94)
Full-text articles assessed for eligibility (n = 40)
39 articles were added by snowball method
Full-text articles assessed for eligibility (n = 79)
Articles included (n = 63)

Database Vroeggeboorte

Codebook

Data Dictionary Codebook

2018-11-22 00:17:06

#	Variable / Field Name	Field Label *Field Note*	Field Attributes (Field Type, Validation, Choices, Calculations, etc.)
Instrument: **Demographics mother** (demographics_mother)			
1	study_id	Study ID	text, Identifier
2	age	Maternal age at admission	text (number, Min: 12, Max: 55), Identifier
3	n	Number of foetus	dropdown, Required 1, 1 2, 2 3, 3 4, 4
4	twin_type Show the field ONLY if: [n] = '2' or [n] = '3' or [n] = '4'	Type of multiple pregnancy	dropdown 1, DCDA 2, MCDA 3, MCMA 4, TCTA 5, DCTA 6, DCDA, triplets 7, MCTA 8, MCDA, triplets 9, MCMA, triplets 10, Unknown
5	interval Show the field ONLY if: [n] = '2' or [n] = '3' or [n] = '4'	Interval delivery?	radio 0, No 1, Yes - first delivery 2, Yes - subsequent delivery
6	interval_description Show the field ONLY if: [interval] = '1' or [interval] = '2'	If it concerns an interval delivery (more than 2 hours between births), please create a study ID for each delivery. For subsequent interval deliveries, please select the study ID of the first birth.	descriptive

7	interval_study_id Show the field ONLY if: [interval] = '2'	Study ID related to first birth	sql (autocomplete) SELECT DISTINCT record FROM redcap_data WHERE project_id=20 AND field_name='interval' AND value='1'
8	date_admission	Date of admission	text (date_dmy), Required, Identifier
9	date_due	Due date	text (date_dmy), Required, Identifier
10	iut	Intra-uterine transfer	yesno, Required 1 Yes 0 No
11	back Show the field ONLY if: [iut] = '1'	Intra-uterine transfer back to referring hospital/home with birth in referral hospital	yesno 1 Yes 0 No
12	home Show the field ONLY if: [iut] = '1'	Intra-uterine discharge home, with birth in maternal intensive care hospital	yesno 1 Yes 0 No
13	back_date Show the field ONLY if: [iut] = '1' and ([back] = '1' or [home] = '1')	Date of transfer/discharge	text (date_dmy), Identifier
14	back_w	Gestational age at transfer (weeks)	calc Calculation: rounddown(roundup (280-datediff([back_date], [date_due], "d", "dmy"), 0)/7, 0) Field Annotation: @HIDDEN
15	back_days	Gestational age at transfer (days)	calc Calculation: roundup(280-datediff ([back_date], [date_due], "d", "dmy"), 0) - (rounddown(roundup(280-datediff([back_date], [date_due], "d", "dmy"),0)/7, 0)*7) Field Annotation: @HIDDEN
16	ga_trans Show the field ONLY if: [iut] = '1' and [back] = '1'	Gestational age at transfer: [back_w] weeks [back_days] day(s)	descriptive
17	g	Gravida	text (number, Min: 1), Required
18	p	Para	text (number), Required

19	art	Fertility treatment	dropdown 0, No 1, ICSI/IVF 2, Ovulation induction 3, KID 4, Donor egg 5, IUI
20	pb_history	History of preterm birth *Preterm birth due to spontaneous preterm labour or PPROM*	dropdown, Required 0, No 1, Immature (< 24 weeks) 2, Extreme (24w - 27w6d) 3, Very (28w - 31w6d) 4, Moderate to late (32w - 36w6d) 5, More than one 99, Not applicable (P0)
21	diab	Diabetes	dropdown 0, No 1, Diabetes gravidarum, diet 2, Diabetes gravidarum, insulin 3, Diabetes type I 4, Diabetes type II, metformin 5, Diabetes type II, insulin 6, Diabetes type II, metformin and insulin 7, Diabetes type MODY
22	length	Maternal length (cm)	text (number, Min: 100, Max: 200)
23	weight_1	Maternal weight before/at start pregnancy (kg)	text (number, Min: 30, Max: 190)
24	bmi_1	BMI before/at start pregnancy	calc Calculation: [weight_1]*10000/ ([length]*[length])
25	weight_2	Maternal weight before delivery (kg)	text (number, Min: 30, Max: 190)
26	bmi_2	BMI before delivery	calc Calculation: [weight_2]*10000/ ([length]*[length])
27	race	Race	dropdown, Identifier 0, White 1, Black 2, Asian 3, Other 98, Not available

28	edu	Education *see COS record*	dropdown 0, No education 1, Primary 2, Secondary 3, Bachelor 4, Master 98, Not available
29	lang	Language *see COS record*	dropdown, Identifier 1, Dutch 2, French 3, English 4, Turkish 5, Arabic 6, 2 or more languages spoken, including Dutch 7, 2 or more languages spoken, not including Dutch 8, Other 98, Not available
30	demographics_mother_complete	Section Header: *Form Status* Complete?	dropdown 0, Incomplete 1, Unverified 2, Complete
Instrument: **Usus** (usus)			
31	smok	Smoking *When stop smoking: indicate number of cigarettes before stop*	dropdown 0, Never smoked 1, 1-10 cig/d 2, 11-20 cig/d 3, > 20 cig/d 4, Number before stop unknown
32	smok_stop	Time of smoking cessation	dropdown 0, Before conception 1, At positive pregnancy test 2, 1st trimester 3, 2nd trimester 4, 3th trimester 98, Not available 99, Not applicable (never smoked/currently smoking)

33	alcohol	Alcohol abusus during pregnancy	dropdown 0 No 3 Yes, < 1U/d 1 Yes, 2-4U/d 2 Yes, >= 5U/d 98 Unknown
34	drug	Drug abusus	dropdown 0 No 1 Cannabis 2 Cocain 3 Heroin 4 Methadon 5 Other 98 Unknown
35	usus_complete	Section Header: *Form Status* Complete?	dropdown 0 Incomplete 1 Unverified 2 Complete
Instrument: **History** (history)			
36	sectio	History of sectio caesarea	dropdown 1 Yes 0 No 99 Not applicable (P0)
37	curettage	History of curettage	dropdown 1 Yes 0 No 98 Unknown (patient had an abortion but curettage no explicitly in file)
38	lletz	History of Large Loop Excision of Transformation Zone	yesno 1 Yes 0 No
39	coni	History of cold knife conisation	yesno 1 Yes 0 No
40	surg_septum	History of excision uterine septum	yesno 1 Yes 0 No

41	surg_adhesio	History of intra-uterine adhesiolysis	yesno 1 Yes 0 No Field Annotation: Asherman
42	utmyom	Uterus myomatosus	yesno 1 Yes 0 No
43	surg_myom	History of myomectomy	yesno 1 Yes 0 No
44	utanomaly	Uterus anomaly (uterus unicornis, bicornis, septatus, ...)	dropdown 1 Yes 0 No/undiagnosed 2 Diagnosis in index pregnancy 3 Corrected
45	history_complete	Section Header: *Form Status* Complete?	dropdown 0 Incomplete 1 Unverified 2 Complete
Instrument: **Pathology at admission** (pathology_at_admission)			
46	spl	Spontaneous preterm labour *Spontaneous onset of contractions/symptoms + cervical change before 34 weeks of gestational age; PPROM excluded*	yesno, Required 1 Yes 0 No
47	pprom	Preterm prelabour rupture of membranes	yesno, Required 1 Yes 0 No
48	pprom_date	Date of preterm prelabour rupture of membranes *Before/at admission OR during admission*	text (date_dmy) Field Annotation: Date of PPROM at or during admission
49	pe	Preeclampsia or growth restriction	yesno 1 Yes 0 No
50	type_pi Show the field ONLY if: [pe] = '1'	Type	checkbox 1 type_pi___1 Preeclampsia 2 type_pi___2 IUGR/doppler abnormalities 3 type_pi___3 HELLP
51	praevia	Placenta praevia	yesno 1 Yes 0 No

52	uti	Urinary tract infection *Positive urine sediment or culture*	dropdown 1, Yes 0, No 98, Not available
53	infect	Infection other than urogenital *Appendicitis, gastro-enteritis, ...*	yesno 1, Yes 0, No
54	pathology_at_admission_complete	Section Header: *Form Status* Complete?	dropdown 0, Incomplete 1, Unverified 2, Complete
Instrument: **Swabs** (swabs)			
55	swab	Section Header: *Antenatal* Vaginal culture swab at admission *Positive = antibiogram available*	dropdown, Required 0, Negative 1, E. coli 2, Enterobacter other than E. coli 3, Candida 4, Bacterial vaginosis 5, P. mirabilis 6, L. monocytogenes 8, Mycoplasma genitalium 9, Ureaplasma urealyticum 7, Other 98, Not available 99, Not applicable (no SPL/PPROM)
56	chlamydia	Chlamydia PCR at admission	dropdown 0, Negative 1, Positive 98, Not available 99, Not applicable
57	gbs	Rectovaginal swab for group B streptococci	dropdown, Required 0, Negative 1, Positive 98, Not available 99, Not applicable (primary caesarean)

58	pswab_f Show the field ONLY if: [back] <> '1' and ([spl] = '1' or [pprom] = '1' or [pprom_date] <> '')	Section Header: *Postnatal* Swab fetal side placenta *if more than one: indicate the most abundant or most relevent species*	dropdown 0, Negative 1, E. coli 2, Enterobacter other than E. coli 3, GBS 4, L. monocytogenes 5, P. mirabilis 6, Other 98, Not available
59	pswab_m Show the field ONLY if: [back] <> '1' and ([spl] = '1' or [pprom] = '1' or [pprom_date] <> '')	Swab maternal side placenta *if more than one: indicate the most abundant or most relevent species*	dropdown 0, Negative 1, E. coli 2, Enterobacter other than E. coli 3, GBS 4, L. monocytogenes 5, P. mirabilis 6, Other 98, Not available
60	swabs_complete	Section Header: *Form Status* Complete?	dropdown 0, Incomplete 1, Unverified 2, Complete
Instrument: **Symptoms at presentation** (symptoms_at_presentation)			
61	dt9 Show the field ONLY if: [spl] <> '1' and [ppro m] <> '1'	Only in case of spontaneous preterm labour or preterm prelabour rupture of membranes, you will be able to fill in this form.	descriptive
62	onlyghent	ONLY FOR GHENT UNIVERSITY HOSPITAL other hospitals are free to fill in or not	descriptive
63	s_contr_reg Show the field ONLY if: [spl] = '1' or [pprom] = '1'	Regular contractions	dropdown 0, No 1, Yes 98, Not available
64	s_contr_irreg Show the field ONLY if: [spl] = '1' or [pprom] = '1'	Irregular contractions	dropdown 0, No 1, Yes 98, Not available

65	s_blood Show the field ONLY if: [spl] = '1' or [pprom] = '1'	Vaginal blood loss	dropdown 0, No 1, Yes 98, Not available
66	s_pain Show the field ONLY if: [spl] = '1' or [pprom] = '1'	Aspecific abdominal pain, other than contractions	dropdown 0, No 1, Yes 98, Not available
67	toco Show the field ONLY if: [spl] = '1' or [pprom] = '1'	Tocography	dropdown 0, Negative 1, Regular contractions 2, Irregular contractions 3, Not interpretable 98, Not available
68	symptoms_at_presentation_complete	Section Header: *Form Status* Complete?	dropdown 0, Incomplete 1, Unverified 2, Complete
Instrument: **Antihypertensive medication** (antihypertensive_medication)			
69	placinsuff Show the field ONLY if: [pe] <> '1'	Only in case of placental insufficiency, you will be able to fill in this form.	descriptive
70	antihyper Show the field ONLY if: [pe] = '1'	Class of medication *MgSO4 is not considered as antihypertensive medication*	radio 0, No antihypertensive medication 1, Methyldopa 2, Beta-blockers 3, Calcium antagonist 4, Dihydralazine 5, Diuretics 6, Ketanserin 7, Combination 8, Start methyldopa, switch to other 9, Start beta-blocker, switch to other 10, Other option

71	antihyper_other Show the field ONLY if: [pe] = '1'	Write down dose and dosage of medication If a combination, a switch to other or another option is given, please write down the class of antihypertensive medication given	notes
72	antihypertensive_medication_complete	Section Header: *Form Status* Complete?	dropdown 0 Incomplete 1 Unverified 2 Complete
Instrument: **Tocolysis** (tocolysis)			
73	tocolysis	Tocolysis	yesno, Required 1 Yes 0 No
74	toco_tot Show the field ONLY if: [tocolysis] = '1'	Total number of courses of tocolysis	dropdown, Required 1 1 course 2 2 courses 3 3 courses 4 4 courses
75	tocom Show the field ONLY if: [tocolysis] = '1'	Maintenance tocolysis *Course > 48 hours*	yesno, Required 1 Yes 0 No
76	tococ Show the field ONLY if: [tocolysis] = '1'	Combination tocolysis	yesno, Required 1 Yes 0 No
77	toco1 Show the field ONLY if: [tocolysis] = '1' and ([toco_tot] = '1' or [toco_tot] = '2' or [toco_tot] = '3' or [toco_tot] = '4')	Date of start first course of tocolysis	text (date_dmy)
78	toco_a_1 Show the field ONLY if: [tocolysis] = '1' and ([toco_tot] = '1' or [toco_tot] = '2' or [toco_tot] = '3' or [toco_tot] = '4')	Type of tocolysis used for first course: atosiban	dropdown 1 Yes 0 No 2 In combination with other tocolytics 3 Maintenance 4 Switch after nifidepine

79	toco_n_1 Show the field ONLY if: [tocolysis] = '1' and ([toco_tot] = '1' or [toco_tot] = '2' or [toco_tot] = '3' or [toco_tot] = '4')	Type of tocolysis used for first course: nifedipine	dropdown 1, Yes 0, No 2, In combination with other tocolytics 3, Maintenance
80	toco_r_1 Show the field ONLY if: [tocolysis] = '1' and ([toco_tot] = '1' or [toco_tot] = '2' or [toco_tot] = '3' or [toco_tot] = '4')	Type of tocolysis used for first course: ritodrine	dropdown 1, Yes 0, No 2, In combination with other tocolytics 3, Maintenance
81	toco_i_1 Show the field ONLY if: [tocolysis] = '1' and ([toco_tot] = '1' or [toco_tot] = '2' or [toco_tot] = '3' or [toco_tot] = '4')	Type of tocolysis used for first course: indomethacine	dropdown 1, Yes 0, No 2, In combination with other tocolytics 3, Maintenance
82	toco2 Show the field ONLY if: [tocolysis] = '1' and ([toco_tot] = '2' or [toco_tot] = '3' or [toco_tot] = '4')	Date of start second course of tocolysis	text (date_dmy)
83	toco_a_2 Show the field ONLY if: [tocolysis] = '1' and ([toco_tot] = '2' or [toco_tot] = '3' or [toco_tot] = '4')	Type of tocolysis used for second course: atosiban	dropdown 1, Yes 0, No 2, In combination with other tocolytics 3, Maintenance 4, Switch after nifidepine
84	toco_n_2 Show the field ONLY if: [tocolysis] = '1' and ([toco_tot] = '2' or [toco_tot] = '3' or [toco_tot] = '4')	Type of tocolysis used for second course: nifedipine	dropdown 1, Yes 0, No 2, In combination with other tocolytics 3, Maintenance

85	toco_r_2 Show the field ONLY if: [tocolysis] = '1' and ([toco_tot] = '2' or [toco_tot] = '3' or [toco_tot] = '4')	Type of tocolysis used for second course: ritodrine	dropdown 1, Yes 0, No 2, In combination with other tocolytics 3, Maintenance
86	toco_i_2 Show the field ONLY if: [tocolysis] = '1' and ([toco_tot] = '2' or [toco_tot] = '3' or [toco_tot] = '4')	Type of tocolysis used for second course: indomethacine	dropdown 1, Yes 0, No 2, In combination with other tocolytics 3, Maintenance
87	toco3 Show the field ONLY if: [tocolysis] = '1' and ([toco_tot] = '3' or [toco_tot] = '4')	Date of start third course of tocolysis	text (date_dmy)
88	toco_a_3 Show the field ONLY if: [tocolysis] = '1' and ([toco_tot] = '3' or [toco_tot] = '4')	Type of tocolysis used for third course: atosiban	dropdown 1, Yes 0, No 2, In combination with other tocolytics 3, Maintenance 4, Switch after nifidepine
89	toco_n_3 Show the field ONLY if: [tocolysis] = '1' and ([toco_tot] = '3' or [toco_tot] = '4')	Type of tocolysis used for third course: nifedipine	dropdown 1, Yes 0, No 2, In combination with other tocolytics 3, Maintenance
90	toco_r_3 Show the field ONLY if: [tocolysis] = '1' and ([toco_tot] = '3' or [toco_tot] = '4')	Type of tocolysis used for third course: ritodrine	dropdown 1, Yes 0, No 2, In combination with other tocolytics 3, Maintenance
91	toco_i_3 Show the field ONLY if: [tocolysis] = '1' and ([toco_tot] = '3' or [toco_tot] = '4')	Type of tocolysis used for third course: indomethacine	dropdown 1, Yes 0, No 2, In combination with other tocolytics 3, Maintenance

92	toco4 Show the field ONLY if: [tocolysis] = '1' and [toco_tot] = '4'	Date of start fourth course of tocolysis	text (date_dmy)
93	toco_a_4 Show the field ONLY if: [tocolysis] = '1' and [toco_tot] = '4'	Type of tocolysis used for fourth course: atosiban	dropdown 1 Yes 0 No 2 In combination with other tocolytics 3 Maintenance 4 Switch after nifidepine
94	toco_n_4 Show the field ONLY if: [tocolysis] = '1' and [toco_tot] = '4'	Type of tocolysis used for fourth course: nifedipine	dropdown 1 Yes 0 No 2 In combination with other tocolytics 3 Maintenance
95	toco_r_4 Show the field ONLY if: [tocolysis] = '1' and [toco_tot] = '4'	Type of tocolysis used for fourth course: ritodrine	dropdown 1 Yes 0 No 2 In combination with other tocolytics 3 Maintenance
96	toco_i_4 Show the field ONLY if: [tocolysis] = '1' and [toco_tot] = '4'	Type of tocolysis used for fourth course: indomethacine	dropdown 1 Yes 0 No 2 In combination with other tocolytics 3 Maintenance
97	tocolysis_complete	Section Header: *Form Status* Complete?	dropdown 0 Incomplete 1 Unverified 2 Complete
Instrument: **Cervix** (cervix)			
98	dt10 Show the field ONLY if: [spl] <> '1' and [ppro m] <> '1' and [tocoly sis] <> '1'	Only in case of spontaneous preterm labour, preterm prelabour rupture of membranes or use of tocolysis, you will be able to fill in this form.	descriptive

99	def_fun Show the field ONLY if: [spl] = '1' or [pprom] = '1' or [tocolysis] = '1'	Funneling is a protrusion of the amniotic membranes of 5 mm or more into the internal os as measured along the lateral border of the funnel.	descriptive
100	cl1 Show the field ONLY if: [spl] = '1' or [pprom] = '1' or [tocolysis] = '1'	Cervical length at start tocolysis / at admission (mm) *if there is dilatation, leave blank; if cervical length and dilatation are unknown before start tocolysis, write 98*	text (number) Field Annotation: @HIDDEN
101	fun1 Show the field ONLY if: [spl] = '1' or [pprom] = '1' or [tocolysis] = '1'	Funneling at start tocolysis / at admission (mm) *if there is dilatation, leave blank; if cervical length and dilatation are unknown before start tocolysis, write 98*	text (number) Field Annotation: @HIDDEN
102	d1 Show the field ONLY if: [spl] = '1' or [pprom] = '1' or [tocolysis] = '1'	Dilatation at start tocolysis / at admission (cm) *leave blank if no digital examination was performed; if cervical length and dilatation are unknown before start tocolysis, write 98*	text (number) Field Annotation: @HIDDEN
103	cl_adm Show the field ONLY if: [spl] = '1' or [pprom] = '1' or [tocolysis] = '1'	Cervical length at admission (mm) *if there is dilatation, leave blank; if cervical length and dilatation are unknown before start tocolysis, write 98*	text (number)
104	funyn_adm Show the field ONLY if: [spl] = '1' or [pprom] = '1' or [tocolysis] = '1'	Funneling at admission	radio 0, No 1, Yes 2, Not available
105	fun_adm Show the field ONLY if: ([spl] = '1' or [ppro m] = '1' or [tocolysis] = '1') and [fun_adm] <> ''	Funneling at admission (mm) *if there is dilatation, leave blank; if cervical length and dilatation are unknown before start tocolysis, write 98*	text (number) Field Annotation: @READONLY
106	d_adm Show the field ONLY if: [spl] = '1' or [pprom] = '1' or [tocolysis] = '1'	Dilatation at admission (cm) *leave blank if no digital examination was performed; if cervical length and dilatation are unknown before start tocolysis, write 98*	text (number)

107	cl_start Show the field ONLY if: [tocolysis] = '1'	Cervical length at start tocolysis (mm) *if there is dilatation, leave blank; if cervical length and dilatation are unknown before start tocolysis, write 98*	text (number)
108	fun_start Show the field ONLY if: [tocolysis] = '1' and [fun_start] <> ''	Funneling at start tocolysis (mm) *if there is dilatation, leave blank; if cervical length and dilatation are unknown before start tocolysis, write 98*	text (number) Field Annotation: @READONLY
109	d_start Show the field ONLY if: [tocolysis] = '1'	Dilatation at start tocolysis (cm) *leave blank if no digital examination was performed; if cervical length and dilatation are unknown before start tocolysis, write 98*	text (number)
110	cl2 Show the field ONLY if: [tocolysis] = '1' and ([toco_tot] = '2' or [toco_tot] = '4' or [toco_tot] = '3')	Cervical length before second course of tocolysis (mm) *if there is dilatation, leave blank; if cervical length and dilatation are unknown before start tocolysis, write 98*	text (number)
111	fun2 Show the field ONLY if: [tocolysis] = '1' and ([toco_tot] = '2' or [toco_tot] = '4' or [toco_tot] = '3') and [fun2] <> ''	Funneling before second course of tocolysis (mm) *if there is dilatation, leave blanc; if cervical length and dilatation are unknown before start tocolysis, write 98*	text (number) Field Annotation: @READONLY
112	d2 Show the field ONLY if: [tocolysis] = '1' and ([toco_tot] = '2' or [toco_tot] = '3' or [toco_tot] = '4')	Dilatation before second course of tocolysis (cm) *leave blank if no digital examination was performed; if cervical length and dilatation are unknown before start tocolysis, write 98*	text (number)
113	cl3 Show the field ONLY if: [tocolysis] = '1' and ([toco_tot] = '3' or [toco_tot] = '4')	Cervical length before third course of tocolysis (mm) *if there is dilatation, leave blank; if cervical length and dilatation are unknown before start tocolysis, write 98*	text (number)
114	fun3 Show the field ONLY if: [tocolysis] = '1' and ([toco_tot] = '3' or [toco_tot] = '4') and [fun3] <> ''	Funneling before third course of tocolysis (mm) *if there is dilatation, leave blank; if cervical length and dilatation are unknown before start tocolysis, write 98*	text (number) Field Annotation: @READONLY

115	d3 Show the field ONLY if: [tocolysis] = '1' and ([toco_tot] = '3' or [toco_tot] = '4')	Dilatation before third course of tocolysis (cm) *leave blank if no digital examination was performed; if cervical length and dilatation are unknown before start tocolysis, write 98*	text (number)
116	cervix_complete	Section Header: *Form Status* Complete?	dropdown 0 Incomplete 1 Unverified 2 Complete
Instrument: **Biomarker** (biomarker)			
117	dt11 Show the field ONLY if: [spl] <> '1' and [tocolysis] <> '1'	Only in case of spontaneous preterm labour or use of tocolysis, you will be able to fill in this form.	descriptive
118	bio_usage Show the field ONLY if: [spl] = '1' or [tocolysis] ='1'	Usage of a biomarker test for preterm labour	yesno 1 Yes 0 No
119	bio Show the field ONLY if: [bio_usage] = '1'	Type of biomarker	dropdown, Required 0 Fibronectin 1 Actim Partus 2 Partosure
120	bio_result Show the field ONLY if: [bio_usage] = '1'	Result biomarker test	dropdown, Required 1 Positive 0 Negative Field Annotation: irrespective of indication based on cervical length/dilatation
121	biomarker_complete	Section Header: *Form Status* Complete?	dropdown 0 Incomplete 1 Unverified 2 Complete
Instrument: **C-reactive protein** (creactive_protein)			
122	dt12 Show the field ONLY if: [spl] <> '1' and [ppprom] <> '1' and [tocolysis] <> '1' and [uti] <> '1' and [infect] <> '1'	Only in case of spontaneous preterm labour, preterm prelabour rupture of membranes, use of tocolysis or infectious diseases, you will be able to fill in this form.	descriptive

123	crp1 Show the field ONLY if: [spl] = '1' or [pprom] = '1' or [tocolysis] = '1' or [uti] = '1' or [infect] = '1'	CRP at start first course of tocolysis (preferably)/at admission (mg/L) *998 = not available*	text (number), Required Field Annotation: @HIDDEN
124	crp1_toco Show the field ONLY if: [toco_tot] = '1' or [toco_tot] = '2' or [toco_tot] = '3' or [toco_tot] = '4'	CRP at start first course of tocolysis (mg/L) *998 = not available*	text (number)
125	crp_adm	CRP at admission (mg/L) *998 = not available*	text (number), Required
126	crp2 Show the field ONLY if: [toco_tot] = '2' or [toco_tot] = '3' or [toco_tot] = '4'	CRP at start second course of tocolysis (mg/L) *998 = not available*	text (number)
127	crp3 Show the field ONLY if: [toco_tot] = '3' or [toco_tot] = '4'	CRP at start third course of tocolysis (mg/L) *998 = not available*	text (number)
128	creactive_protein_complete	Section Header: *Form Status* Complete?	dropdown 0 Incomplete 1 Unverified 2 Complete
Instrument: **MgSO4** (mgso4)			
129	mg_pe	Section Header: *Prevention eclampsia* MgSO4 indication preëclampsia	yesno, Required 1 Yes 0 No
130	mg_np	Section Header: *Neuroprotection* MgSO4 indication neuroprotection, first course *When already MgSO4 for preeclampsia: fill in yes when delivery < 32w (MIC Genk: 34w)*	yesno, Required 1 Yes 0 No
131	mg_np_2 Show the field ONLY if: [mg_np] = '1'	MgSO4 indication neuroprotection, second course	yesno 1 Yes 0 No Field Annotation: fill in yes when already MgSO4 for preeclampsia and delivery < 32w

132	mg_np_3 Show the field ONLY if: [mg_np] = '1' and [mg_np_2] = '1'	MgSO4 indication neuroprotection, third course	yesno 1 Yes 0 No Field Annotation: fill in yes when already MgSO4 for preeclampsia and delivery < 32w
133	mg_np_4 Show the field ONLY if: [mg_np] = '1' and [mg_np_2] = '1' and [mg_np_3] = '1'	MgSO4 indication neuroprotection, fourth course	yesno 1 Yes 0 No Field Annotation: fill in yes when already MgSO4 for preeclampsia and delivery < 32w
134	mgso4_complete	Section Header: *Form Status* Complete?	dropdown 0 Incomplete 1 Unverified 2 Complete
Instrument: **Neuroprotection in detail** (neuroprotection_in_detail)			
135	dt13	Only in case of administration of MgSO4, this form will appear.	descriptive
136	mg_conc	Mg concentration (mmol/L) *Last available value, under MgSO4, before delivery*	text (number)
137	lab_date	Date and time of lab with Mg concentration	text (datetime_dmy)
138	creat	Creatinine (mg/dL) (new value) *Last value available, before delivery*	text (number)
139	lab_date_creat	Date and time of lab with creatinine value	text (datetime_dmy)
140	mg_start1 Show the field ONLY if: [mg_pe] = '1' or [mg_np] = '1' or [mg_np_2] = '1' or [mg_np_3] = '1' or [mg_np_4] = '1'	Startdate and -time of first course of neuroprotection	text (datetime_dmy)
141	mg_stop1 Show the field ONLY if: [mg_pe] = '1' or [mg_np] = '1' or [mg_np_2] = '1' or [mg_np_3] = '1' or [mg_np_4] = '1'	Stopdate and -time of first course of neuroprotection	text (datetime_dmy)

142	mg_duration_1 Show the field ONLY if: [mg_pe] = '1' or [mg_np] = '1' or [mg_np_2] = '1' or [mg_np_3] = '1' or [mg_np_4] = '1'	Duration of MgSO4 administration, first course (minutes)	calc Calculation: datediff([mg_stop1], [mg_start1], "m","dmy")
143	mg_start2 Show the field ONLY if: [mg_np_2] = '1' or [mg_np_3] = '1' or [mg_np_4] = '1'	Startdate and -time of second course of neuroprotection	text (datetime_dmy)
144	mg_stop2 Show the field ONLY if: [mg_np_2] = '1' or [mg_np_3] = '1' or [mg_np_4] = '1'	Stopdate and -time of second course of neuroprotection	text (datetime_dmy)
145	mg_duration_2 Show the field ONLY if: [mg_np_2] = '1' or [mg_np_3] = '1' or [mg_np_4] = '1'	Duration of MgSO4 administration, second course (minutes)	calc Calculation: datediff([mg_stop2], [mg_start2], "m","dmy")
146	mg_start3 Show the field ONLY if: [mg_np_3] = '1' or [mg_np_4] = '1'	Startdate and -time of third course of neuroprotection	text (datetime_dmy)
147	mg_stop3 Show the field ONLY if: [mg_np_3] = '1' or [mg_np_4] = '1'	Stopdate and -time of third course of neuroprotection	text (datetime_dmy)
148	mg_duration_3 Show the field ONLY if: [mg_np_3] = '1' or [mg_np_4] = '1'	Duration of MgSO4 administration, third course (minutes)	calc Calculation: datediff([mg_stop3], [mg_start3], "m","dmy")
149	mg_start4 Show the field ONLY if: [mg_np_4] = '1'	Startdate and -time of fourth course of neuroprotection	text (datetime_dmy)
150	mg_stop4 Show the field ONLY if: [mg_np_4] = '1'	Stopdate and -time of fourth course of neuroprotection	text (datetime_dmy)

151	mg_duration_4 Show the field ONLY if: [mg_np_4] = '1'	Duration of MgSO4 administration, fourth course (minutes)	calc Calculation: datediff([mg_stop4], [mg_start4], "m","dmy")
152	totalmag Show the field ONLY if: [mg_pe] = '1' or [mg_np] = '1' or [mg_np_2] = '1' or [mg_np_3] = '1' or [mg_np_4] = '1'	Total maternal dose (g)	text
153	neuroprotection_in_detail_complete	Section Header: *Form Status* Complete?	dropdown 0, Incomplete 1, Unverified 2, Complete
Instrument: **Prevention** (prevention)			
154	dt15 Show the field ONLY if: [spl] <> '1' and [pprom] <> '1' and [pprom_date] = ''	Only in case of spontaneous preterm labour or preterm prelabour rupture of membranes, you will be able to fill in this form.	descriptive
155	prog Show the field ONLY if: [spl] = '1' or [pprom] = '1' or [pprom_date] <> ''	Progesterone	yesno 1, Yes 0, No
156	utrop Show the field ONLY if: [prog] = '1'	Progesterone, primary prevention preterm birth, start at 12-16w	dropdown 1, Yes 0, No
157	utros Show the field ONLY if: [prog] = '1' and [utrop] = '0'	Progesterone, secondary prevention preterm birth, start at 19-26w	dropdown 1, Yes 0, No
158	utrot Show the field ONLY if: [prog] = '1' and [utrop] = '0' and [utros] = '0'	Progesterone, tertiary prevention preterm birth, start after tocolysis	dropdown 1, Yes 0, No

159	utrod Show the field ONLY if: [prog] = '1'	Progesterone, dosage	dropdown 1, 1dd 200 mg 2, 2dd 200 mg 3, 3dd 200 mg 4, Other dosage 98, Not available
160	utror Show the field ONLY if: [prog] = '1'	Progesterone, route of administration	dropdown 1, Per os 2, Per vaginam 3, Both routes during index pregnancy 98, Not available
161	cerclage Show the field ONLY if: [spl] = '1' or [pprom] = '1' or [pprom_date] <> ''	Cerclage during index pregnancy *Primary = prophylactic cerclage based on history at 10-16 weeks Secondary = cerclage before 24 weeks for cervical length < 25 mm Tertiary = cerclage before 24 weeks for cervical dilatation with exposition of the membranes*	dropdown 0, No 1, Primary 2, Secondary 3, Tertiary 4, Abdominal
162	arabin Show the field ONLY if: [spl] = '1' or [pprom] = '1' or [pprom_date] <> ''	Arabin pessary	yesno 1, Yes 0, No
163	prevention_complete	Section Header: *Form Status* Complete?	dropdown 0, Incomplete 1, Unverified 2, Complete
Instrument: **Fetal lung maturation** (fetal_lung_maturation)			
164	acs	Antenatal corticosteroids	yesno, Required 1, Yes 0, No
165	typeacs Show the field ONLY if: [acs] = '1'	Type of antenatal corticosteroid	dropdown 0, Betamethasone 1, Dexamethasone 98, Unknown
166	celw Show the field ONLY if: [acs] = '1'	Weekly repeat course of antenatal corticosteroids (ACS) *not applicable = born < 1 week after first course / term related (in UZ Gent: no indication for weekly courses)*	radio, Required 1, Yes 0, No 99, Not applicable

167	celr Show the field ONLY if: [acs] = '1'	Repeat course of antenatal corticosteroids *not applicable = born < 1 week after first course / term related (in UZ Ghent: indication for weekly courses)*	radio, Required 1 Yes 0 No 99 Not applicable
168	cel_tot	Number of courses of antenatal corticosteroids	radio, Required 0 No course 12 1 complete course (2x 12 mg beta or 4x 6 mg dexa or 2x 15 mg dexa) 11 1 incomplete first course (1x 12 mg beta or < 4x 6mg dexa or 1x 15 mg dexa) 22 2 complete courses (2x (2x12 mg) beta or 2x (4x6 mg dexa or 2x (2x15 mg dexa)) 5 1 complete and 1 incomplete repeat course 21 1 weekly repetition (2x 12 mg + 1x 12 mg beta or 4x 6 mg + 2x 6 mg dexa or 2x 15 mg + 1x 15 mg dexa) 3 2 weekly repetitions (2x 12 mg + 2x (1x 12 mg) beta or 4x 6 mg + 2x (2x 6mg) dexa or 2x 15 mg + 2x (1x 15 mg) dexa) 4 3 weekly repetitions (2x 12 mg + 3x (1x 12 mg) beta or 4x 6 mg + 3x (3x 6mg) dexa or 2x 15 mg + 3x (1x 15 mg) dexa)
169	celd1 Show the field ONLY if: [acs] = '1'	Date of first course antenatal corticosteroids *betamethasone: 2x12 mg or dexamethasone: 4x6 mg*	text (date_dmy), Required
170	celh1 Show the field ONLY if: [acs] = '1'	Hour of first injection of first course of ACS	text (time) Field Annotation: 01:01 = not applicable blanc it not available
171	cel_interval1 Show the field ONLY if: [acs] = '1'	Duration of interval	radio 1 12h 2 24h 3 Incomplete course 4 Unknown 5 Not applicable (dexa)

172	celd22 Show the field ONLY if: [acs] = '1' and ([cel_tot] = '22' or [cel_tot] = '5')	Date of second course antenatal corticosteroids *betamethasone: 2x12 mg or dexamethasone: 4x6 mg*	text (date_dmy), Required
173	celh22 Show the field ONLY if: [acs] = '1' and ([cel_tot] = '22' or [cel_tot] = '5')	Hour of first injection of second course of ACS	text (time) Field Annotation: 01:01 = not applicable blanc of not available
174	cel_interval2 Show the field ONLY if: [acs] = '1' and [cel_tot] = '22'	Duration of interval	radio 1, 12h 2, 24h 3, Incomplete course 4, Unknown 5, Not applicable (dexa 4 x 6 mg)
175	celd21 Show the field ONLY if: [acs] = '1' and ([cel_tot] = '21' or [cel_tot] = '3' or [cel_tot] = '4')	Date of first weekly administration of antenatal corticosteroids *betamethasone: 2x12 mg or dexamethasone: 4x6 mg*	text (date_dmy), Required
176	celh21 Show the field ONLY if: [acs] = '1' and ([cel_tot] = '21' or [cel_tot] = '3' or [cel_tot] = '4')	Hour of first weekly repeat injection	text (time) Field Annotation: 01:01 = not applicable blanc if not available
177	celd3 Show the field ONLY if: [acs] = '1' and ([cel_tot] = '3' or [cel_tot] = '4')	Date of second weekly administration of antenatal corticosteroids *betamethasone: 2x12 mg or dexamethasone: 4x6 mg*	text (date_dmy), Required
178	celh3 Show the field ONLY if: [acs] = '1' and ([cel_tot] = '3' or [cel_tot] = '4')	Hour of second weekly repeat injection	text (time) Field Annotation: 01:01 = not applicable blanc if not available
179	celd4 Show the field ONLY if: [acs] = '1' and [cel_tot] = '4'	Date of third weekly administration of antenatal corticosteroids *betamethasone: 2x12 mg or dexamethasone: 4x6 mg*	text (date_dmy), Required

180	celh4 Show the field ONLY if: [acs] = '1' and [cel_tot] = '4'	Hour of third weekly repeat injection	text (time) Field Annotation: 01:01 = not applicable blanc if not available
181	fetal_lung_maturation_complete	Section Header: *Form Status* Complete?	dropdown 0, Incomplete 1, Unverified 2, Complete
Instrument: **Antibiotics** (antibiotics)			
182	ab_maint	Maintenance antibiotics in setting of PPROM or exposed membranes	dropdown 0, No 1, Yes, erythromycin 2, Yes, clarithromycin 3, Yes, ampicillin 4, Yes, ampicillin and gentamycin 5, Yes, amoxicillin with clavulanic acid 6, Yes, azithromycin and amoxicillin 7, Yes, azithromycin 8, Yes, josamycin 99, Not applicable
183	ab_mat	Maternal intake of antibiotics Excluded: - maintenance antibiotics (PPROM) - GBS prophylaxis - perioperative prophylaxis Included: switch to broader spectrum antibiotics (PPROM)	yesno 1, Yes 0, No
184	gbs_pro Show the field ONLY if: [back] <> '1'	GBS prophylaxis	dropdown 99, not indicated 0, indicated, not administred 1, indicated, complete prophylaxis (penicillin >= 4 hours before delivery) 2, indicated, incomplete prophylaxis
185	exit	To continue: Save and Exit form, and start neonate data input.	descriptive

186	antibiotics_complete	Section Header: *Form Status* Complete?	dropdown 0, Incomplete 1, Unverified 2, Complete
Instrument: **Birth** (birth)			
187	dt3 Show the field ONLY if: [mother_arm_1][back] = '1'	If this instrument is almost empty, your patient has been transferred to the referral hospital and has given birth there.	descriptive
188	active	Active management: parental decision for intensive neonatal care when born at less than 26 weeks gestational age	dropdown 1, Yes 0, No 2, No decision made 99, > 26 weeks
189	date_birth Show the field ONLY if: [mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1'	Date of delivery	text (date_dmy), Identifier
190	birth_hour Show the field ONLY if: [mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1'	Hour of birth	text (time), Required
191	ga_w Show the field ONLY if: [mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1'	Gestational age at birth (weeks)	calc Calculation: rounddown(roundup(280-datediff([date_birth], [mother_arm_1][date_due], "d", "dmy", true), 0)/7, 0) Field Annotation: @HIDDEN
192	ga_d Show the field ONLY if: [mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1'	Gestational age at birth (days)	calc Calculation: roundup(280-datediff([date_birth], [mother_arm_1][date_due], "d", "dmy", true), 0) - (rounddown(roundup(280-datediff([date_birth], [mother_arm_1][date_due], "d", "dmy", true),0)/7, 0) *7) Field Annotation: @HIDDEN
193	ga Show the field ONLY if: [mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1'	Gestational age at birth: [ga_w] weeks [ga_d] day(s)	descriptive

194	present Show the field ONLY if: [mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1'	Fetal presentation	dropdown 1, Cephalic 2, Breech 3, Transverse
195	vb Show the field ONLY if: [mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1'	Vaginal birth	yesno, Required 1, Yes 0, No
196	ps Show the field ONLY if: [vb] = '0'	Primary caesarean section *No labour; intact membranes*	yesno, Required 1, Yes 0, No
197	ss Show the field ONLY if: [vb] = '0' and [ps] = '0'	Secondary caesarean section *Caesarean section during labour and/or after rupture of membranes (with or without contractions)*	yesno, Required 1, Yes 0, No
198	iol Show the field ONLY if: ([mother_arm_1][back] <> '1' AND [vb] ='1') or ([vb] = '0' and [ps] = '0')	Induction of labour	radio 0, No 1, Yes
199	lifebirth Show the field ONLY if: [mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1'	Neonate born alive	yesno, Required 1, Yes 0, No
200	birth_weight Show the field ONLY if: [mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1'	Birth weight (g)	text (number, Min: 300, Max: 5500), Required
201	iugr Show the field ONLY if: [mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1'	Intra uterine growth restriction *True birth weight < p10*	yesno 1, Yes 0, No

202	birth_length Show the field ONLY if: [mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1'	Length at birth (cm)	text (number, Min: 15, Max: 60)
203	birth_headc Show the field ONLY if: [mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1'	Headcircumference at birth (cm)	text (number, Min: 15, Max: 50)
204	pha Show the field ONLY if: [mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1'	Umbilical cord arterial pH at birth	text (number)
205	bea Show the field ONLY if: [mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1'	Umbilical cord arterial base excess at birth	text (number)
206	phv Show the field ONLY if: [mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1'	Umbilical cord venous pH at birth	text (number)
207	bev Show the field ONLY if: [mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1'	Umbilical cord venous base excess at birth	text (number)
208	mec Show the field ONLY if: [mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1'	Meconium stained amniotic fluid	dropdown 1, Yes 0, No 98, Not available
209	poly Show the field ONLY if: [mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1'	Polyhydramnios *AFI > 20 cm and/or SDP > 8 and/or diagnosis in file*	yesno 1, Yes 0, No

210	apd_itis Show the field ONLY if: [mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1'	Histology of the placenta, inflammation	dropdown 0, No inflammation/infection 1, Chorionitis 2, Amnionitis 3, Funisitis 4, Chorioamnionitis with our without funisitis 98, Not available
211	apd_vasc Show the field ONLY if: [mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1'	Histology of the placenta, vascular events	dropdown 0, No vascular event 1, Vascular event 98, Not available
212	thread Show the field ONLY if: ([mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1') and ([mother_arm_1][cerclage] = '1' or [mother_arm_1][cerclage] = '2' or [mother_arm_1][cerclage] = '3')	Culture thread cerclage	dropdown 0, Negative 1, E. coli 2, Enterobacter other than E. coli 3, GBS 4, L. monocytogenes 5, P. mirabilis 6, Other 98, Not available
213	birth_complete	Section Header: *Form Status* Complete?	dropdown 0, Incomplete 1, Unverified 2, Complete
Instrument: **Demographics baby** (demographics_baby)			
214	dt2 Show the field ONLY if: [mother_arm_1][back] = '1'	If this instrument is empty, your patient has been transferred to the referral hospital and has given birth there.	descriptive
215	cos Show the field ONLY if: ([mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1') and [lifebirth] = '1'	COS number	text (number), Identifier

216	sex Show the field ONLY if: [mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1'	Sex of the child	dropdown, Required, Identifier 1, Male 2, Female
217	demographics_baby_complete	Section Header: *Form Status* Complete?	dropdown 0, Incomplete 1, Unverified 2, Complete
Instrument: **Neonatal morbidity** (neonatal_morbidity)			
218	dt14 Show the field ONLY if: [lifebirth] = '0' or [mother_arm_1][back] = '1'	If this form is empty, your patient - has been transferred to the referral hospital and has given birth there or - experienced an intrapartum death	descriptive
219	nicu_in Show the field ONLY if: ([mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1') and [lifebirth] = '1'	Date of admission at NICU [date_birth]	descriptive, Identifier
220	nicu_out Show the field ONLY if: ([mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1') and [lifebirth] = '1'	Date of discharge from NICU	text (date_dmy), Required, Identifier
221	disch_to Show the field ONLY if: ([mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1') and [lifebirth] = '1'	Discharge to	radio 1, Home 2, Maternity 3, Referral hospital 4, Neonatal mortality
222	rds Show the field ONLY if: ([mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1') and [lifebirth] = '1'	Section Header: *Respiratory system* Respiratory distress syndrome	yesno, Required 1, Yes 0, No

223	surf Show the field ONLY if: ([mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1') and [lifebirth] = '1'	Administration of surfactant	yesno 1 Yes 0 No
224	surfh Show the field ONLY if: [surf] = '1'	Time first administration surfactant	dropdown 1 < 2 hours after birth 2 2 - 6 hours 3 6 - 12 hours 4 > 12 hours
225	pnc Show the field ONLY if: ([mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1') and [lifebirth] = '1'	Postnatal administration of corticosteroids *Multiple answers possible*	checkbox 0 pnc___0 No 1 pnc___1 Yes, one course 2 pnc___2 Yes, two courses 3 pnc___3 Yes, three courses 4 pnc___4 Yes, maintenance
226	type_pnc Show the field ONLY if: [pnc(1)] = '1' or [pnc(2)] = '1' or [pnc(3)] = '1' or [pnc(4)] = '1'	Type of postnatal corticosteroids *Multiple answers possible*	checkbox 1 type_pnc___1 First course: dexamethasone 2 type_pnc___2 First course: hydrocortisone 3 type_pnc___3 Second course: dexamethasone 4 type_pnc___4 Second course: hydrocortisone 5 type_pnc___5 Third course: dexamethasone 6 type_pnc___6 Third course: hydrocortisone 7 type_pnc___7 Maintenance: dexamethasone 8 type_pnc___8 Maintenance: hydrocortisone
227	start_pnc_1 Show the field ONLY if: [pnc(1)] = '1' or [pnc(2)] = '1' or [pnc(3)] = '1'	Start date postnatal corticosteroids first course	text (date_dmy)
228	stop_pnc_1 Show the field ONLY if: [pnc(1)] = '1' or [pnc(2)] = '1' or [pnc(3)] = '1'	Stop date postnatal corticosteroids first course	text (date_dmy)

229	start_pnc_2 Show the field ONLY if: [pnc(2)] = '1' or [pnc(3)] = '1'	Start date postnatal corticosteroids second course	text (date_dmy)
230	stop_pnc_2 Show the field ONLY if: [pnc(2)] = '1' or [pnc(3)] = '1'	Stop date postnatal corticosteroids second course	text (date_dmy)
231	start_pnc_3 Show the field ONLY if: [pnc(3)] = '1'	Start date third course postnatal corticosteroids	text (date_dmy)
232	stop_pnc_3 Show the field ONLY if: [pnc(3)] = '1'	Stop date third course postnatal corticosteroids	text (date_dmy)
233	start_pnc_maint Show the field ONLY if: [pnc(4)] = '1'	Start date maintenance postnatal corticosteroids	text (date_dmy)
234	stop_pnc_maint Show the field ONLY if: [pnc(4)] = '1'	Stop date maintenance postnatal corticosteroids	text (date_dmy)
235	postnat_cort_stop Show the field ONLY if: [pnc(1)] = '1' or [pnc(2)] = '1' or [pnc(3)] = '1' or [pnc(4)] = '1'	Neonatal life day of final stop administration postnatal corticosteroids	text (number)
236	respsup Show the field ONLY if: ([mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1') and [lifebirth] = '1'	Need for respiratory support	yesno, Required 1, Yes 0, No
237	respsupmeth Show the field ONLY if: [respsup] = '1'	Respiratory support	checkbox, Required 1, respsupmeth___1, Nasal cannula 2, respsupmeth___2, CPAP 3, respsupmeth___3, Ventilation 4, respsupmeth___4, NO 5, respsupmeth___5, High frequency oscillation

238	o2 Show the field ONLY if: [respsup] = '1'	Total number of days of oxygen administration	text (number)
239	o2_stop Show the field ONLY if: [respsup] = '1'	Neonatal day of life of final stop oxygen	text (number)
240	cpap Show the field ONLY if: [respsup] = '1' and [respsupmeth(2)] = '1'	Total number of days of CPAP	text (number)
241	cpap_stop Show the field ONLY if: [respsup] = '1' and [respsupmeth(2)] = '1'	Neonatal day of life of final stop CPAP	text (number)
242	vent Show the field ONLY if: [respsup] = '1' and [respsupmeth(3)] = '1'	Total number of days of ventilation	text (number)
243	vent_stop Show the field ONLY if: [respsup] = '1' and [respsupmeth(3)] = '1'	Neonatal day of life of final stop ventilation	text (number)
244	no Show the field ONLY if: [respsup] = '1' and [respsupmeth(4)] = '1'	Total number of days of NO	text
245	no_stop Show the field ONLY if: [respsup] = '1' and [respsupmeth(4)] = '1'	Neonatal day of life of final stop NO	text (number)
246	hfo Show the field ONLY if: [respsup] = '1' and [respsupmeth(5)] = '1'	Total number of days of high frequency oscillation (HFO)	text (number)
247	hfo_stop Show the field ONLY if: [respsup] = '1' and [respsupmeth(5)] = '1'	Neonatal day of life of final stop HFO	text (number)

248	cld36 Show the field ONLY if: [respsup] = '1'	Chronic lung disease at 36 weeks postmenstrual age	dropdown, Required 1, Yes 0, No 2, Death < 36 weeks 3, Oxygen at time of transfer (< 36 weeks)
249	food Show the field ONLY if: ([mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1') and [lifebirth] = '1'	Section Header: *Gastro-intestinal system* Type of feeding at discharge	dropdown 1, Breast feeding 2, Formula feeding, start breast feeding 3, Formula feeding, start formula feeding 4, Mixed, start exclusive breast feeding 5, Mixed, start mixed
250	breast Show the field ONLY if: [food] = '2' or [food] = '4'	Date of cessation exclusive breast feeding	text (date_dmy)
251	nec Show the field ONLY if: ([mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1') and [lifebirth] = '1'	Gastro-intestinal complications	checkbox, Required 0, nec___0, No 1, nec___1, Necrotizing enterocolitis 2, nec___2, Solitary gastro-intestinal perforation 3, nec___3, Other
252	rop Show the field ONLY if: ([mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1') and [lifebirth] = '1'	Section Header: *Cerebral and visual* Retinopathy of prematurity, treated (laser or intravitreal injections)	dropdown, Required 1, Yes 0, No 2, No indication for screening 3, Mortality

253	ich Show the field ONLY if: ([mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1') and [lifebirth] = '1'	Intracerebral hemorrhage (ICH)	checkbox, Required 0, ich___0, No ICH 1, ich___1, Grade 1 intraventricular hemorrhage (IVH): subependymal hemorrhage 2, ich___2, Grade 2 IVH: without ventricular dilatation 3, ich___3, Grade 3 IVH: with ventricular dilatation 4, ich___4, Fronto-parietal intraparenchymal echodense lesion (IPE) 5, ich___5, Focal minor IPE 6, ich___6, Sub- or epidural hemorrhage 7, ich___7, Cerebral hemorrhage 8, ich___8, Thalamoventricular hemorrhage 9, ich___9, Subarachnoidal hemorrhage 10, ich___10, Cerebellar hemorrhage
254	pvl Show the field ONLY if: ([mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1') and [lifebirth] = '1'	Periventricular leucomalacia (PVL)	checkbox, Required 0, pvl___0, No PVL 1, pvl___1, Isolated flares, > 7 days 2, pvl___2, Flares + ventriculomegaly 3, pvl___3, Irregular echographic densities, no ventriculomegaly 4, pvl___4, Regular echographic densities, with ventriculomegaly 5, pvl___5, Cystic PVL 6, pvl___6, Cystic subcortical/mixed leucomalacia
255	pda Show the field ONLY if: ([mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1') and [lifebirth] = '1'	Section Header: *Other* Persistent ductus arteriosus, with need for treatment	yesno 1, Yes 0, No

256	hemc Show the field ONLY if: ([mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1') and [lifebirth] = '1'	Positive hemoculture during NICU admission	dropdown 0 No 1 On one occasion, pathogen 2 On one occasion, possibly contamination 3 On more than one occasion, at least one pathogen
257	pt Show the field ONLY if: ([mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1') and [lifebirth] = '1'	Phototherapy	yesno 1 Yes 0 No
258	neonatal_morbidity_complete	Section Header: *Form Status* Complete?	dropdown 0 Incomplete 1 Unverified 2 Complete
Instrument: **Neonatal mortality** (neonatal_mortality)			
259	dt4 Show the field ONLY if: [lifebirth] = '0' or [mother_arm_1][back] = '1'	If this form is empty, your patient - has been transferred to the referral hospital and has given birth there or - experienced an intrapartum death	descriptive
260	mortality Show the field ONLY if: ([mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1') and [lifebirth] = '1'	Mortality *Yes = including termination of intensive care*	yesno, Required 1 Yes 0 No
261	stop_ic Show the field ONLY if: [mortality] = '1'	Termination or abstinence of neonatal intensive care (IC) due to negative prognosis	dropdown 2 IC until decease 3 Abstinence of IC 4 IC stopped
262	death_date Show the field ONLY if: [mortality] = '1'	Date of death	text (date_dmy), Required, Identifier
263	death_hour Show the field ONLY if: [mortality] = '1'	Time of death	text (time)

264	neonatal_mortality_complete	Section Header: *Form Status* Complete?	dropdown 0 Incomplete 1 Unverified 2 Complete

Instrument: **Neonatal magnesemia** (neonatal_magnesemia)

265	neonatal_magnesemia	Day Date/time Mg (mmol/l) Na (mmol/l) Cl (mmol/l) Ca (mmol/l) P (mmol/l) Ureum (mg/dl) Creatinine (mg/dl) 0 labdh00 mg00 na00 cl00 ca00 p00 ureum00 creat00 1 labdh01 mg01 na01 cl01 ca01 p01 ureum01 creat01 2 labdh02 mg02 na02 cl02 ca02 p02 ureum02 creat02 3 labdh03 mg03 na03 cl03 ca03 p03	descriptive

		ureum03 creat03 4 labdh04 mg04 na04 cl04 ca04 p04 ureum04 creat04 5 labdh05 mg05 na05 cl05 ca05 p05 ureum05 creat05 6 labdh06 mg06 na06 cl06 ca06 p06 ureum06 creat06 7 labdh07 mg07 na07 cl07 ca07 p07 ureum07 creat07 8 labdh08 mg08 na08 cl08 ca08 p08 ureum08 creat08 9		

		labdh09 mg09 na09 cl09 ca09 p09 ureum09 creat09 10 labdh10 mg10 na10 cl10 ca10 p10 ureum10 creat10 11 labdh11 mg11 na11 cl11 ca11 p11 ureum11 creat11 12 labdh12 mg12 na12 cl12 ca12 p12 ureum12 creat12 13 labdh13 mg13 na13 cl13 ca13 p13 ureum13 creat13 14 labdh14 mg14 na14 cl14 ca14	

		p14 ureum14 creat14	
266	labdh00	Date and time of first results (ideally date of birth)	text (datetime_dmy), Identifier Field Annotation: @HIDEBUTTON
267	mg00	Magnesium concentration (mmol/l), first result after birth	text (number, Min: 0, Max: 10)
268	na00 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Natrium concentration (mmol/l), first result after birth	text (number, Min: 0, Max: 200)
269	cl00 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Chloride concentration (mmol/l), first result after birth	text
270	ca00 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Calcium concentration (mmol/l), first result after birth	text (number, Min: 0, Max: 100)

271	p00 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Phosphor concentration (mmol/l), first result after birth	text (number, Min: 0, Max: 200)
272	ureum00 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Ureum concentration (mg/dl), first result after birth	text
273	creat00	Creatinine (mg/dl), first result after birth	text (number, Min: 0, Max: 50)
274	labdh01	Date and time of first laboratory results, day one	text (datetime_dmy), Identifier Field Annotation: @HIDEBUTTON
275	mg01	Magnesium concentration (mmol/l), first result of day one	text (number, Min: 0, Max: 10)
276	na01 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Natrium concentration (mmol/l), first result of day one	text (number, Min: 0, Max: 200)
277	cl01 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Chloride concentration (mmol/l), first result of day one	text

278	ca01 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Calcium concentration (mmol/l), first result of day one	text (number, Min: 0, Max: 100)
279	p01 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Phosphor concentration (mmol/l), first result of day one	text (number, Min: 0, Max: 200)
280	ureum01 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Ureum concentration (mg/dl), first result of day one	text
281	creat01	Creatinine (mg/dl), first result of day one	text (number, Min: 0, Max: 50)
282	labdh02	Date and time of first laboratory results, day two	text (datetime_dmy), Identifier Field Annotation: @HIDEBUTTON
283	mg02	Magnesium concentration (mmol/l), first result of day two	text (number, Min: 0, Max: 10)
284	na02 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Natrium concentration (mmol/l), first result of day two	text (number, Min: 0, Max: 200)

285	cl02 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Chloride concentration (mmol/l), first result of day two	text
286	ca02 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Calcium concentration (mmol/l), first result of day two	text (number, Min: 0, Max: 100)
287	p02 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Phosphor concentration (mmol/l), first result of day two	text (number, Min: 0, Max: 200)
288	ureum02 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Ureum concentration (mg/dl), first result of day two	text
289	creat02	Creatinine (mg/dl), first result of day two	text (number, Min: 0, Max: 50)
290	labdh03	Date and time of first laboratory results, day three	text (datetime_dmy), Identifier Field Annotation: @HIDEBUTTON
291	mg03	Magnesium concentration (mmol/l), first result of day three	text (number, Min: 0, Max: 10)

292	na03 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Natrium concentration (mmol/l), first result of day three	text (number, Min: 0, Max: 200)
293	cl03 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Chloride concentration (mmol/l), first result of day three	text
294	ca03 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Calcium concentration (mmol/l), first result of day three	text (number, Min: 0, Max: 100)
295	p03 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Phosphor concentration (mmol/l), first result of day three	text (number, Min: 0, Max: 200)

296	ureum03 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Ureum concentration (mg/dl), first result of day three	text
297	creat03	Creatinine (mg/dl), first result of day three	text (number, Min: 0, Max: 50)
298	labdh04	Date and time of first laboratory results, day four	text (datetime_dmy), Identifier Field Annotation: @HIDEBUTTON
299	mg04	Magnesium concentration (mmol/l), first result of day four	text (number, Min: 0, Max: 10)
300	na04 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Natrium concentration (mmol/l), first result of day four	text (number, Min: 0, Max: 200)
301	cl04 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Chloride concentration (mmol/l), first result of day four	text
302	ca04 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Calcium concentration (mmol/l), first result of day four	text (number, Min: 0, Max: 100)

303	p04 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Phosphor concentration (mmol/l), first result of day four	text (number, Min: 0, Max: 200)
304	ureum04 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Ureum concentration (mg/dl), first result of day four	text
305	creat04	Creatinine (mg/dl), first result of day four	text (number, Min: 0, Max: 50)
306	labdh05	Date and time of first laboratory results, day five	text (datetime_dmy), Identifier Field Annotation: @HIDEBUTTON
307	mg05	Magnesium concentration (mmol/l), first result of day five	text (number, Min: 0, Max: 10)
308	na05 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Natrium concentration (mmol/l), first result of day five	text (number, Min: 0, Max: 200)
309	cl05 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Chloride concentration (mmol/l), first result of day five	text

310	ca05 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Calcium concentration (mmol/l), first result of day five	text (number, Min: 0, Max: 100)
311	p05 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Phosphor concentration (mmol/l), first result of day five	text (number, Min: 0, Max: 200)
312	ureum05 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Ureum concentration (mg/dl), first result of day five	text
313	creat05	Creatinine (mg/dl), first result of day five	text (number, Min: 0, Max: 50)
314	labdh06	Date and time of first laboratory results, day six	text (datetime_dmy), Identifier Field Annotation: @HIDEBUTTON
315	mg06	Magnesium concentration (mmol/l), first result of day six	text (number, Min: 0, Max: 10)
316	na06 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Natrium concentration (mmol/l), first result of day six	text (number, Min: 0, Max: 200)

317	cl06 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Chloride concentration (mmol/l), first result of day six	text
318	ca06 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Calcium concentration (mmol/l), first result of day six	text (number, Min: 0, Max: 100)
319	p06 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Phosphor concentration (mmol/l), first result of day six	text (number, Min: 0, Max: 200)
320	ureum06 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Ureum concentration (mg/dl), first result of day six	text
321	creat06	Creatinine (mg/dl), first result of day six	text (number, Min: 0, Max: 50)
322	labdh07	Date and time of first laboratory results, day seven	text (datetime_dmy), Identifier Field Annotation: @HIDEBUTTON
323	mg07	Magnesium concentration (mmol/l), first result of day seven	text (number, Min: 0, Max: 10)

324	na07 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Natrium concentration (mmol/l), first result of day seven	text (number, Min: 0, Max: 200)
325	cl07 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Chloride concentration (mmol/l), first result of day seven	text
326	ca07 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Calcium concentration (mmol/l), first result of day seven	text (number, Min: 0, Max: 100)
327	p07 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Phosphor concentration (mmol/l), first result of day seven	text (number, Min: 0, Max: 200)

328	ureum07 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Ureum concentration (mg/dl), first result of day seven	text
329	creat07	Creatinine (mg/dl), first result of day seven	text (number, Min: 0, Max: 50)
330	labdh08	Date and time of first laboratory results, day eight	text (datetime_dmy), Identifier Field Annotation: @HIDEBUTTON
331	mg08	Magnesium concentration (mmol/l), first result of day eight	text (number, Min: 0, Max: 10)
332	na08 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Natrium concentration (mmol/l), first result of day eight	text (number, Min: 0, Max: 200)
333	cl08 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Chloride concentration (mmol/l), first result of day eight	text
334	ca08 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Calcium concentration (mmol/l), first result of day eight	text (number, Min: 0, Max: 100)

335	p08 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Phosphor concentration (mmol/l), first result of day eight	text (number, Min: 0, Max: 200)
336	ureum08 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Ureum concentration (mg/dl), first result of day eight	text
337	creat08	Creatinine (mg/dl), first result of day eight	text (number, Min: 0, Max: 50)
338	labdh09	Date and time of first laboratory results, day nine	text (datetime_dmy), Identifier Field Annotation: @HIDEBUTTON
339	mg09	Magnesium concentration (mmol/l), first result of day nine	text (number, Min: 0, Max: 10)
340	na09 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Natrium concentration (mmol/l), first result of day nine	text (number, Min: 0, Max: 200)
341	cl09 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Chloride concentration (mmol/l), first result of day nine	text

342	ca09 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Calcium concentration (mmol/l), first result of day nine	text (number, Min: 0, Max: 100)
343	p09 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Phosphor concentration (mmol/l), first result of day nine	text (number, Min: 0, Max: 200)
344	ureum09 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Ureum concentration (mg/dl), first result of day nine	text
345	creat09	Creatinine (mg/dl), first result of day nine	text (number, Min: 0, Max: 50)
346	labdh10	Date and time of first laboratory results, day ten	text (datetime_dmy), Identifier Field Annotation: @HIDEBUTTON
347	mg10	Magnesium concentration (mmol/l), first result of day ten	text (number, Min: 0, Max: 10)
348	na10 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Natrium concentration (mmol/l), first result of day ten	text (number, Min: 0, Max: 200)

349	cl10 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Chloride concentration (mmol/l), first result of day ten	text
350	ca10 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Calcium concentration (mmol/l), first result of day ten	text (number, Min: 0, Max: 100)
351	p10 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Phosphor concentration (mmol/l), first result of day ten	text (number, Min: 0, Max: 200)
352	ureum10 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Ureum concentration (mg/dl), first result of day ten	text
353	creat10	Creatinine (mg/dl), first result of day ten	text (number, Min: 0, Max: 50)
354	labdh11	Date and time of first laboratory results, day eleven	text (datetime_dmy), Identifier Field Annotation: @HIDEBUTTON
355	mg11	Magnesium concentration (mmol/l), first result of day eleven	text (number, Min: 0, Max: 10)

356	na11 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Natrium concentration (mmol/l), first result of day eleven	text (number, Min: 0, Max: 200)
357	cl11 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Chloride concentration (mmol/l), first result of day eleven	text
358	ca11 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Calcium concentration (mmol/l), first result of day eleven	text (number, Min: 0, Max: 100)
359	p11 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Phosphor concentration (mmol/l), first result of day eleven	text (number, Min: 0, Max: 200)

360	ureum11 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Ureum concentration (mg/dl), first result of day eleven	text
361	creat11	Creatinine (mg/dl), first result of day eleven	text (number, Min: 0, Max: 50)
362	labdh12	Date and time of first laboratory results, day twelve	text (datetime_dmy), Identifier Field Annotation: @HIDEBUTTON
363	mg12	Magnesium concentration (mmol/l), first result of day twelve	text (number, Min: 0, Max: 10)
364	na12 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Natrium concentration (mmol/l), first result of day twelve	text (number, Min: 0, Max: 200)
365	cl12 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Chloride concentration (mmol/l), first result of day twelve	text
366	ca12 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Calcium concentration (mmol/l), first result of day twelve	text (number, Min: 0, Max: 100)

367	p12 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Phosphor concentration (mmol/l), first result of day twelve	text (number, Min: 0, Max: 200)
368	ureum12 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Ureum concentration (mg/dl), first result of day twelve	text
369	creat12	Creatinine (mg/dl), first result of day twelve	text (number, Min: 0, Max: 50)
370	labdh13	Date and time of first laboratory results, day thirteen	text (datetime_dmy), Identifier Field Annotation: @HIDEBUTTON
371	mg13	Magnesium concentration (mmol/l), first result of day thirteen	text (number, Min: 0, Max: 10)
372	na13 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Natrium concentration (mmol/l), first result of day thirteen	text (number, Min: 0, Max: 200)
373	cl13 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Chloride concentration (mmol/l), first result of day thirteen	text

374	ca13 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Calcium concentration (mmol/l), first result of day thirteen	text (number, Min: 0, Max: 100)
375	p13 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Phosphor concentration (mmol/l), first result of day thirteen	text (number, Min: 0, Max: 200)
376	ureum13 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Ureum concentration (mg/dl), first result of day thirteen	text
377	creat13	Creatinine (mg/dl), first result of day thirteen	text (number, Min: 0, Max: 50)
378	labdh14	Date and time of first laboratory results, day fourteen	text (datetime_dmy), Identifier Field Annotation: @HIDEBUTTON
379	mg14	Magnesium concentration (mmol/l), first result of day fourteen	text (number, Min: 0, Max: 10)
380	na14 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Natrium concentration (mmol/l), first result of day fourteen	text (number, Min: 0, Max: 200)

381	cl14 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Chloride concentration (mmol/l), first result of day fourteen	text
382	ca14 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Calcium concentration (mmol/l), first result of day fourteen	text (number, Min: 0, Max: 100)
383	p14 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Phosphor concentration (mmol/l), first result of day fourteen	text (number, Min: 0, Max: 200)
384	ureum14 Show the field ONLY if: [mother_arm_1][mg_pe] = '1' or [mother_arm_1][mg_np] = '1' or [mother_arm_1][mg_np_2] = '1' or [mother_arm_1][mg_np_3] = '1' or [mother_arm_1][mg_np_4] = '1'	Ureum concentration (mg/dl), first result of day fourteen	text
385	creat14	Creatinine (mg/dl), first result of day fourteen	text (number, Min: 0, Max: 50)

386	neonatal_magnesemia_complete	Section Header: *Form Status* Complete?	dropdown 0, Incomplete 1, Unverified 2, Complete

Instrument: **4 months COS follow-up** (months_cos_follow_up)

387	dt5 Show the field ONLY if: [mother_arm_1][back] = '1' or [mortality] = '1' or [lifebirth] = '0'	If this form is empty - your patient has been transferred to the referral hospital and has given birth there or - the neonate passed away	descriptive
388	cos_indicated Show the field ONLY if: ([mother_arm_1][back] <> '1' or [mother_arm_1][home] = '1') and [lifebirth] = '1' and [mortality] = '0'	COS follow-up indicated? * on indication * year of birth < 2015: gestational age < 30 weeks and/or birth weight < 1250 g >= 2015: gestational age < 32 weeks and/or birth weight < 1500 g	yesno 1, Yes 0, No
389	m4_drop Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [cos_indicated] = '1'	Drop out of long-term follow-up?	yesno 1, Yes 0, No
390	m4_date Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m4_drop] = '0'	Date of consultation	text (date_dmy), Identifier
391	m4_hosp Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m4_drop] = '0'	Number of hospitalisations after discharge from NICU	text (number)

392	m4_weight Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m4_drop] = '0'	Weight (kg)	text (number, Min: 2, Max: 50)
393	m4_weight_perc Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m4_drop] = '0'	Weight (%)	dropdown 1 | < p3 2 | >= p3 - < p10 3 | >= p10 - < p25 4 | >= p25 - < p50 5 | >= p50 - < p75 6 | >= p75 - < p90 7 | >= p90 - < p97 8 | >= p97
394	m4_height Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m4_drop] = '0'	Height (cm)	text (number, Min: 40, Max: 160)
395	m4_height_perc Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m4_drop] = '0'	Height (%)	dropdown 1 | < p3 2 | >= p3 - < p10 3 | >= p10 - < p25 4 | >= p25 - < p50 5 | >= p50 - < p75 6 | >= p75 - < p90 7 | >= p90 - < p97 8 | >= p97
396	m4_headc Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m4_drop] = '0'	Head circumference (cm)	text (number, Min: 30, Max: 70)

397	m4_headc_perc Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m4_drop] = '0'	Head circumference (%)	dropdown 1, < p3 2, >= p3 - < p10 3, >= p10 - < p25 4, >= p25 - < p50 5, >= p50 - < p75 6, >= p75 - < p90 7, >= p90 - < p97 8, >= p97
398	m4_genpeds Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m4_drop] = '0'	General pediatric evaluation	checkbox 1, m4_genpeds___1, normal 2, m4_genpeds___2, on oral/inhalat respiratory therapy 3, m4_genpeds___3, limited respirat exercise toleran 4, m4_genpeds___4, requires oxyge 5, m4_genpeds___5, requires continued respiratory support 6, m4_genpeds___6, renal impairme requiring treatment or special diet 7, m4_genpeds___7, requires dialysi or awaiting org transplant 8, m4_genpeds___8, feeding problems/aver 9, m4_genpeds___9, requires nasogastric or percutaneous endoscopic gastrostomy feeding 10, m4_genpeds___10, on semi-eleme diet 11, m4_genpeds___11, stoma 12, m4_genpeds___12, requires TPN 13, m4_genpeds___13, cardiac dysfunction 14, m4_genpeds___14, endocrine dysfunction

399	m4_neuroex Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m4_drop] = '0'	Neurological examination	dropdown 1, normal 2, suspect psychomotor 3, suspect cerebral palsy 4, cerebral palsy
400	m4_epilepsy Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m4_drop] = '0'	Epilepsy, treated or not	dropdown 0, no 1, yes, under medication 2, yes, without medication
401	m4_mri Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m4_drop] = '0'	Cranial MRI taken after discharge at NICU and before bilan at 4 months	checkbox 0, m4_mri___0, no MRI taken 1, m4_mri___1, normal 2, m4_mri___2, maldevelopments 3, m4_mri___3, periventricular leucomalacia (PVL) 4, m4_mri___4, sequelae interventricular hemorrhage (IVH) or periventricular hemorrhagic infarction 5, m4_mri___5, combination PVL and IVH 6, m4_mri___6, basal ganglia/thalami injury 7, m4_mri___7, parasagittal lesions 8, m4_mri___8, middle cerebral artery infarctions 9, m4_mri___9, miscellaneous

402	m4_cus_ich Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m4_drop] = '0'	Cranial ultrasound taken after discharge from NICU and before bilan at 4 months, evaluation of intracerebral hemorrhage	checkbox

0	m4_cus_ich___0	no cranial ultrasound take
1	m4_cus_ich___1	no cerebral hemorrhage
2	m4_cus_ich___2	intraventricular hemorrhage (IVH grade 1: subependymal hemorrhage
3	m4_cus_ich___3	IVH without dilatation
4	m4_cus_ich___4	IVH with dilatatio
5	m4_cus_ich___5	focal periventricular hemorrhagic infarction
6	m4_cus_ich___6	extensive periventricular hemorrhagic infarction
7	m4_cus_ich___7	sub- or epidural hemorrhage
8	m4_cus_ich___8	lobar cerebral hemorrhage
9	m4_cus_ich___9	thalamoventricu hemorrhage
10	m4_cus_ich___10	subarachnoidal hemorrhage
11	m4_cus_ich___11	cerebellar hemorrhage

403	m4_cus_pvl Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m4_drop] = '0'	Cranial ultrasound taken after discharge from NICU and before bilan at 4 months, evaluation of periventricular leucomalacia (PVL)	dropdown 0, no cUS taken 1, no PVL 2, periventricular echodense area (isolated flares) more than 7 days 3, isolated ventriculomegaly 4, irregular echodensities, no ventriculomegaly 5, grade II: transient periventricular echodense areas evolving into frontoparietal cysts 6, grade III: periventricular echodense areas evolving into multiple cysts in the frontoparietal and/or occipital white matter 7, grade IV: echodense areas in the deep white matter with evolution into multiple subcortical cysts
404	m4_ophtalmo Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m4_drop] = '0'	Ophtalmological examination	dropdown 0, not done 1, normal 2, retinopathy, treated 3, retinopathy, untreated 4, other
405	m4_eye Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m4_drop] = '0'	Vision	checkbox 1, m4_eye___1, normal 2, m4_eye___2, strabismus 3, m4_eye___3, nystagmus 4, m4_eye___4, retinopathy 5, m4_eye___5, characteristics of cortical visual impairment 6, m4_eye___6, other
406	m4_eyefct Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m4_drop] = '0'	Functionality of vision	dropdown 1, normal 2, impaired without spectacles 3, impaired with spectacles 4, severely impaired: blind or no useful vision (after correction, on the better eye)

407	m4_ear Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m4_drop] = '0'	Functionality of hearing	dropdown 1, normal 2, impaired without hearing aids 3, impaired with hearing aids 4, severely impaired: hearing loss > 70dB (before correction, on the better ear)
408	m4_motor Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m4_drop] = '0'	Neuromotor evaluation	dropdown 0, no consultation with physiotherapist 1, excellent 2, normal 3, suboptimal 4, deviant
409	m4_aims_raw Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m4_drop] = '0'	Alberta Infant Motor Scale (AIMS) score	text (number, Min: 0, Max: 58)
410	m4_aims_perc Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m4_drop] = '0'	AIMS score in percentile (minimum) *if exact %: give same value for min and max %*	text (number, Min: 0, Max: 100)
411	m4_aims_perc_max Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m4_drop] = '0'	AIMS score in percentile (maximum) *if exact %: give same value for min and max %*	text (number, Min: 0, Max: 100)
412	m4_concl_normal Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m4_drop] = '0'	Section Header: *Conclusions* Normal development	yesno, Required 1, Yes 0, No

413	m4_concl_prem Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m4_drop] = '0'	Typical characteristics of prematurity	yesno, Required 1 Yes 0 No
414	m4_concl_mild Show the field ONLY if: [m4_concl_normal] = '0'	Mild neurodevelopmental impairment	checkbox, Required 0 m4_concl_mild___0 No 1 m4_concl_mild___1 Grof Motorisch Functionerings Classificatie Systeem (GMFCS) I 2 m4_concl_mild___2 Cognitive 3 m4_concl_mild___3 Motor 4 m4_concl_mild___4 Other 5 m4_concl_mild___5 Hearing loss < 40dbHL 6 m4_concl_mild___6 Impaired vision but appears to have useful vision
415	m4_concl_mod Show the field ONLY if: [m4_concl_normal] = '0' and [m4_concl_mild(0)] = '1'	Moderate neurodevelopmental impairment	checkbox, Required 0 m4_concl_mod___0 No 1 m4_concl_mod___1 GMFCS II 2 m4_concl_mod___2 Cognitive 3 m4_concl_mod___3 Hearing 4 m4_concl_mod___4 Words 5 m4_concl_mod___5 Vision 6 m4_concl_mod___6 Other
416	m4_concl_sev Show the field ONLY if: [m4_concl_normal] = '0' and [m4_concl_mild(0)] = '1' and [m4_concl_mod(0)] = '1'	Severe neurodevelopmental impairment	checkbox, Required 0 m4_concl_sev___0 No 1 m4_concl_sev___1 GMFCS III-IV 2 m4_concl_sev___2 Cognitive 3 m4_concl_sev___3 Hearing 4 m4_concl_sev___4 Words 5 m4_concl_sev___5 Vision 6 m4_concl_sev___6 Other

417	months_cos_follow_up_complete	Section Header: *Form Status* Complete?	dropdown 0, Incomplete 1, Unverified 2, Complete

Instrument: **10 months COS follow-up** (months_cos_follow_up_0c76)

418	dt6 Show the field ONLY if: [mother_arm_1][back] = '1' or [mortality] = '1' or [lifebirth] = '0'	If this form is empty - your patient has been transferred to the referral hospital and has given birth there or - the neonate passed away	descriptive
419	m10_drop Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [cos_indicated] = '1'	Drop out of long-term follow-up?	yesno 1, Yes 0, No
420	m10_date Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m10_drop] = '0'	Date of consultation	text (date_dmy), Identifier
421	m10_hosp Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m10_drop] = '0'	Number of hospitalisations after discharge from NICU	text (number)
422	m10_weight Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m10_drop] = '0'	Weight (kg)	text (number, Min: 2, Max: 50)

423	m10_weight_perc Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m10_drop] = '0'	Weight (%)	dropdown 1, < p3 2, >= p3 - < p10 3, >= p10 - < p25 4, >= p25 - < p50 5, >= p50 - < p75 6, >= p75 - < p90 7, >= p90 - < p97 8, >= p97
424	m10_height Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m10_drop] = '0'	Height (cm)	text (number, Min: 40, Max: 150)
425	m10_height_perc Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m10_drop] = '0'	Height (%)	dropdown 1, < p3 2, >= p3 - < p10 3, >= p10 - < p25 4, >= p25 - < p50 5, >= p50 - < p75 6, >= p75 - < p90 7, >= p90 - < p97 8, >= p97
426	m10_headc Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m10_drop] = '0'	Head circumference (cm)	text (number, Min: 30, Max: 80)
427	m10_headc_perc Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m10_drop] = '0'	Head circumference (%)	dropdown 1, < p3 2, >= p3 - < p10 3, >= p10 - < p25 4, >= p25 - < p50 5, >= p50 - < p75 6, >= p75 - < p90 7, >= p90 - < p97 8, >= p97

428	m10_genpeds Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m10_drop] = '0'	General pediatric evaluation	checkbox

1	m10_genpeds___1	normal
2	m10_genpeds___2	on oral/inhala respiratory therapy
3	m10_genpeds___3	limited respira exercise toler
4	m10_genpeds___4	requires oxyg
5	m10_genpeds___5	requires continued respiratory support
6	m10_genpeds___6	renal impairm requiring treatment or special diet
7	m10_genpeds___7	requires dialy or awaiting or transplant
8	m10_genpeds___8	feeding problems/ave
9	m10_genpeds___9	requires nasogastric or percutaneous endoscopic gastrostomy feeding
10	m10_genpeds___10	on semi-elem diet
11	m10_genpeds___11	stoma
12	m10_genpeds___12	requires TPN
13	m10_genpeds___13	cardiac dysfunction
14	m10_genpeds___14	endocrine dysfunction

429	m10_neuroex Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m10_drop] = '0'	Neurological examination	checkbox

1	m10_neuroex___1	normal
2	m10_neuroex___2	suspect psychomotor
3	m10_neuroex___3	suspect cerebral palsy
4	m10_neuroex___4	cerebral palsy, spastic, diplegy
5	m10_neuroex___5	cerebral palsy, spastic, quadriplegy
6	m10_neuroex___6	cerebral palsy, unilateral
7	m10_neuroex___7	cerebral palsy, dyskinetic
8	m10_neuroex___8	cerebral palsy, ataxic
9	m10_neuroex___9	cerebral palsy, GMFCS I
10	m10_neuroex___10	cerebral palsy, GMFCS II
11	m10_neuroex___11	cerebral palsy, GMFCS III
12	m10_neuroex___12	cerebral palsy, GMFCS IV
13	m10_neuroex___13	cerebral palsy, GMFCS V

430	m10_epilepsy Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m10_drop] = '0'	Epilepsy, treated or not	dropdown

0	no
1	yes, under medication
2	yes, without medication

431	m10_mri Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m10_drop] = '0'	Cranial MRI taken after bilat at 4 months and before bilan at 10 months	checkbox 0, m10_mri___0, no MRI taken 1, m10_mri___1, normal 2, m10_mri___2, maldevelopments 3, m10_mri___3, periventricular leucomalacia (PVL) 4, m10_mri___4, sequelae interventricular hemorrhage (IVH) or periventricular hemorrhagic infarction 5, m10_mri___5, combination PVL and IVH 6, m10_mri___6, basal ganglia/thalami injury 7, m10_mri___7, parasagittal lesions 8, m10_mri___8, middle cerebral artery infarctions 9, m10_mri___9, miscalleneous
432	m10_ophtalmo Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m10_drop] = '0'	Ophtalmological examination	dropdown 0, not done 1, normal 2, retinopathy, treated 3, retinopathy, untreated 4, other
433	m10_eye Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m10_drop] = '0'	Vision	checkbox 1, m10_eye___1, normal 2, m10_eye___2, strabismus 3, m10_eye___3, nystagmus 4, m10_eye___4, retinopathy 5, m10_eye___5, characteristics of cortical visual impairment 6, m10_eye___6, other
434	m10_eyefct Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m10_drop] = '0'	Functionality of vision	dropdown 1, normal 2, impaired without spectacles 3, impaired with spectacles 4, severely impaired: blind or no useful vision (after correction, on the better eye)

435	m10_ear Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m10_drop] = '0'	Functionality of hearing	dropdown 1, normal 2, impaired without hearing aids 3, impaired with hearing aids 4, severely impaired: hearing loss > 70dB (before correction, on the better ear)
436	m10_bii_raw Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m10_drop] = '0'	Bayley-II score, mental, raw score	text (number, Min: 0, Max: 178)
437	m10_bii_index Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m10_drop] = '0'	Bayley-II score, mental, index	text (number, Min: 55, Max: 145)
438	m10_biii_cogn_raw Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m10_drop] = '0'	Bayley III score, cognition, raw score	text (number, Min: 0, Max: 91)
439	m10_biii_scaled Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m10_drop] = '0'	Bayley-III score, cognition, scaled score	text (number, Min: 1, Max: 19)
440	m10_biii_cogn_index Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m10_drop] = '0'	Bayley-III score, cognition, index *if score < 55, fill in 0*	text (number, Min: 0, Max: 145)

441	m10_biii_rec_raw Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m10_drop] = '0'	Bayley-III score, receptive communication, raw score	text (number, Min: 0, Max: 49)
442	m10_biii_rec_scaled Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m10_drop] = '0'	Bayley-III score, receptive communication, scaled score	text (number, Min: 1, Max: 19)
443	m10_biii_exp_raw Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m10_drop] = '0'	Bayley-III score, expressive communication, raw score	text (number, Min: 0, Max: 46)
444	m10_biii_exp_scaled Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m10_drop] = '0'	Bayley-III score, expressive communication, scaled score	text (number, Min: 1, Max: 19)
445	m10_biii_comm_index Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m10_drop] = '0'	Bayley-III score, receptive and expressive communication, index	text (number, Min: 47, Max: 153)
446	m10_social Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m10_drop] = '0'	Social behaviour	dropdown 0, normal 1, abnormal

447	m10_motor Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m10_drop] = '0'	Neuromotor evaluation	dropdown 0, no consultation with psychotherapist 1, excellent 2, normal 3, suboptimal 4, deviant
448	m10_aims_raw Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m10_drop] = '0'	Alberta Infant Motor Scale (AIMS) score	text (number, Min: 0, Max: 58)
449	m10_aims_perc Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m10_drop] = '0'	AIMS score in percentile (minimum) *if exact %: give same value for min and max %*	text (number, Min: 0, Max: 100)
450	m10_aims_perc_max Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m10_drop] = '0'	AIMS score in percentile (maximum) *if exact %: give same value for min and max %*	text (number, Min: 0, Max: 100)
451	m10_concl_normal Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m10_drop] = '0'	Section Header: *Conclusions* Normal development	yesno, Required 1, Yes 0, No
452	m10_concl_prem Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [m10_drop] = '0'	Typical characteristics of prematurity	yesno 1, Yes 0, No

453	m10_concl_mild Show the field ONLY if: [m10_concl_normal] = '0'	Mild neurodevelopmental impairment	checkbox, Required

0	m10_concl_mild___0	No
1	m10_concl_mild___1	Grof Motorisch Functionering Classificatie Systeem (GMFCS) I
2	m10_concl_mild___2	Cognitive
3	m10_concl_mild___3	Motor
4	m10_concl_mild___4	Other
5	m10_concl_mild___5	Hearing loss < 40dBHL
6	m10_concl_mild___6	Impaired vision but appears to have useful vision
7	m10_concl_mild___7	Mild behavorial and/or social-emotional problems

454	m10_concl_mod Show the field ONLY if: [m10_concl_normal] = '0' and [m10_concl_mild(0)] = '1'	Moderate neurodevelopmental impairment	checkbox, Required

0	m10_concl_mod___0	No
1	m10_concl_mod___1	GMFCS II
2	m10_concl_mod___2	Cognitive
3	m10_concl_mod___3	Hearing
4	m10_concl_mod___4	Words
5	m10_concl_mod___5	Vision
6	m10_concl_mod___6	Other
7	m10_concl_mod___7	Motor
8	m10_concl_mod___8	Moderate behavioral and/or social-emotional problems

455	m10_concl_sev Show the field ONLY if: [m10_concl_normal] = '0' and [m10_concl_mild(0)] = '1' and [m10_concl_mod(0)] = '1'	Severe neurodevelopmental impairment	checkbox, Required 0, m10_concl_sev___0, No 1, m10_concl_sev___1, GMFCS III-IV 2, m10_concl_sev___2, Cognitive 3, m10_concl_sev___3, Hearing 4, m10_concl_sev___4, Words 5, m10_concl_sev___5, Vision 6, m10_concl_sev___6, Other 7, m10_concl_sev___7, Motor 8, m10_concl_sev___8, Severe behavorial and/or social-emotional problems
456	months_cos_follow_up_0c76_complete	Section Header: *Form Status* Complete?	dropdown 0, Incomplete 1, Unverified 2, Complete
Instrument: **2 years COS follow-up** (years_cos_follow_up)			
457	dt7 Show the field ONLY if: [mother_arm_1][back] = '1' or [mortality] = '1' or [lifebirth] = '0'	If this form is empty - your patient has been transferred to the referral hospital and has given birth there or - the neonate passed away	descriptive
458	y2_drop Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [cos_indicated] = '1'	Drop out of long-term follow-up?	yesno 1, Yes 0, No
459	y2_date Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y2_drop] = '0'	Date of consultation	text (date_dmy), Identifier

460	y2_hosp Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y2_drop] = '0'	Number of hospitalisations after discharge from NICU	text (number)
461	y2_weight Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0'	Weight (kg)	text (number, Min: 4, Max: 60)
462	y2_weight_perc Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0'	Weight (%)	dropdown 1, < p3 2, >= p3 - < p10 3, >= p10 - < p25 4, >= p25 - < p50 5, >= p50 - < p75 6, >= p75 - < p90 7, >= p90 - < p97 8, >= p97
463	y2_height Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y2_drop] = '0'	Height (cm)	text (number, Min: 50, Max: 150)
464	y2_height_perc Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0'	Height (%)	dropdown 1, < p3 2, >= p3 - < p10 3, >= p10 - < p25 4, >= p25 - < p50 5, >= p50 - < p75 6, >= p75 - < p90 7, >= p90 - < p97 8, >= p97

465	y2_headc Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y2_drop] = '0'	Head circumference (cm)	text (number, Min: 30, Max: 80)
466	y2_headc_perc Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0'	Head circumference (%)	dropdown 1, < p3 2, >= p3 - < p10 3, >= p10 - < p25 4, >= p25 - < p50 5, >= p50 - < p75 6, >= p75 - < p90 7, >= p90 - < p97 8, >= p97

467	y2_genpeds Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y2_drop] = '0'	General pediatric evaluation	checkbox

1	y2_genpeds___1	normal
2	y2_genpeds___2	on oral/inhalatic respiratory therapy
3	y2_genpeds___3	limited respirat exercise toleran
4	y2_genpeds___4	requires oxyger
5	y2_genpeds___5	requires continued respiratory support
6	y2_genpeds___6	renal impairmer requiring treatment or special diet
7	y2_genpeds___7	requires dialysis or awaiting orga transplant
8	y2_genpeds___8	feeding problems/avers
9	y2_genpeds___9	requires nasogastric or percutaneous endoscopic gastrostomy feeding
10	y2_genpeds___10	on semi-elemer diet
11	y2_genpeds___11	stoma
12	y2_genpeds___12	requires TPN
13	y2_genpeds___13	cardiac dysfunction
14	y2_genpeds___14	endocrine dysfunction

468	y2_neuroex Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y2_drop] = '0'	Neurological examination	checkbox

1	y2_neuroex___1	normal
2	y2_neuroex___2	suspect psychomotor
3	y2_neuroex___3	suspect cerebral palsy
4	y2_neuroex___4	cerebral palsy, spastic, diplegy
5	y2_neuroex___5	cerebral palsy, spastic, quadriplegy
6	y2_neuroex___6	cerebral palsy, unilateral
7	y2_neuroex___7	cerebral palsy, dyskinetic
8	y2_neuroex___8	cerebral palsy, ataxic
9	y2_neuroex___9	cerebral palsy, GMFCS I
10	y2_neuroex___10	cerebral palsy, GMFCS II
11	y2_neuroex___11	cerebral palsy, GMFCS III
12	y2_neuroex___12	cerebral palsy, GMFCS IV
13	y2_neuroex___13	cerebral palsy, GMFCS V
14	y2_neuroex___14	cerebral palsy

469	y2_epilepsy Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y2_drop] = '0'	Epilepsy, treated or not	dropdown

0	no
1	yes, under medication
2	yes, without medication

470	y2_mri Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y2_drop] = '0'	Cranial MRI taken after bilan at 10 months and before bilan at 2 years	checkbox 0, y2_mri___0, no MRI taken 1, y2_mri___1, normal 2, y2_mri___2, maldevelopments 3, y2_mri___3, periventricular leucomalacia (PVL) 4, y2_mri___4, sequelae interventricular hemorrhage (IVH) or periventricular hemorrhagic infarction 5, y2_mri___5, combination PVL and IVH 6, y2_mri___6, basal ganglia/thalami injury 7, y2_mri___7, parasagittal lesions 8, y2_mri___8, middle cerebral artery infarctions 9, y2_mri___9, miscalleneous
471	y2_ophtalmo Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y2_drop] = '0'	Ophtalmological examination	dropdown 0, not done 1, normal 2, retinopathy, treated 3, retinopathy, untreated 4, other
472	y2_eye Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y2_drop] = '0'	Vision	checkbox 1, y2_eye___1, normal 2, y2_eye___2, strabismus 3, y2_eye___3, nystagmus 4, y2_eye___4, retinopathy 5, y2_eye___5, characteristics of cortical visual impairment 6, y2_eye___6, other
473	y2_eyefct Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y2_drop] = '0'	Functionality of vision	dropdown 1, normal 2, impaired without spectacles 3, impaired with spectacles 4, severely impaired: blind or no useful vision (after correction, on the better eye)

474	y2_ear Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y2_drop] = '0'	Functionality of hearing	dropdown 1, normal 2, impaired without hearing aids 3, impaired with hearing aids 4, severely impaired: hearing loss > 70dB (before correction, on the better ear)
475	y2_bii_raw Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y2_drop] = '0'	Bayley-II score, mental, raw score	text (number, Min: 0, Max: 178)
476	y2_bii_index Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y2_drop] = '0'	Bayley-II score, mental, index	text (number, Min: 55, Max: 145)
477	y2_biii_cogn_raw Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y2_drop] = '0'	Bayley III score, cognition, raw score	text (number, Min: 0, Max: 91)
478	y2_biii_scaled Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y2_drop] = '0'	Bayley-III score, cognition, scaled score	text (number, Min: 1, Max: 19)
479	y2_biii_cogn_index Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y2_drop] = '0'	Bayley-III score, cognition, index *if score < 55, fill in 0*	text (number, Min: 0, Max: 145)

480	y2_biii_rec_raw Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y2_drop] = '0'	Bayley-III score, receptive communication, raw score	text (number, Min: 0, Max: 49)
481	y2_biii_rec_scaled Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y2_drop] = '0'	Bayley-III score, receptive communication, scaled score	text (number, Min: 1, Max: 19)
482	y2_biii_exp_raw Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y2_drop] = '0'	Bayley-III score, expressive communication, raw score	text (number, Min: 0, Max: 46)
483	y2_biii_exp_scaled Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y2_drop] = '0'	Bayley-III score, expressive communication, scaled score	text (number, Min: 1, Max: 19)
484	y2_biii_comm_index Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y2_drop] = '0'	Bayley-III score, receptive and expressive communication, index	text (number, Min: 47, Max: 153)

<table>
<tr><td>485</td><td>y2_behaviour

Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y2_drop] = '0'</td><td>Behaviour</td><td>checkbox<table><tr><td>0</td><td>y2_behaviour___0</td><td>normal</td></tr><tr><td>1</td><td>y2_behaviour___1</td><td>ADHD</td></tr><tr><td>2</td><td>y2_behaviour___2</td><td>autism spectrum disorder</td></tr><tr><td>3</td><td>y2_behaviour___3</td><td>self-regulation difficulties</td></tr><tr><td>4</td><td>y2_behaviour___4</td><td>anxiety</td></tr><tr><td>5</td><td>y2_behaviour___5</td><td>attachment disorder</td></tr><tr><td>6</td><td>y2_behaviour___6</td><td>obsessive compulsive disorder</td></tr><tr><td>7</td><td>y2_behaviour___7</td><td>other disorder</td></tr><tr><td>8</td><td>y2_behaviour___8</td><td>further investigation</td></tr></table></td></tr>
<tr><td>486</td><td>asd_2

Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y2_drop] = '0'</td><td>Autism Spectrum Disorder (ASD)</td><td>dropdown<table><tr><td>0</td><td>no suspicion of ASD</td></tr><tr><td>1</td><td>suspicion of ASD</td></tr><tr><td>2</td><td>diagnosis of ASD</td></tr></table></td></tr>
<tr><td>487</td><td>y2_motor

Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y2_drop] = '0'</td><td>Neuromotor evaluation</td><td>dropdown<table><tr><td>0</td><td>no consultation with psychotherapist</td></tr><tr><td>1</td><td>excellent</td></tr><tr><td>2</td><td>normal</td></tr><tr><td>3</td><td>suboptimal</td></tr><tr><td>4</td><td>deviant</td></tr></table></td></tr>
<tr><td>488</td><td>y2_biii_fine_raw

Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y2_drop] = '0'</td><td>Bayley III score, fine motor, raw score</td><td>text (number, Min: 0, Max: 66)</td></tr>
</table>

489	y2_biii_fine_scaled Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y2_drop] = '0'	Bayley III score, fine motor, scaled score	text (number, Min: 1, Max: 19)
490	y2_biii_fine_ageq Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y2_drop] = '0'	Bayley III score, fine motor, age equivalent	text (number)
491	y2_biii_gros_raw Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y2_drop] = '0'	Bayley III score, gros motor, raw score	text (number, Min: 0, Max: 72)
492	y2_biii_gros_scaled Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y2_drop] = '0'	Bayley III score, gros motor, scaled score	text (number, Min: 1, Max: 19)
493	y2_biii_gros_ageq Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y2_drop] = '0'	Bayley III score, gros motor, age equivalent	text (number)
494	y2_biii_gros_index Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y2_drop] = '0'	Bayley III score, gros motor, index	text (number, Min: 46, Max: 154)

495	y2_concl_normal Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y2_drop] = '0'	Section Header: *Conclusions* Normal development	yesno, Required 1, Yes 0, No
496	y2_concl_mild Show the field ONLY if: [y2_concl_normal] = '0'	Mild neurodevelopmental impairment	checkbox, Required 0, y2_concl_mild___0, No 1, y2_concl_mild___1, Grof Motorisch Functionerings Classificatie Systeem (GMFCS) I 2, y2_concl_mild___2, Cognitive 3, y2_concl_mild___3, Motor 4, y2_concl_mild___4, Other
497	y2_concl_mod Show the field ONLY if: [y2_concl_normal] = '0' and [y2_concl_mild(0)] = '1'	Moderate neurodevelopmental impairment	checkbox, Required 0, y2_concl_mod___0, No 1, y2_concl_mod___1, GMFCS II 2, y2_concl_mod___2, Cognitive 3, y2_concl_mod___3, Hearing 4, y2_concl_mod___4, Words 5, y2_concl_mod___5, Vision 6, y2_concl_mod___6, Other
498	y2_concl_sev Show the field ONLY if: [y2_concl_normal] = '0' and [y2_concl_mild(0)] = '1' and [y2_concl_mod(0)] = '1'	Severe neurodevelopmental impairment	checkbox, Required 0, y2_concl_sev___0, No 1, y2_concl_sev___1, GMFCS III-IV 2, y2_concl_sev___2, Cognitive 3, y2_concl_sev___3, Hearing 4, y2_concl_sev___4, Words 5, y2_concl_sev___5, Vision 6, y2_concl_sev___6, Other
499	years_cos_follow_up_complete	Section Header: *Form Status* Complete?	dropdown 0, Incomplete 1, Unverified 2, Complete

Instrument: **4 years COS follow-up** (years_cos_follow_up_d1ea)

500	dt8 Show the field ONLY if: [mother_arm_1][back] = '1' or [mortality] = '1' or [lifebirth] = '0'	If this form is empty - your patient has been transferred to the referral hospital and has given birth there or - the neonate passed away	descriptive
501	y4_drop Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [cos_indicated] = '1'	Drop out of long-term follow-up?	yesno 1, Yes 0, No
502	y4_date Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	Date of consultation	text (date_dmy), Identifier
503	y4_hosp Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	Number of hospitalisations after discharge from NICU	text (number)
504	y4_edu Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	Current education	dropdown 1, regular education 2, regular education with additional support 3, regular education, repeat school year 4, special education
505	y4_weight Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	Weight (kg)	text (number, Min: 5, Max: 50)

506	y4_weight_perc Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	Weight (%)	dropdown 1 | < p3 2 | >= p3 - < p10 3 | >= p10 - < p25 4 | >= p25 - < p50 5 | >= p50 - < p75 6 | >= p75 - < p90 7 | >= p90 - < p97 8 | >= p97
507	y4_height Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	Height (cm)	text (number, Min: 50, Max: 150)
508	y4_height_perc Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	Height (%)	dropdown 1 | < p3 2 | >= p3 - < p10 3 | >= p10 - < p25 4 | >= p25 - < p50 5 | >= p50 - < p75 6 | >= p75 - < p90 7 | >= p90 - < p97 8 | >= p97
509	y4_headc Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	Head circumference (cm)	text (number, Min: 30, Max: 80)
510	y4_headc_perc Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	Head circumference (%)	dropdown 1 | < p3 2 | >= p3 - < p10 3 | >= p10 - < p25 4 | >= p25 - < p50 5 | >= p50 - < p75 6 | >= p75 - < p90 7 | >= p90 - < p97 8 | >= p97

511	y4_genpeds Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	General pediatric evaluation	checkbox

1	y4_genpeds___1	normal
2	y4_genpeds___2	on oral/inhalatic respiratory therapy
3	y4_genpeds___3	limited respirat exercise toleran
4	y4_genpeds___4	requires oxyger
5	y4_genpeds___5	requires continued respiratory support
6	y4_genpeds___6	renal impairmer requiring treatment or special diet
7	y4_genpeds___7	requires dialysis or awaiting orga transplant
8	y4_genpeds___8	feeding problems/avers
9	y4_genpeds___9	requires nasogastric or percutaneous endoscopic gastrostomy feeding
10	y4_genpeds___10	on semi-elemer diet
11	y4_genpeds___11	stoma
12	y4_genpeds___12	requires TPN
13	y4_genpeds___13	cardiac dysfunction
14	y4_genpeds___14	endocrine dysfunction

512	y4_neuroex Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	Neurological examination	checkbox

1	y4_neuroex___1	normal
2	y4_neuroex___2	suspect psychomotor
3	y4_neuroex___3	suspect cerebral palsy
4	y4_neuroex___4	cerebral palsy, spastic, diplegy
5	y4_neuroex___5	cerebral palsy, spastic, quadriplegy
6	y4_neuroex___6	cerebral palsy, unilateral
7	y4_neuroex___7	cerebral palsy, dyskinetic
8	y4_neuroex___8	cerebral palsy, ataxic
9	y4_neuroex___9	cerebral palsy, GMFCS I
10	y4_neuroex___10	cerebral palsy, GMFCS II
11	y4_neuroex___11	cerebral palsy, GMFCS III
12	y4_neuroex___12	cerebral palsy, GMFCS IV
13	y4_neuroex___13	cerebral palsy, GMFCS V

513	y4_epilepsy Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	Epilepsy, treated or not	dropdown

0	no
1	yes, under medication
2	yes, without medication

514	y4_mri Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	Cranial MRI taken after bilan at 2 years and before bilan at 4 years	checkbox 0, y4_mri___0, no MRI taken 1, y4_mri___1, normal 2, y4_mri___2, maldevelopments 3, y4_mri___3, periventricular leucomalacia (PVL) 4, y4_mri___4, sequelae interventricular hemorrhage (IVH) or periventricular hemorrhagic infarction 5, y4_mri___5, combination PVL and IVH 6, y4_mri___6, basal ganglia/thalami injury 7, y4_mri___7, parasagittal lesions 8, y4_mri___8, middle cerebral artery infarctions 9, y4_mri___9, miscalleneous
515	y4_ophtalmo Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	Ophtalmological examination	dropdown 0, not done 1, normal 2, retinopathy, treated 3, retinopathy, untreated
516	y4_eye Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	Vision	checkbox 1, y4_eye___1, normal 2, y4_eye___2, strabismus 3, y4_eye___3, nystagmus 4, y4_eye___4, retinopathy 5, y4_eye___5, characteristics of cortical visual impairment 6, y4_eye___6, other
517	y4_eyefct Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	Functionality of vision	dropdown 1, normal 2, impaired without spectacles 3, impaired with spectacles 4, severely impaired: blind or no useful vision (after correction, on the better eye)

518	y4_ear Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	Functionality of hearing	dropdown 1, normal 2, impaired without hearing aids 3, impaired with hearing aids 4, severely impaired: hearing loss > 70dB (before correction, on the better ear)
519	y4_iq_tot Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	Wechsler Preschool and Primary Scale of Intelligence (WPPSI)-III test, total IQ score	text (number, Min: 55, Max: 145)
520	y4_iq_perf Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	WPPSI-III test, performal IQ score	text (number, Min: 55, Max: 145)
521	y4_iq_verb Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	WPPSI-III test, verbal IQ score	text (number, Min: 55, Max: 145)
522	y4_process Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	WPPSI-III test, processing speed	text (number, Min: 55, Max: 145)
523	y4_nonverb Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	WPPSI-III test, nonverbal index	text (number)

524	y4_behaviour Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	Behaviour	checkbox 0, y4_behaviour___0, normal 1, y4_behaviour___1, ADHD 2, y4_behaviour___2, autism spectrum disorder 3, y4_behaviour___3, self-regulation difficulties 4, y4_behaviour___4, anxiety 5, y4_behaviour___5, attachment disorder 6, y4_behaviour___6, obsessive compulsive disorder 7, y4_behaviour___7, other disorder 8, y4_behaviour___8, further investigation
525	asd_4 Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	Autism Spectrum Disorder	dropdown 0, no suspicion of ASD 1, suspicion of ASD 2, diagnosis of ASD
526	y4_motor Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	Neuromotor evaluation	dropdown 0, no consultation with psychotherapist 1, excellent 2, normal 3, suboptimal 4, deviant
527	y4_mabc_tot_raw Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	Movement Assessment Battery for Children (MABC) test, total raw score	text (number)

528	y4_mabc_tot_perc Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	MABC test, total score, percentile	text (number, Min: 0, Max: 100)
529	y4_mabc_ac_raw Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	MABC test, aiming and catchin, raw score	text (number)
530	y4_mabc_ac_perc Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	MABC test, aiming and catching, percentile	text (number, Min: 0, Max: 100)
531	y4_mabc_bal_raw Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	MABC test, balance, raw score	text (number)
532	y4_mabc_bal_perc Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	MABC test, balance, percentile	text (number, Min: 0, Max: 100)
533	y4_mabc_dex_raw Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	MABC test, dexterity, raw score	text (number)

534	y4_mabc_dex_perc Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	MABC test, dexterity, percentile	text (number, Min: 0, Max: 100)
535	y4_vmi_integr_raw Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	Visual Motor Integration (VMI) Beery test, visual motor integration, raw score	text (number, Min: 1, Max: 30)
536	y4_vmi_integr_perc Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	VMI Beery test, visual motor integration, percentile	text (number, Min: 0, Max: 100)
537	y4_vmi_integr_ageq Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	VMI Beery test, visual motor integration, age equivalent	text (number)
538	y4_vmi_perc_raw Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	VMI Beery test, visual perception, raw score	text (number, Min: 1, Max: 30)
539	y4_vmi_perc_perc Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	VMI Beery test, visual perception, percentile	text (number, Min: 0, Max: 100)

540	y4_vmi_perc_ageq Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	VMI Beery test, visual perception, age equivalent	text (number)
541	y4_vmi_motor_raw Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	VMI Beery test, motor coordination, raw score	text (number, Min: 1, Max: 30)
542	y4_vmi_motor_perc Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	VMI Beery test, motor coordination, percentile	text (number, Min: 0, Max: 100)
543	y4_vmi_motor_ageq Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	VMI Beery test, motor coordination, age equivalent	text (number)
544	y4_lang Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	Language	dropdown 0, no test 1, CELF preschool-2_NL 2, Schlichting 3, both 4, other
545	y4_phon_rec Show the field ONLY if: [y4_lang] = '1' or [y4_lang] = '2' or [y4_lang] = '3' or [y4_lang] = '4'	Phonology reception	dropdown 1, excellent 2, normal 3, suboptimal 4, deviant

546	y4_phon_pro Show the field ONLY if: [y4_lang] = '1' or [y4_lang] = '2' or [y4_lang] = '3' or [y4_lang] = '4'	Phonology production	dropdown 1 excellent 2 normal 3 suboptimal 4 deviant
547	y4_art Show the field ONLY if: [y4_lang] = '1' or [y4_lang] = '2' or [y4_lang] = '3' or [y4_lang] = '4'	Articulation	dropdown 1 excellent 2 normal 3 suboptimal 4 deviant
548	y4_voc_comp Show the field ONLY if: [y4_lang] = '1' or [y4_lang] = '2' or [y4_lang] = '3' or [y4_lang] = '4'	Vocabulary comprehension	dropdown 1 excellent 2 normal 3 suboptimal 4 deviant
549	y4_voc_pro Show the field ONLY if: [y4_lang] = '1' or [y4_lang] = '2' or [y4_lang] = '3' or [y4_lang] = '4'	Vocabulary production	dropdown 1 excellent 2 normal 3 suboptimal 4 deviant
550	y4_synt_comp Show the field ONLY if: [y4_lang] = '1' or [y4_lang] = '2' or [y4_lang] = '3' or [y4_lang] = '4'	MorphoSyntax comprehension	dropdown 1 excellent 2 normal 3 suboptimal 4 deviant
551	y4_synt_pro Show the field ONLY if: [y4_lang] = '1' or [y4_lang] = '2' or [y4_lang] = '3' or [y4_lang] = '4'	MorphoSyntax production	dropdown 1 excellent 2 normal 3 suboptimal 4 deviant
552	y4_prag Show the field ONLY if: [y4_lang] = '1' or [y4_lang] = '2' or [y4_lang] = '3' or [y4_lang] = '4'	Pragmatics	dropdown 1 normal 2 abnormal

553	y4_concl_normal Show the field ONLY if: [mother_arm_1][back] <> '1' and [lifebirth] = '1' and [mortality] = '0' and [y4_drop] = '0'	Section Header: *Conclusions* Normal development	yesno, Required 1, Yes 0, No
554	y4_concl_mild Show the field ONLY if: [y4_concl_normal] = '0'	Mild neurodevelopmental impairment	checkbox, Required 0, y4_concl_mild___0, No 1, y4_concl_mild___1, Grof Motorisch Functionerings Classificatie Systeem (GMFCS) I 2, y4_concl_mild___2, Cognitive 3, y4_concl_mild___3, Motor 4, y4_concl_mild___4, Other
555	y4_concl_mod Show the field ONLY if: [y4_concl_normal] = '0' and [y4_concl_mild(0)] = '1'	Moderate neurodevelopmental impairment	checkbox, Required 0, y4_concl_mod___0, No 1, y4_concl_mod___1, GMFCS II 2, y4_concl_mod___2, Cognitive 3, y4_concl_mod___3, Hearing 4, y4_concl_mod___4, Words 5, y4_concl_mod___5, Vision 6, y4_concl_mod___6, Other
556	y4_concl_sev Show the field ONLY if: [y4_concl_normal] = '0' and [y4_concl_mild(0)] = '1' and [y4_concl_mod(0)] = '1'	Severe neurodevelopmental impairment	checkbox, Required 0, y4_concl_sev___0, No 1, y4_concl_sev___1, GMFCS III-IV 2, y4_concl_sev___2, Cognitive 3, y4_concl_sev___3, Hearing 4, y4_concl_sev___4, Words 5, y4_concl_sev___5, Vision 6, y4_concl_sev___6, Other
557	years_cos_follow_up_d1ea_complete	Section Header: *Form Status* Complete?	dropdown 0, Incomplete 1, Unverified 2, Complete

Universitair Ziekenhuis Gent

UNIVERSITEIT GENT

1. Samenvatting

Onderstaand document beschrijft de richtlijnen voor de aanpak van dreigende vroeggeboorte in het UZ Gent.

2. Inleiding/doel

Onderstaand document beschrijft de richtlijnen voor de aanpak van dreigende vroeggeboorte in het UZ Gent. Deze richtlijn is een leidraad. De Vrouwenkliniek afdeling verloskunde is niet verantwoordelijk voor de gevolgen van de toepassing ervan buiten het UZ Gent.

3. Afkortingen en definities

CTG: Cardiotocografie
NPW: Negatief Predictieve Waarde
PBO: Perifeer Bloed Onderzoek
PPROM: Preterm Prelabour Rupture Of Membranes
RR: Bloeddruk

4. Toepassingsgebied

Deze procedure is van toepassing voor de Vrouwenkliniek, afdeling verloskunde

5. Verantwoordelijkheden en bevoegdheden

Artsen dragen de verantwoordelijkheid, maar vroedvrouwen moeten de procedure ook in acht houden.

6. Grafische voorstelling

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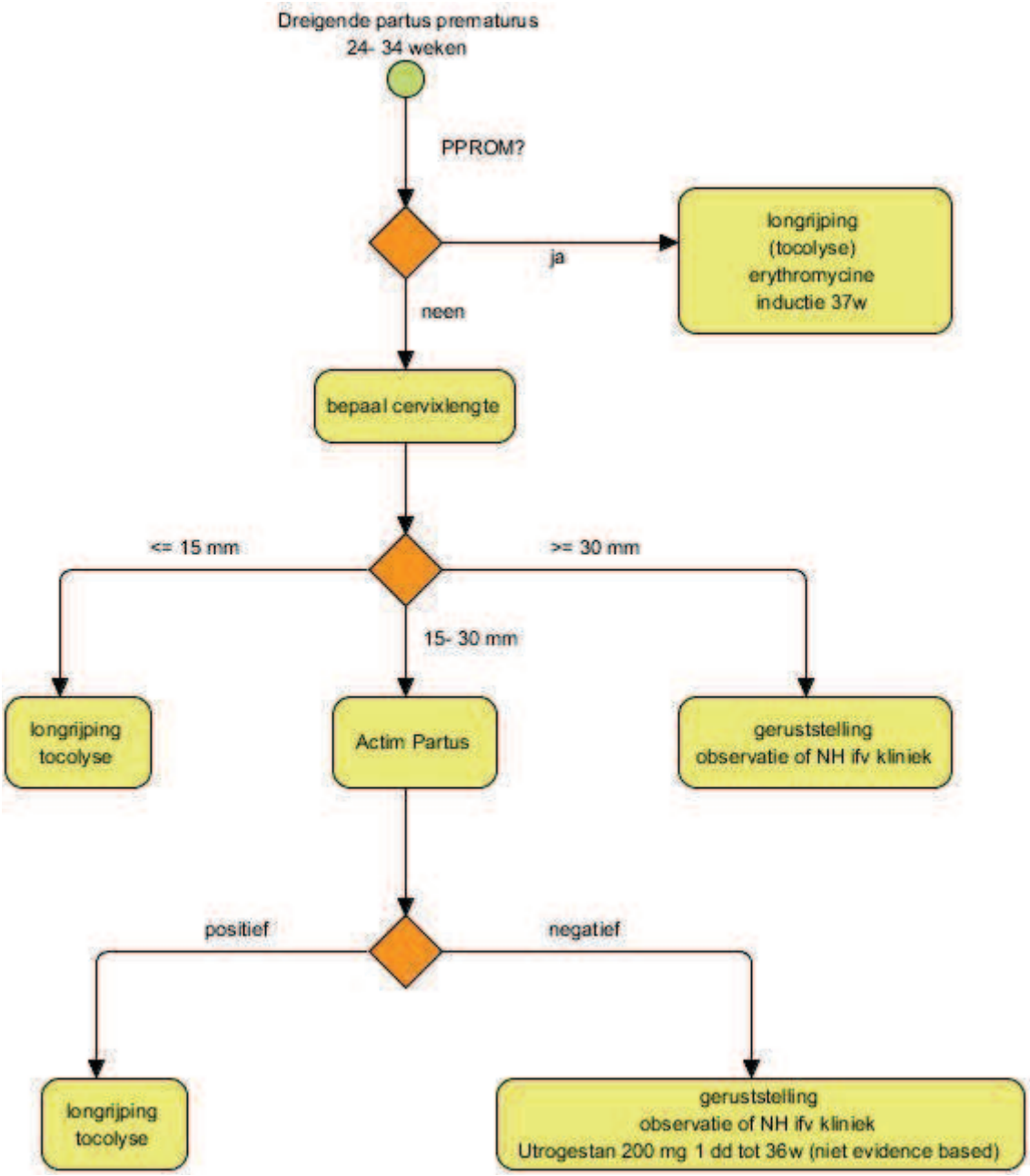

7. Benodigdheden

NVT

8. Procedure

8.1 Definitie

Dreigende partus prematurus:

Het optreden vóór de 37ste zwangerschapsweek van **uteriene contracties** (pijnlijke, bij palpatie voelbare opspanningen van de uterus) **en** die leiden tot **cervicale verandering**.

PPROM:
Gebroken vliezen zonder contracties voor 37 weken zwangerschap.

8.2 Prevalentie

Partus < 37 weken: 7,5 % (SPE, 2012, Vlaanderen).
Partus < 34 weken: 1,1 % (SPE, 2012, Vlaanderen).

8.3 Etiologie/risicofactoren (deze lijst is niet bedoeld om volledig te zijn)

- vaak ongekend
- voorgeschiedenis van vroeggeboorte (belangrijkste risicofactor)
- chorioamnionitis (vaginaal of hematogeen)
- PPROM
- meerling
- verkorte cervix (bvb bij screening in het tweede trimester)
- iatrogeen (foetale of maternele indicatie)
- maternele ziekte: gastro-enteritis, cystitis, …
- roken
- …

8.4 Preventie

Enkele interventies in de algemene populatie verminderen het risico op vroeggeboorte: **rookstop** en screenen op en behandeling van asymptomatische **bacteriurie** (screening bij 16 weken).

a. Vaginale kweek

In **eerste trimester** afname vaginale kweek bij voorgeschiedenis van vroeggeboorte. De evidentie hierrond is niet eensluitend.
Bacteriële vaginose: Clindamycine 2 dd 300 mg po, gedurende 5 dagen. Flagyl eveneens toegelaten in eerste trimester.
Candida: te behandelen met éénmalig Miconazole ovule 1200mg.

b. Cervixlengtemeting

Bij **asymptomatische** patiënten:

- partus immaturus in voorgeschiedenis
  termijn: 16 weken
  afkapwaarde: zie protocol cervixinsufficiëntie
  consequentie: overwegen cerclage

- partus prematurus in voorgeschiedenis
  termijn: 20 weken
  afkapwaarde: 25 mm
  consequentie: overwegen cerclage (in combinatie met (reeds opgestarte) progesteron)

- alle patiënten
  termijn: 20 weken igv hoog risico, 24 weken bij laagrisico patiënte
  afkapwaarde: 25 mm
  consequentie: progesteron (Utrogestan ® 1 dd 200 mg vaginaal voor slapengaan)

Bij **symptomatische** patiënten: cfr infra.

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c. Progesteron

Blijft anno 2013 een hot topic. De evoluties op dit domein dienen verder opgevolgd te worden en kunnen een beleidsverandering teweeg brengen.

Indicaties volgens de tot op heden verworven kennis:
- **partus prematurus in voorgeschiedenis**
  dosering: 1 dd 200 mg vaginaal voor slapengaan
  termijn: van 16 tot 36 weken

- **cxlengte < 25 mm** bij asymptomatische patiënte, **19-24 weken zwanger**
  dosering: 1 dd 200 mg vaginaal voor slapengaan

Er zijn geen studies over progesteron bij meerlingen beschreven. Evenmin weinig gegevens over progesteron na toedienen tocolyse (eventueel kan bij verkorte cervix 200 mg vaginaal progesteron voorgeschreven worden).

8.5 Diagnostiek, opvolging en aanpak

a. Diagnostiek **cfr schema 1**

Vermoeden dreigende vroeggeboorte obv **kliniek**:
- voelbare uteriene contracties en/of tocografie positief
- PPROM
- tekenen, bloedverlies

Diagnose op basis van **cervixlengte**. Eventueel aangevuld met vaginaal toucher.
Al dan niet in combinatie met **Actim Partus® test** (niet bij PPROM).
Afname Actim Partus® test alvorens TVE!!
Aparte wattenstaafjes voor Actim Partus test beschikbaar. Afname cfr infra.
Indien cervixlengte <15 of > 30 mm: wattenstaafje wegwerpen. Indien cervixlengte 15-30 mm: verpakking van Actim Partus test openen en test uitvoeren.

DIAGNOSE PRETERME CONTRACTIES
- cervixlengte **≥ 30 mm**: geen tocolyse - cervixlengte **≤ 15 mm**: tocolyse en longrijping - cervixlengte **15-30 mm**: Actim Partus als negatief: geen tocolyse als positief: tocolyse en longrijping

Afname Actim Partus® test:
Wattenstaafje ter hoogte van os cervici gedurende 10-15 seconden. In medium roeren gedurende 10-15 seconden (1) en verwijderen. Teststrip in medium (2). Wanneer verzadigd kan deze uit medium gehaald worden (3). Af te lezen na de 5 minuten: 1 streepje = negatief, 2 streepjes = positief (4).

1 2 3 4

bron: www.medixbiochemica.com

Actim Partus® test

spoort ph IGFBP – 1 op
vanaf 22
hoge NPW
afname swab **thv os cervici**
afname **voor TVE**
PPROM: contra-indicatie (CI)
overvloedig vaginaal bloedverlies: CI weinig/matig: vals positief mogelijk, geen vals negatief
coïtus laatste 24 u: geen contra-indicatie
praktische test (idem als Actim PROM test)
duur test: max 5 min

Diagnostiek PPROM:
Speculumonderzoek: afvloei van liquor zichtbaar, al dan niet na hoesten of Valsalva.

varentest	uitstrijkje op een draagglaasje en laten opdrogen onder microscoop typisch varenpatroon (onafhankelijk van de zwangerschapsduur)
PROM-test (Actim-PROM®)	2 streepjes = positief uit te voeren wanneer varentest niet conclusief

Afname Actim Prom® test: bijgeleverd wattenstaafje vaginaal gedurende 10-15 seconden. In medium roeren gedurende 10-15 seconden en verwijderen. Teststrip in medium. Wanneer verzadigd kan deze uit medium gehaald worden. Af te lezen na de 5 minuten: 1 streepje = negatief, 2 streepjes = positief.

Actim Prom® test
spoort IGFBP – 1 op
elke zwangerschapsduur
hoge sensitiviteit
afname swab thv os cervici of fornix posterior
vaginaal bloedverlies, semen, urine, gel: geen contra-indicatie
duur test: max 5 min

b. Bijkomende investigaties

- vitale parameters (temperatuur, pols, RR), fundushoogte
- speculumonderzoek + Chlamydia PCR, vaginale kweek, rectovaginale GBS kweek
- echografie (morfologie, biometrie, biofysisch profiel, ligging, placenta, Doppler a.umbilicalis)
- urinesediment en kweek (gesondeerd, zeker bij PPROM)
- labo (PBO, elektrolyten, glycemie, lever- en nierfunctie, CRP)
- CTG (vanaf 24 – 26 weken afhankelijk van de wens tot intensieve zorg voor preterme neonaat bij patiënte)
- igv PPROM: cervixlengte met steriele handschoen over sonde en steriele KY gel

c. Indicaties voor hospitalisatie

- Patiënte met contracties en cervix ≤ 15mm
- Patiënte met contracties, verkorte cervix (> 15 mm en < 30 mm) en positieve Actim Partus®
- Patiënte waarbij men twijfelt: 24 uur opname, zeker bij zwangerschapsduur < 34 weken
- PPROM

d. Aanpak en opvolging

Zwangerschapsduur tussen 34 en 37 weken
▪ expectatief, geen tocolyse ▪ relatieve bedrust ▪ CTG 1 x/dag ▪ ontslag indien niet evolutief en na geruststelling patiënte, tenzij bij gebroken vliezen
Zwangerschapsduur < 34 weken
▪ relatieve bedrust ▪ foetale longrijping (zie "**Longrijping**", pt 8.6) ▪ antibiotica (zie: "**Antibiotica**", pt 8.7) ▪ tocolyse (zie: "**Tocolytica**", pt 8.8) ▪ bij partus imminens, denk aan GBS profylaxie ▪ vitale parameters 2dd ▪ CTG 1dd ▪ cervixlengte/vaginaal toucher (en eventueel Actim Partus test opnieuw doen) op indicatie (menstruatie-achtig gevoel, harde buiken, positieve tocografie, bloedverlies,…) ▪ vaginale kweek, PBO + CRP, urinesediment en midstream: herhalen op indicatie ▪ echografie wekelijks, biometrie tweewekelijks ▪ GBS kweek 1x/4 weken ▪ gesprek neonatoloog regelen indien gewenst, altijd indien 24-26weken ▪ < 32 weken en evolutieve arbeid: neuroprotectie (zie: "**Neuroprotectie**", pt 8.9)
PPROM

▪ cfr supra +
▪ tocolyse niet herstarten na 28 weken
▪ erythromycine (vb Erythro forte®) 4 dd 500mg per os gedurende 10 dagen
▪ infectieuze parameters dagelijks, nadien 2-3x/week
▪ vaginakweek wekelijks
▪ inductie bij 37 weken (manier van inleiding cfr PROM)
▪ indien tekenen van chorioamnionitis
  ○ GEEN tocolyse
  ○ partus inleiden
  ○ amoxicilline + clavulaanzuur (vb Augmentin®) 4 dd 1g IV tot 24 uur na de partus igv afebriele patiënte (als koorts en/of pos hemocultuur moet antibiotica langer gecontinueerd worden); te overwegen postpartaal 24-48u Augmentin Retard ® po 2 dd 2g
  ○ Igv peni-allergie: clindamycine-gentamycine

8.6 Longrijping

Indicatie: partus verwacht binnen de 7 dagen bij eenling < 34 weken of meerling < 32 weken

Suggestief voor partus < 7 dagen:
- symptomatisch en cervixlengte < 15 mm
- symptomatisch en cervixlengte 15 – 30 mm met pos Actim Partus® test
- contracties en vaginaal bloedverlies
- PPROM
- indicatie voor preterme verlossing (IUGR, MCMA tweeling, …)

Product en dosering:
- Betamethason (**Celestone**® Chronodose)
- 1 kuur = **2 x 12 mg** IM, met tussentijd van **24 uur** (1 kuur = 2 maal 2 flacons Celestone® Chronodose (5,7 mg betamethason))

- Alternatief in geval van stockbreuk: Diprophos (betamethason (natriumfosfaat) 2mg + betamethason (dipropionaat) 5mg / ml), spuitampul van 2 mL: 2x1 ampul IM, met tussentijd van 24 uur
- 2e keus alternatief: Aacidexam (dexamethasone) 4 x 6 mg IM met 12u tussen.

Schema:
- Dreigende vroeggeboorte (<28 weken):
  - gesprek met neonatoloog ter bepaling van termijn waarop start intensieve zorgen; longrijping moet 48u voor vooropgestelde termijn gestart worden

- start **1 kuur** longrijping **vanaf 25 5/7 weken**, of ten vroegste vanaf **23 5/7** weken, afhankelijk van de keuze van de patiënte na overleg met neonatoloog
- **wekelijks halve kuur** (1 x 2 flacons of 1 x 12 mg) te herhalen bij persisterende dreigende vroeggeboorte tot en met de termijn van 28 6/7 weken of een maximale cumulatieve dosis van 6 (6 x 12 mg = initiële kuur + 4 herhaal ½ kuren)

- Dreigende vroeggeboorte (**28-34 weken**):
  - **1 kuur** longrijping

8.7 Antibiotica

- Positief urinesediment:
  - amoxicilline 3 dd 500 mg ged 5d
  - eventueel aanpassen na antibiogram
- Bacteriële vaginose:
  - metronidazole (Flagyl®, Fasigyn ®) 2 dd 500mg 7d of
  - clindamycine 2 x 300mg/d 7d
  - onmiddellijk te starten indien RO diagnostisch voor bacteriële vaginose, zoniet op geleide van kweekuitslag
- Chlamydia trachomatis:
  - azithromycine 1g po eenmalig of
  - amoxicilline 3 dd 500mg 7d
- GBS pos:
  - partus imminens: GBS profylaxie volgens protocol
  - geen partus imminens: geen behandeling
- Chorioamnionitis:
  - CRP stijging van >20 g/dl én geen andere haarden van Infectie en klnische tekenen van dreigende vroeggeboorte: amoxicilline-clavulaanzuur 4 dd 1g IV, op basis van kliniek over te schakelen op per os, totale duur 7d
- PPROM:
  - erythromycine 4 dd 500 mg po ged 10d

8.8 Tocolyse

8.8.1 Vuistregels

- Tocolytica hebben als DOEL :
  - de mogelijkheid te geven LONGRIJPING toe te dienen
  - een INTRA-UTERIENE TRANSFER naar een MIC/NIC centrum mogelijk te maken

Er is geen enkele evidentie voor gebruik van tocolyse om andere redenen.

In geval van dreigende premature partus < 34 weken (32 weken voor tweeling) **herhaaltocolyse** (tot maximaal 3 kuren) te overwegen (op vraag van de patiënte en op gevoel van de arts).
Het is belangrijk aan de patiënte duidelijk te maken dat hier geen evidentie voor is.
In geval van herhaaltocolyse, moet er een bewezen cervixlengte-verandering zijn. Eventueel kan herhaling van de Actim Partus test overwogen worden.
Herhaaltocolyse is tegenaangewezen bij (tekenen van) infectie of preëclampsie.
Geen verlenging van 48u durende kuren om een 'kantooruurpartus' na te streven!

PPROM: tocolyse **niet herhalen na 28 weken**

Chronische tocolyse uitzonderlijk bij de niet-infectieuze patiënte, met intacte vliezen, die bij contracties begint te bloeden (bijv. placenta praevia). Bijvoorbeeld onderstaand schema (nationale richtlijn KCE):

- 4 dd 20 mg nifedipine retard maximum 12 dagen na de 2 dagen van initiële tocolyse en longrijping
- afbouwen vanaf D10:
  - D10 60 mg/d (in 3 dosissen)
  - D11 40 mg/d (2 dosissen)
  - D12 20 mg

Combineren van tocolytica is niet evidence-based, is geassocieerd met meer bijwerkingen en wordt zeker niet meer toegepast na 28 weken.

8.8.2 Algemene contra-indicaties van tocolyse:

- < 23-25+5 weken (afhankelijk van wens ouders) of > 34+0 weken (bij meerling 32 weken)
- (pre)eclampsie
- chorioamnionitis
- abruptio/solutio placentae
- IUGR en afwijkende Doppler/CTG
- intra-uteriene vruchtdood
- foetale aandoeningen die niet met het leven verenigbaar zijn

8.8.3 Welk tocolyticum?

Voorkeurspreparaten:
1. Calciumblokker: Nifedipine (Adalat®)
2. Oxytocine antagonisten: Atosiban (Tractocile®)

Tweede keuze:
1. Prostaglandine synthetaseremmers: Indomethacine (Dolcidium®, Indocid®)
2. [Betamimetica: Ritodrine (Prepar®)]

CAVE:
Tractocile® eerste keuze bij:
- contra-indicaties voor Adalat®
- meerlingen
- cardiaal belaste patiënten
- reeds opgestart in doorverwijzend ziekenhuis.

a. Calciumblokkers

Nifedipine (Adalat ®)

- even effectief als beta-mimetica
- minder bijwerkingen (hoofdpijn, enkeloedeem, warmte-opwellingen, hypotensie en reflectoire tachycardie)

Toedieningswijze: per os.

Schema:

In het eerste uur **nifedipine 2 comprimés van 10 mg**, daarna **20 mg nifedipine retard** per 6 uur voor de volgende 47h.

t 0h: 1 co 10 mg Adalat®	t 24h: 20 mg Adalat® Retard
t 15': 1 co 10 mg Adalat®	t 30h: 20 mg Adalat® Retard
t 06h: 20 mg Adalat® Retard	t 36h: 20 mg Adalat® Retard
t 12h: 20 mg Adalat® Retard	t 42h: 20 mg Adalat® Retard
t 18h: 20 mg Adalat® Retard	

b. Oxytocine antagonisten

Atosiban (Tractocile ®)

- even effectief als beta-mimetica
- minder bijwerkingen (nausea, braken, hoofdpijn, opvliegers, tachycardie, hypotensie, hyperglycemie)

Toedieningswijze: intraveneus.

Schema:

Bolus	1A Solution for injection (bleekblauw)= 0,9 ml van 7.5 mg/ml over 1 min = 6.75 mg over 1 min
Oplaaddosis	2A Concentrate for Solution (donkerpaars) 5 ml van 7.5 mg/ml (37,5 mg per A) in 90 ml fysiologisch of glucose 5% à 24 ml/u gedurende 3u = 300 µg/min
Onderhoudsdosis	zelfde oplossingsconcentraat als oplaaddosis maar a rato van 8ml/u = 100µg/min

c. Prostaglandinesynthetase-remmers

Indomethacine (Indocid®)

- Contra-indicaties
  - actieve maagdarmbloedingen, gastroduodenaal ulcus of gastritis
  - ernstige nierinsufficiëntie
  - voorgeschiedenis van allergische reacties door salicylaten en NSAID
- Neveneffecten
  - Foetaal: inductie van vroegtijdig sluiten van de foetale ductus arteriosus met risico op pulmonaire hypertensie, verminderde diurese met tot gevolg oligohydramnion (bij langdurig gebruik)
  - Maternaal: gastro-intestinale effecten

Toedieningswijze: rectaal.

Dosering:

100 mg per suppo maximum 2 suppo's per dag **niet** gebruiken na zwangerschapsduur van 32 weken

d. β-sympaticomimetica

Ritodrine (Pre-Par®)

- Contra-indicaties
  - hartpatiënten! EKG niet systematisch te nemen; enkel o.b.v. aanwijzingen in anamnese
  - diabetes
  - manifeste hyperthyreoïdie met tachycardie
  - Meerling
- Neveneffecten:
  - Materneel: tachycardie, palpitaties, tremor, hypotensie, hyperglycemie en gestoorde glucosetolerantie, voorbijgaande hypokaliëmie (<3 mEq/l), longoedeem, zeldzaam: nausea, zweten en flush

Toedieningswijze: intraveneus.

8.8.4 Ernstige complicatie van tocolyse: longoedeem

- mogelijke complicatie van ritodrine, vooral indien samen met indomethacine en corticosteroïden, en in combinatie met ruime intraveneuze vochttoediening; kan eveneens, maar minder frequent, complicatie zijn van nifedipine
- therapie: medicatie staken, O2, Furosemide (vb Lasix®), eventueel digitalisatie (overleg met internist)

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8.9 Neuroprotectie

- Middel: **MgSO4**.
- Indicatie:
  Dreigende partus **binnen 24 uur tussen 24-26** (afhankelijk van wens ouders) **en 32 weken**
- Suggestief voor partus < 24u:
  - ≥ 4 cm ontsluiting (max 8 cm)
  - contractiel (en cervixverandering) ondanks tocolyse
  - PPROM en contractiel
  - iatrogeen (geplande preterme partus om foetale of maternale reden)
  - ….
- Dosering: volgens preeclampsie protocol **(bolus 4 g, onderhoudsdosis 1g/u)**
- Duur toediening: tot partus of **maximaal 24 uur**.
- Neonatoloog dient op de hoogte gesteld te worden van toediening van MgSO4: kan neonatale behandelingsimplicaties hebben.

9. Evaluatie

NVT

10. Referenties

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ENTERALE EN PARENTERALE VOEDING OP DE NEONATOLOGIE

"Preterm birth is a nutritional emergency"

Linde Goossens
Update december 2018

PARENTERALE VOEDING

Samenstelling

Oplossing **A** = glucose 12% + calcium + magnesium + wateroplosbare vitaminen
Oplossing **B** = eiwitten (Vaminolact 6,5%®) + elektrolieten + sporenelementen
Oplossing **C** = vetten (SMOF-lipid 20%®) + vetoplosbare vitaminen

AB_1 = 85 ml A + 15 ml B
AB_2 = 75 ml A + 25 ml B

Manier van opklimmen

Dag 1: AB_1
Dag 2: AB_2 + C
Dag 3 en volgende: AB_2 + C

Hoeveelheid

- Baby's > 34w PML : Dag 1: **60** ml/kg/dag
  Dag 2: **80** ml/kg/dag, waarvan C aan **5** ml/kg/dag (=1g/kg/dag)
  Dag 3: **100** ml/kg/dag, waarvan C aan **10** ml/kg/dag
  Dag 4: **120** ml/kg/dag, waarvan C aan **15** ml/kg/dag
  Dag 5: **140** ml/kg/dag, waarvan C aan **15** ml/kg/dag
  Dag 6 en volgende: **160** ml/kg/d met C **15** ml/kg/d

- Baby's ≤ 34w PML: Dag 1: start met **80** ml/kg/dag
  en klim op met 20 ml/kg/d tot **160** ml/kg/dag
  C wordt eveneens verder opgekommen met 5 ml/kg/dag tot:
  15 ml/kg/dag als G ≤ 1.000g
  18 ml/kg/dag als G > 1.000g

- Dysmature baby's (<p10): starten ook aan **80** ml/kg/dag
  klimmen op met 20 ml/kg/dag tot **160** ml/kg/dag

Controle TG-spiegel (max 250 mg/dl) op dag 5 of 6 (als maximale hoeveelheid vetten toegediend wordt) en daarna *gemiddeld* 1x/week; strikt per week indien > 3g vet/kg/dag.

- Baby's met **GG < 1.001g èn op een OPEN incubator:**

  Het vochtbeleid van 'ELBW' baby's verzorgd op een '*open incubator*' is verschillend van bovenstaande omwille van de exponentiële toename van de 'perspiratio insensibilis' bij dalend geboortegewicht (in tegenstelling tot de lineaire toename bij een *gesloten* incubator).

Het voorgesteld schema bij **OPEN** INCUBATOR is als volgt (ml/kg/24 uur) :

	500 - 800 g	**801 - 1000 g**
Dag 1	120*	100
Dag 2	160*	140
Dag 3	200*	160
Dag 4 of >	200* of ↓	160 of ↓

** glucoseconcentratie in oplossing A = 6 % ipv 12 % !*

PS: 1. Indien totaal vocht > 150 ml/kg/d: AB_1 ook na dag 3 en Calciumgluconaat 10 % 25 ml per 500 ml baxter A (ipv 35 ml).

! Bovenstaand is slechts richtinggevend; het opklimmen van de totale hoeveelheid vocht gebeurt tevens op geleide van vochtbalans en waarden van serum-elektrolieten.

AANDACHTSPUNTEN

Beademde baby's met **RDS** en **G > 1.000g** :

het totaal vocht wordt niet verder opgeklommen dan **120** ml/kg/dag
tot extubatie
of tenzij de vochtbalans/elektrolietenbalans in onevenwicht is
of indien noodzaak tot opdrijven calorie-aanbod (in overleg)

Oplossing C wordt verminderd tot 5 ml/kg/dag:

- bij vermoeden of bewezen sepsis (niet bij geïsoleerde CRP-stijging)
- bij cholestase (zie protocol cholestase)

Andere bronnen van vochttoevoer worden van het **totaal vocht afgetrokken** :

arteriële katheter (zie protocol "Neonatale TPN" p15), continue IV medicatie worden meestal 'extra' gegeven : bloed, SOPP,…

Alle voorschriften lopen **over 24u** toediening en het aantal **ml/uur** wordt genoteerd:

Opl A: ml/u
Opl B_1 of B_2: ml/u
Opl C: ml/u

Elektrolietensupplementen :

- K wordt voorgeschreven per 500ml A-oplossing
- NaCl (10%-20%) wordt in een continue zijlijn gegeven

Bij kortdurende onderbreking van de enterale voeding

zal bij de a terme baby bij voorkeur gebruik gemaakt worden van volgende oplossing: Ped 1: 100-150 ml/kg/dag.

ENTERALE VOEDING

Soort voeding (lokaal beleid)

- ***Colostrum***: (zie protocol "Colostrum")

Is rijk aan immunoglobulines en immuuncellen, wordt gedurende de eerste 24-72u postpartum geproduceerd. Mag de eerste dagen 'rauw' toegediend worden.

- ***Moedermelk / borstvoeding***

Overgangsmelk wordt geproduceerd in de 3de-14de dag postpartum. Deze is rijk aan vet, lactose en vitaminen. Mature melk wordt verkregen vanaf ongeveer 2 weken postpartum en heeft een lagere dichtheid aan nutriënten.

(N.a.v. het advies van de Hoge Gezondheidsraad nr. 8734 (juni 2016) wordt in afwachting van een aangepast lokaal protocol, tot nader bericht (ter plaatse) afgekolfde moedermelk rechtstreeks opgeslagen in de koelkast (gevolgd door transport naar de melkkeuken om in te vriezen) en voorlopig dus niet rauw toegediend).

- ***Indien geen moedermelk voorhanden is***:

Pre-Nan *Stage 1* (Nestlé): bij preterme baby met gewicht < 1.800g
(100% gehydrol. wei-eiw.) bij dysmature baby met gewicht < 1.800g
(80 kcal/100ml; 40% MCT-vet)
(enkel onder vloeibare vorm)

Pre-Nan *Stage 2* (Nestlé): bij preterme baby met gewicht > 1.800g
(100% gehydrol. wei-eiw) bij dysmature baby met gewicht > 1.800g
(73 kcal/100ml; géén MCT)
(vloeibaar èn poeder-vorm)
(probiotica enkel in Stage 2 *poeder*)

Nan Evolia 1 (Nestlé): (HMO & probiotica) bij a terme baby met gewicht > 2.300g
(Pre-Nan Stage 2 kan aangehouden worden bij ex-pretermen met: slechte G-evolutie, dysmaturiteit zonder inhaalgroei, osteopenie, vochtbeperking)
(100% lactose)
(1,2 g eiwitten/100ml: "Optipro"-formule)
(LCPUFA's)
(67 kcal/100ml)

Nan Optipro HA 1 (Nestlé):
(partieel wei-hydrolysaat) bij a terme baby met atopische ouders/broers/zussen – na overleg supervisor

Nutrilon AR 1 (Nutricia) : bij a terme baby met reflux èn overleg SV
(verrijkt met johannesbroodpitmeel)

Nan AR 1 (Nestlé) bij a terme baby met reflux en atopie èn overleg SV
(hypoallergeen; probiotica)
(verrijkt met zetmeel)

Manier van toedienen

PER OS: starten bij een postmenstruele leeftijd van 33 weken bij BV,
bij flesvoeding vanaf 34 weken.

Deze "richtlijn" wordt gehanteerd voor de uniformiteit en werkbaarheid op de afdeling maar kan individueel verschillen. Indien medisch en praktisch mogelijk mag, na overleg met arts-supervisor en verantwoordelijke verpleegkundige, vroeger gestart worden, onafhankelijk van gewicht en zws-leeftijd, op geleide van de 'Early Feeding Skills' – (EFS) schaal (ook wel 'Orale Voedingsbereidheid Schaal' genoemd: OVB - schaal).
Voorzichtigheid bij enteraal starten en opklimmen blijft evenwel geboden bij baby's met een (geboorte)gewicht lager dan 1.500g !

PER SONDE (bolusvoeding geniet de voorkeur over continue toediening omwille van het risico van vastkleven van vetten aan de leidingen): indien niet aan bovenvermelde criteria voldaan wordt of om medische redenen.

DE OVERSCHAKELING VAN SV NAAR PO : recentelijk baseren we ons op de EFS schaal en "bieden we voeding aan, rest SV". Nooit forceren !

Aantal voedingen

G < 1.000 g:	~ 10 voedingen
G 1.000 - 1.300g:	~ 8 voedingen
G > 1.300g:	~ 7 voedingen
G > 2.300g:	~ 6 voedingen bij KV
	~ 7 (8) voedingen is meer fysiologisch indien volledig enteraal èn partiële BV; alsook bij de combinatie PO/sondevoeding onder exclusieve MM; *(individueel te bekijken per patiënt !)*
	~ onbeperkt, op vraag, bij exclusieve BV

(7 x 60 ml Pre-Nan Stage 2 wordt dan 6 x 70 ml Nan Evolia 1, tenzij bij (partiële) BV/moedermelk: dan kunnen 7 (8) voedingen aangehouden worden om "fysiologische" redenen)

Opklimmen van enterale voeding

INDIEN UITSLUITEND ENTERALE VOEDING

a terme baby:	dag 1:	**40** (tot 60) ml/kg/dag
	dag 2:	**60** (80) ml/kg/dag
	dag 3:	**80** (100) ml/kg/dag
	dag 4 en volgende :	**+ 20** ml/kg/dag tot **180ml/kg/dag** (soms tot 200 ml/kg/dag)
a terme dysmatuur:	dag 1:	**60** (80)ml/kg/dag en verder opklimmen tot **180** (soms 200-220) **ml/kg/dag**
preterme baby: (bij GG > 1.500g)	dag 1:	**60** ml/kg/dag
	dag 2:	**80** ml/kg/dag
	dag 3:	**100** ml/kg/dag
	dag 4 en meer :	**+ 20** ml/kg/dag tot **160** (afhankelijk van tolerantie en gewichtsevolutie) of **180 ml/kg/dag**
preterme dysmatuur: (bij GG > 1.500g)	dag 1:	**80** ml/kg/dag en verder opklimmen tot **160**-**180 ml/kg/dag**

(indien GG < 1.500g wordt TPN gestart ev. aangevuld met enterale voeding)

IN COMBINATIE MET PARENTERALE VOEDING

Bij beademde patiënten die hemodynamisch-respiratoir stabiel zijn:

minimale enterale voeding (MEV) per sonde wordt zo snel mogelijk (binnen de eerste 48u) opgestart en aangehouden gedurende meerdere dagen (individueel te beoordelen; meestal gedurende 5-7 dagen) vooraleer verder op te klimmen:

- bij MM: colostrum vanaf dag 1 zo mogelijk (*zie protocol colostrum*)
- **10 ml/kg/dag** aanhouden tot "enterale tolerantie" (=weinig maagresidu's)

Opstarten *perorale* voeding bij baby zonder respiratoire ondersteuning ≥34w:

- starten met **20 ml/kg/dag** en

het volume aftrekken van het IV vocht (AB-opl.); verder opklimmen met 20 ml/kg/dag

Opstarten *sonde*voeding :

- starten met **10-20 ml/kg/dag** tot "enterale tolerantie"
- opklimmen met 10-20 ml/kg/dag (>1.000g)
- *strikte maximum 20 ml/kg/dag indien <1.000g*
- vanaf 100 ml/kg/dag kan ev. sneller opgeklommen worden (individueel te beoordelen)

Als het totaal enteraal volume **100 ml/kg/dag** bedraagt, wordt de IV voeding enkel nog onder de vorm van opl. A gegeven (bevat wateroplosbare vitaminen). De vetoplosbare vitaminen kunnen dan gestart worden volgens protocol (p9).

Van zodra het totaal enteraal volume **120 à 140 ml/kg/dag** bedraagt, kan men overwegen de IV voeding te stoppen (in overleg met supervisor !) en verder enteraal op te klimmen. De vitamine-supplementen worden dan aangevuld volgens protocol (zie p 9).

"NEC-preventie":

Starten met **10 ml/kg /dag** (niet minder!) en verder opklimmen met 10 ml/kg/dag; vanaf 100ml/kg/dag ev. sneller opklimmen.

Wordt toegepast bij neonaten met een verhoogd risico op necrotiserende enterocolitis:

- bij sommige preterme dysmature baby's
- soms ook bij uitgesproken a terme dysmature baby
- asfyxie, hypoxie, shock, polycythemie
- sommige congenitale hartgebreken
- na een doorgemaakte NEC

*Een maagresidu van **minder dan 20% (of minder dan 1ml)** valt zeer waarschijnlijk binnen de normale grenzen.*

Er is geen evidentie dat de kleur van het maagresidu een vroeg teken van NEC is.

Het stoppen of tijdelijk onderbreken van enterale voeding op basis van grote maagresidu's is niet altijd zinvol en verhoogt potentieel het risico op infectie door verlengd TPN-gebruik.

Openhouden centrale lijn bij totale enterale voeding:

Indien de baby op volledig enterale voeding staat maar men de centrale lijn nog niet wenst te verwijderen, wordt deze bij voorkeur opengehouden met NaCl 0,9%.

Er kan ook gekozen worden voor glucose 5%-10%-15% indien men het calorie-aanbod wil verhogen (géén oplossing A gebruiken hiervoor !).

Suppletie met vitaminen PO/PS wordt dan eveneens gestart volgens het huidige protocol.

Toevoegingen voor enterale voeding

Bij *exclusieve* SV:
PreNan HMF® à 4% (1maatje (per 25 ml) = 1gram)(Nestlé):

- toevoeging aan moedermelk bij preterme en dysmature baby's
- energie-inhoud van ongeveer 17 kcal èxtra per 100 ml bereide melk; eiwit 1,42g èxtra/100 ml (koemelkeiwitten)
- *! wordt gestart als de baby enteraal 100 ml/kg/dag krijgt*
- bevat een mengsel van eiwitten (niet-gehydrolyseerd), KH, mineralen, vitaminen en vetten
    - noodzakelijk voor de preterme baby (<35w)
    - en/of de baby met een gewicht <1.800g
- wordt "standaard" gestopt bij een gewicht > 2.000g èn zws-duur >35w, op voorwaarde dat de gewichtsevolutie gunstig is !
- kan ook bij "grotere baby's" met slechte gewichtsevolutie of vochtbeperking
- verhoogt de osmolariteit (die nog verder stijgt als het moment tussen toevoegen en toedienen groter wordt; kan vertraagde maaglediging geven)
- (er zijn geen publicaties voorhanden die de veiligheid en efficiëntie kunnen aantonen van het verhogen van de standaardconc. van 4% naar hogere waarden)

Bij partiële SV of volledig PO:
BMF® à 4% (1,1 gram per 25 ml):

- energie-inhoud van 15 kcal èxtra per 100ml bereide melk; eiwit: 0,8g èxtra/100ml
- bevat géén vetten

Calogen® à 6% (6ml/100ml)(Nutricia) :

- kan aan kunstvoeding toegevoegd worden
- over toevoeging aan MM zijn geen literatuurgegevens voorhanden
- bestaat uit een 'emulsie' van soja-olie en water
- bevat LCT vetten (géén MCT vetten);
- energie-inhoud van 27 kcal per 100 ml bereide melk

Glucose-polymeren:

- Resource® Dextrine maltose (Nestlé) (381 kcal/100g)
    - toevoegen aan 5% tot max. 10% (zowel bij preterme als a terme baby)

VITAMINEN

Zolang intraveneuze voeding gegeven wordt:

A terme baby:	**Konakion •**	**1 mg/24u** IV
Preterme baby (<36w):	**Konakion•:**	**1mg/24u** IV tot D6, **dan 3x/week 1 mg** IV
Niet bij baby's die bij geboorte	Konakion•	IM kregen toegediend

Bij uitsluitend enterale voeding zijn de belangrijke tijdstippen : dag 7, dag14, dag 60

Dag 7:

D-Cure• : preterm met exclusief MM : **12dr./dag** tot ontslag nr huis
dan **6dr./dag** tot aanpassing door kinderarts/huisarts
preterm en a term met KV : **6dr./dag** tot aanpassing door kinderarts/huisarts
a term met MM : **6dr./dag** (400 IE)
9dr/dag (600 IE): negroïde baby
tot aanpassing dr kinderarts/huisarts

vitamine K: indien uitsluitend MM gegeven wordt :

- op de afdeling:
  Konakion • 2 mg/week naast ev. andere vitaminen zolang > 50% MM en maximaal tot 3 maanden
  ! niet nodig indien de baby bij geboorte vitamine K intramusculair gekregen heeft (verwijzend ziekenhuis)
- bij ontslag: **Vitamon K•** 5dr/dag

vitamine K op de materniteit:
éénmalig 2 mg PO op dag 1
bij borstvoeding:
Vitamon K• 5dr/dag gedurende maximaal 3 maanden
(mag gestopt indien > 50% kunstvoeding gegeven wordt)

Dag 14:

vitamine C : **25 mg/dag**	bij term < 34 weken (bij geboorte)
foliumzuur : **0.1 mg/dag**	bij term ≤ 32 weken (bij geboorte) of GG < 2.000g
	stoppen op de chronologische leeftijd van 3 maanden
vitamine E: **10 mg /dag**	bij term ≤ 32 weken (bij geboorte) of GG < 2.000g

Dag 60:

stop Vit C en Vit E

start **Ferricure•** : **2 x 3dr/dag** tot minimaal 6 maanden

VOEDING bij de preterme/dysmature baby bij ONTSLAG: *voorstel*

I. **AGA** (Appropriate for Gestational Age) bij geboorte en 'appropriate for postconceptional age' bij ontslag (p10-p90)

- Borstvoeding / moedermelk
- "Normale" eerste leeftijdsmelk (met LCPUFA)

II. **AGA** bij geboorte en gewicht bij ontslag beneden de p10 ('postnatal growth restriction')

- Moedermelk (aangerijkt met 'human milk fortifier' indien afgekolfde MM)
- Aangepaste kunstvoeding bij ontslag tot 40-52 weken postconceptionele leeftijd
    - PreNAN Stage 2 (Nestlé)
    - speciale "postdischarge" melk: Nutrilon Ex-prematuur (Nutricia)

III. **SGA** (Small for Gestational age) bij geboorte en gewicht bij ontslag nog steeds beneden de p10 (IUGR)

- Moedermelk (aangerijkt met 'human milk fortifier' indien afgekolfde MM)
- Aangepaste kunstvoeding bij ontslag tot 40-52 weken postconceptionele leeftijd
    - PreNAN Stage 2 (Nestlé)
    - speciale "postdischarge" melk: Nutrilon Ex-prematuur (Nutricia)

IV. **SGA** die bij ontslag een gewicht hebben dat 'appropriate for postconceptional age'is (p10-p90) ('early postnatal catch-up growth')

- Borstvoeding / Moedermelk
- "Normale" eerste leeftijdsmelk (met LCPUFA's)

Op korte termijn ziet men een positief effect op de groei met bovenstaand beleid. Lange termijnvoordelen zijn evenwel nog niet met zekerheid aangetoond.

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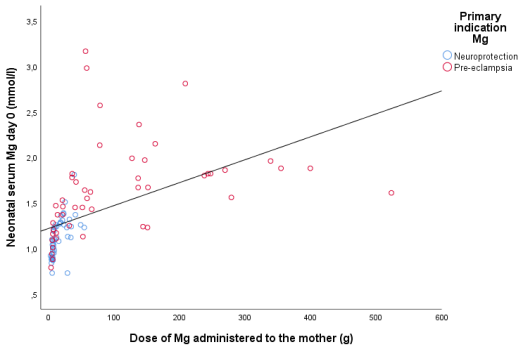
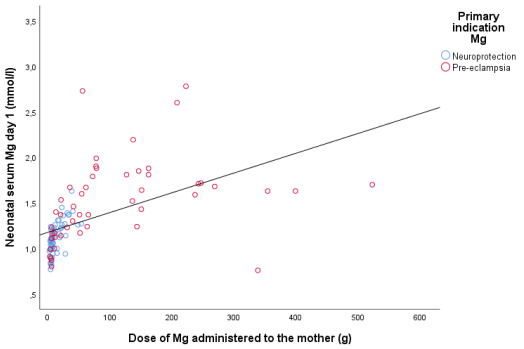
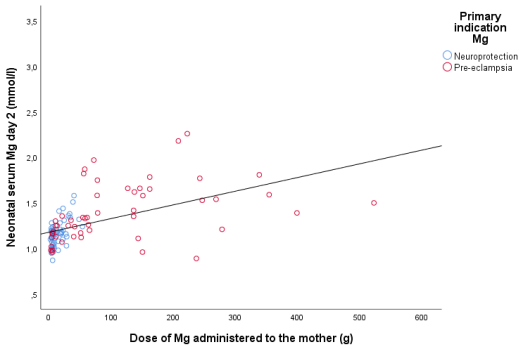
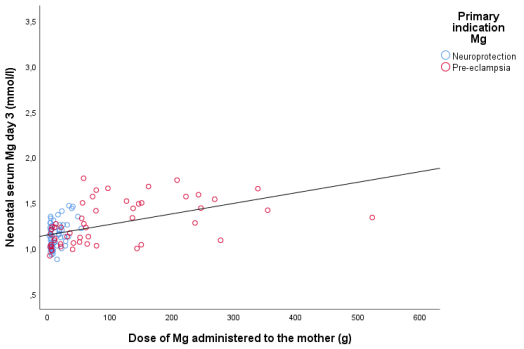
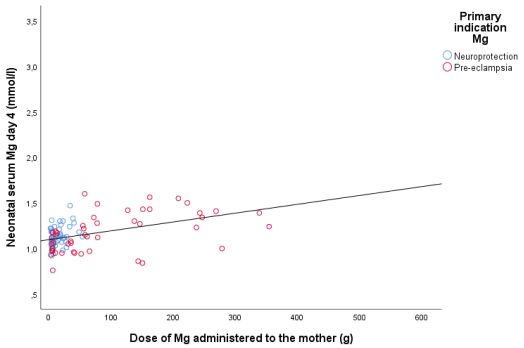
Association between total maternal dose $MgSO_4$ and neonatal magnesemia (day 0-7, 10, 14)

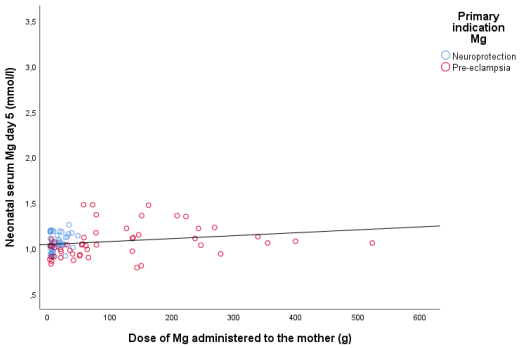


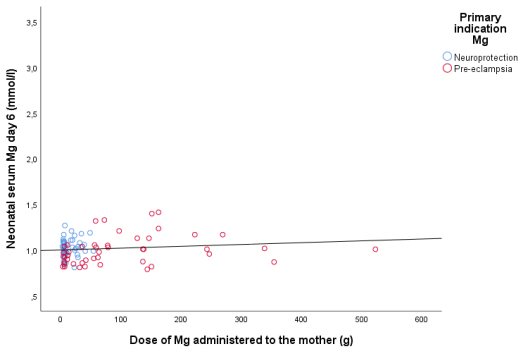


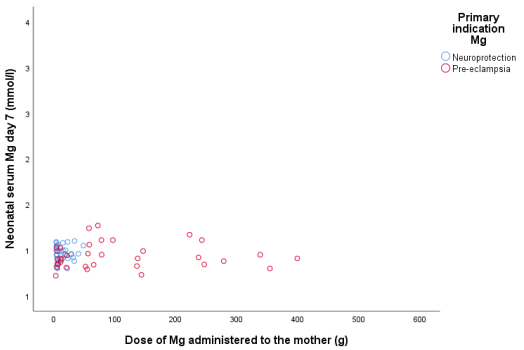












Attachment 5: Non-log transformed graphs