A systematic review and time-response meta-analysis of the optimal timing of elective caesarean sections for best maternal and neonatal health outcomes

Barbara Prediger1*, Tim Mathes1, Stephanie Polus1, Angelina Glatt1, Stefanie Bühn1, Sven Schiermeier2, Edmund A. M. Neugebauer3,4 and Dawid Pieper1

Abstract

Background: The rate of caesarean sections (CS) has increased in the last decades to about 30% of births in high income countries. Many CSs are electively planned without an urgent medical reason for mother or child. An early CS though may harm the newborn. Our aim was to evaluate the gestational time point after the 37 + 0 week of gestation (WG) (after prematurity = term) of performing an elective CS with the lowest morbidity for mother and child by assessing the time course from 37 + 0 to 42+ 6 WG.

Methods: We performed a systematic literature search in MEDLINE, EMBASE, CENTRAL and CINAHL in November 2018. We included studies that compared different time points of elective CS at term no matter the reason for elective CS. Our primary outcomes were the rate of admissions to the neonatal intensive care unit (NICU), neonatal death and maternal death in early versus late term elective CS. Various binary and dose response random effects meta-analyses were performed.

Results: We identified 35 studies including 982,749 women. Except one randomised controlled trial, all studies were cohort studies. We performed a linear time-response meta-analysis on the primary outcome NICU admission on 14 studies resulting in a decrease of the relative risk (RR) to 0.63 (95% CI 0.56, 0.71) from 37 + 0 to 39 + 6 WG. RR for neonatal death showed a decrease to 39 + (0–6) WG (RR 0.59 95% CI 0.43 to 0.83) and increase from then on (RR 2.09 95% CI 1.18 to 3.70) assuming a U-shape course and using a cubic spline model for meta-analysis of four studies. We only identified one study analyzing maternal death resulting in RR of 0.38 (95% CI 0.04 to 3.40) for 37 + 0 + 38 + 6 WG versus ≥39 + 0 WG.

Conclusion: Our systematic review showed that elective CS (primary and repeated) before the 39 + 0 WG lead to more NICU admissions and neonatal deaths, although death is rare and increases again after 39 + 6 WG. We did not find enough evidence on maternal outcomes. There is a need for more research, considering maternal outcomes to provide a balanced decision between neonatal and maternal health.

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**Background**

While the World Health Organization (WHO) states that there is no medical reason for a higher rate of CSs than 10–15%, the rates of Caesarean Section (CS) in high income countries have increased to about 30% of all births in the last decades [1–3]. It is assumed that a high number of CSs is electively planned without an urgent medical need neither in women nor the unborn. A previous CS is the most common reason for performing an elective CS. Researchers from the UK and USA showed that only 50% of women in the UK undergo vaginal birth after CS (VBAC) while there are with only 10% even less in the USA, even though it is recommended for the majority of women with prior CS [4, 5]. Withal there is no unanimity when the optimal time point of performing an elective CS could be. While 97% of elective CSs are performed beyond 37 + 0 WG, about 60% of elective CSs are performed in, or beyond 39 (39 + 0 to 39 + 6) WG, according to an analysis of 63 English NHS trusts [6].

The reason behind is that women with a scarred uterus may have diverse risks in following pregnancies and placentation abnormalities may occur more often. The risk of scar rupture may increase with the growing unborn in the last weeks of pregnancy [7]. Injuries to the bladder and a higher risk of bleeding needing transfusion is assumed. And because of this even a higher mortality rate might be connected to late term elective caesareans compared to early term caesareans before the beginning of labor [8]. Women without prior CS/intact uterus are not touched by those risks. Still labor can occur before the planned time point of CS which may result in an emergency CS which is connected with higher risks [9].

But in childbirth the risks for the neonate may not go along with those for the mother and is even though at term (37 + 0 WG) under various health risk. Lungs are mature in 37 + 0 WG, but neonates born by CS have a general higher risk of respiratory disorders. This is especially linked to early term CS [10].

The two guidelines “Caesarean Section” by NICE and “Birth after previous caesarean birth” by the Royal College for Obstetricians & Gynecologists examine if early term CS increases respiratory morbidity of the neonate. Both recommend to perform elective CS not before the 39 + 0 WG [11, 12]. Furthermore the American College of Obstetricians and Gynecologists recommend in their committee opinions 764 and 765 to not perform any indicated deliveries (both induction of labor and caesarean section) before the 39 + 0 WG, except for some specific pregnancy complications or comorbidities [13, 14]. In uncomplicated dichorionic diamniotic twin pregnancies, elective delivery (vaginal or by CS) should be offered in 37 + (0–6) WG according to the guideline “Twin and triplet pregnancy” from NICE. Risks are increasing from 38 + 0 WG onwards. Nevertheless, about 60% of neonates, are born spontaneously preterm – before 37 + 0 WG [15]. This fact may result in a relevant number of elective CS performed late preterm.

But high level evidence is lacking. There are currently no meta-analyses available which sum up the existing evidence.

As there is an ongoing trend towards more electively planned CSs, it is essential to provide a time point for the CS with the lowest risk for both, mother and child, comparing early term (37 + 0 to 38 + 6 WG) and late term (≥39 + 0 WG) delivery.

We performed a systematic review of the literature to evaluate the optimal time point with

- low risk of mortality and morbidity for mothers
- low risk for the neonate for mortality and morbidity

Beforehand, in 2016, we performed a systematic review on behalf of the German Federal Ministry of Health to answer the present question [16]. Herewith we updated this review and also aimed to expand the reach of the findings with this update in English. Moreover in the original review we performed a random-effects meta-analysis only comparing 37 + 0 to 38 + 6 WG with ≥39 + 0 WG, in this update we performed another type of meta-analysis showing a linear time-response relationship.

**Methods**

**Protocol and registration**

We registered our review at PROSPERO (CRD42017078231) and published the protocol [17].

**Eligibility criteria**

We included women with a planned CS at term (≥37 + 0 WG), regardless if it was first caesarean or repeated CS. We included studies with singleton and multiple pregnancies. Even though multiple pregnancies deviate much from singleton pregnancies we assumed similar uncertainties.
about the timing of elective CS. Our interest were planned
CSs at various time points. The primary outcomes were
neonatal death, NICU admission and maternal death. Sec-
ondary outcomes are for neonates: hospitalization ≥5 days,
respiratory morbidity, respiratory distress syndrome
(RDS), transient tachypnea of the neonate (TTN),
pneumothorax, hypoglycemia (Depending on the age at
assessment: 0–3 h: < 2.0 mmol/l; 3–24 h < 2.2 mmol/l; >
24 h < 2.5 mmol/l) [18], Apgar Score < 7, hyperbilirubine-
mia needing phototherapy (jaundice), near miss (a new-
born infant who nearly died but who survived a
complication occurring during pregnancy, childbirth, or in
the first 7 days after the termination of pregnancy). For
mothers we included following outcomes: hysterec-
tomy, bleeding needing transfusion, and near miss (a
woman who nearly died but survived a complication that
occurred during pregnancy, childbirth or within 42 days of
termination of pregnancy). We report outcomes with un-
specific definition like respiratory morbidity as it is defined
in the relevant study. The inclusion was limited to studies
in WHO Stratum A. This covers states with very low child
and very low adult mortality including western Europe,
North-America and various Western-Pacific states [19].
We chose this stratum because of the very low general
(and child) mortality and comparable access to health ser-
dices, but also because of comparable CS rates and similar
indications for CS, such as organizational reasons on hos-
pital, personal maternal and clinical base [20]. We did not
define any other exclusion criteria regarding the popula-
tion. We considered randomized controlled trials (RCTs),
 quasi RCTs and cohort studies. RCTs are much more dif-
ficult to conduct (E.g. due to spontaneous onset of labor)
and we expected low numbers of RCTs. Even though co-
hort studies are suspected to have higher risks of system-
atic biases, we assumed a high amount of data owing to
birth registries. We did not make any restrictions regard-
ing the language and publication date.

Information sources
We searched MEDLINE, EMBASE, CENTRAL and
CINAHL on 29th of November 2018. We did not re-
strict the search to any language or publication date.
Study registries were searched for new and unpublished
studies (ClinicalTrials, Deutsches Register Klinischer
Studien and EU clinical trials register). To identify grey
literature we searched Google Scholar additionally.
We also checked the references of included studies,
guidelines and systematic reviews and if necessary con-
tacted authors for additional data.

Search strategy
The search strategy was developed using MeSH terms
and text words and a librarian checked the strategy by
applying the PRESS checklist [21]. The search strategies
are available in Additional file 1.

Study selection
Records identified through the searches were added to
an Endnote X7 database and duplicates were removed.
Two reviewers independently assessed the relevance of
the identified titles and abstracts according to the inclu-
sion criteria. Studies which were included for full text
review again were independently assessed by the same
two reviewers. Differences were discussed until a consen-
sus was found or a third reviewer was included.

Data collection
Data was collected in an a priori-piloted abstraction
table by one reviewer, the other reviewer monitored all
entries for completeness and accuracy. We extracted
data directly in an excel sheet. If the study authors only
reported adjusted effect measures in their publications
we raised enquiries to the authors for unadjusted data.

Data items
We extracted following study characteristics: Author,
publication year, region, setting, study design, recruit-
ment period, exclusion criteria, patient characteristics
(Age, body-mass index, ethnicity, diseases, parity, prior
CS, indication for CS, marital/educational/socioecono-
mical status, payer, smoking status), time points mea-
sured, outcomes. All outcomes are collected as
dichotomous variables and for each time point.

Risk of bias assessment
Two reviewers independently assessed risk of bias. We
discussed differences until we found a consensus or a
third reviewer was included. For RCTs we used the
Cochrane Risk of Bias Tool [22]. For cohort studies we
used the ROBINS-I Tool [23]. We first assessed risk of
bias on study level and summarized it on outcome level.

Data synthesis
We only pooled studies that were assessed to be suffi-
cient clinical homogenous judged by reviewers with clin-
iclal expertise. If studies were sufficiently clinically
homogenous, a random-effects meta-analysis was per-
formed. We performed a multivariate dose-response
meta-analysis for pooling outcomes where time starting
with 37 + 0 WG up to 42 + 6 WG in weekly steps repre-
sented the different doses. We examined visually for
each outcome if the assumed time-response relationship
was effectively present and how the relationship was
shaped [24]. Therefore, we created plots showing the
intervention effect for each study over time. Based on
these curves we determined the shape (e.g. linear, U-
shape) specified in the dose-response meta-analysis. For
most neonatal (adverse) outcomes we recognized a regressive or u-shape (with a minimum at week 39) and for maternal (adverse) outcomes a progressive trend [10, 16, 25]. In the first stage of our analysis, we estimated a time-response curve (i.e. gestational week-outcome) for each study across WG values observed in the whole dataset. In the second stage these curves were pooled into an overall gestational week-outcome curve. The time-response analysis followed the two-stage method for dose-response-meta-analysis by Greenland & Longnecker [26]. We calculated study-specific slopes (linear trends) and 95% confidence intervals from the natural logs of the reported effect measures and confidence intervals across WG taking the correlations between RRs into account. In case of the reference category being not the lowest category we first recalculated the data in such a way that (depending on the shape) week 39 or the lowest category was the reference category. In cases where this was not possible, we excluded the categories below the reference category for the linear time-response analysis. For studies reporting ranges of weeks the midpoint of the lower and upper cut-off was assigned for each category. When upper and lower categories were open ended, the lower and upper cut-off value was 37 and 42 weeks. Again the midpoint of the lower and upper cut-off was assigned for each category. When authors reported the median or mean per category this was used off was assigned for each category. When authors re-
included in any meta-analysis. Patient numbers of the included studies ranged from 96 to 785,340 with a median of 13,888. Twenty-two studies reported the exclusion of pregnancies with fetal congenital anomalies. In 24 studies exclusion criteria for mothers with any morbidity influencing the timing of birth (e.g. hypertension, diabetes, placenta previa) were reported. Nineteen

Additional analyses
We performed subgroup analyses for repeat CS vs. first CS and for studies including exclusively multiple pregnancies. Besides general deviations in multiple pregnancies compared to singleton pregnancies we assumed that CS is planned earlier than 37 + 0 WG to 42 + 6 WG more often, and may need a time-response analysis considering other comparisons of WG.

In a sensitivity analysis for primary outcomes, we conducted a univariate random effects meta-analysis (37 + 0 to 38 + 6 vs ≥39 + 0 WG) to demonstrate reliability of the results. We used the Paule and Mandel heterogeneity variance estimator and modified Hartung-Knapp confidence intervals for the pooled estimates [34, 35].

Results
Study selection
We identified 3200 hits in the databases after duplicate removal. One hundred twenty publications were screened in full text of which we included 29 in the review. Moreover we identified six references by screening the reference lists of five systematic reviews. The references from the guidelines, the search in Google Scholar and the search in registries resulted in no additional inclusions. The included and excluded (with reason) studies are presented in Additional file 1 and Fig. 1.

Study characteristics
Of the 35 included publications, three, Brookfield, Chiossi and Tita et al. used the same birth registry [36–38]. Also Vilchez et al. and Zanardo et al. published two papers from the same cohort [39, 40]. We used the first publications and added outcome data from the following publications. Except for one RCT from Glavind et al. all studies were cohort studies [25]. One study, Wilmink et al. examined only twin births. Two studies from Japan, Nakashima et al. and Yamazaki et al., and one from Germany, Gawlik et al., only compared the 37 + (0–6) to the 38 + (0–6) WG and four, Doan, McAlister, Nir and Zanardo et al., did not report the single WG but compared 37 + (0–6) + 38 + (0–6) to ≥39 + (0–6) week [41–49]. These eight studies could not be included in any meta-analysis. Patient numbers of the included studies ranged from 96 to 785,340 with a median of 13,888. Twenty-two studies reported the exclusion of women with multiple pregnancies and 15 studies the exclusion of pregnancies with fetal congenital anomalies. In 24 studies exclusion criteria for mothers with any morbidity influencing the timing of birth (e.g. hypertension, diabetes, placenta previa) were reported.
Studies evaluated NICU admission and six studies evaluated neonatal death. Maternal death was only assessed in one study. None of the studies reported or considered near miss for neonates or mothers. One study, Terada et al., reported outcomes exclusively on oxygen supplementation and respiratory support with overlapping patients, so we did not include this in the meta-analysis [50]. For detailed study and patient characteristics see Additional file 1 and Table 1.

### Risk of bias within studies

Risk of bias was assessed with the Cochrane Risk of Bias tool in the RCT from Glavind et al. see Fig. 2. We assumed a moderate overall risk of bias for the study of Glavind et al. attributable to the missing blinding. All other studies were assessed with the ROBINS-I tool. Consistently throughout all studies confounding and selection of participants were the main issues and we assumed at least serious risk of bias in these domains, see Table 2. The detailed ratings to each bias domain can be found in Additional file 1.

A number of studies attempted to control confounding by multivariable logistic regression but we could not use these data for the meta-analyses because the regarded adjustment factors varied widely. Because we pooled and mainly reported the univariate analysis, risk of confounding was assessed for this analysis. Frequent confounders were maternal age, ethnicity, maternal and neonatal comorbidities, methods to determine gestational age and study setting. Women, who were planned to have elective CS in later term ≥39 + (0–6) WG but needed unplanned CS before term because of complications, are at higher risk for drop out, so the number of healthy women with uncomplicated pregnancies potentially rises in late term CS. In contrast, women who are suspected to have more complications during birth are terminated to an earlier CS, which leads to increasing numbers of complicated pregnancies in early term CS. Therefore, we rated almost all studies as critical or serious risk of bias.

We could not see any risk of bias regarding the classification nor deviation from the intended intervention. We could not determine if there was a risk of bias because of missing data, as none of the studies described how missing data was dealt with, nor if there was missing data. Risk of bias in measurement of outcomes was driven by the suspected influence of the knowledge about the timing of CS on outcome measures. The outcome measure for death or hysterectomy is not influenced by the knowledge of term (objective outcome) whereas the neonatologists/obstetricians judgement about NICU admission is highly influenced (subjective outcome). We did

![Flow-diagram of study selection](image)
| Study                          | Study type          | Setting                        | Recruiting period | n     | Week of gestation | ≥1 C-Section |
|-------------------------------|---------------------|--------------------------------|-------------------|-------|-------------------|--------------|
| Alderdice et al. 2005 [51]   | Cohort study        | Northern Ireland, multicentric | 2001–2002         | 2553  | 37, 38, 39, 40, 41| No           |
| Bailit et al. 2010 [52]      | Cohort study        | USA, multicentric              | 2002–2008         | 3959  | 34, 35, 36, 37, 38, 39, 40, 41 | No           |
| Balchin et al. 2008 [53]     | Cohort study        | England, multicentric          | 1988–2000         | 20,891| 37, 38, 39, 40    | No           |
| Brookfield et al. 2017 [36]  | Cohort study        | USA, multicentric, see Tita 2009, Chiossi 2013 | 1999–2002 | 15,602 | 37, 38, 39, 40, 41 | Yes          |
| Chiossi et al. 2013 [37]     | Cohort study        | USA, multicentric, see Tita 2009, Brookfield 2017 | 1999–2002 | 14,865 | 37, 38, 39, 40, 41 | Yes          |
| Clark et al. 2009 [54]       | Cohort study        | USA, multicentric              | 2007              | 1851  | 37, 38, 40, 41    | Both         |
| Doan et al. 2014 [44]        | Cohort study        | Australia, 1 center            | 1998–2009         | 14,447| 37–38, 39–41      | No           |
| Farchi 2010                   | Cohort study        | Italy, multicentric            | 2003–2005         | 13,329| 37, 38, 39, 40–41 | Yes          |
| Finn et al. 2016 [55]        | Cohort study        | Ireland, 1 center              | 2008–2012         | 4242  | 37, 38, 39, 40, 41| No           |
| Gawlik et al. 2015 [43]      | Cohort study        | Germany, 1 center              | 2006–2011         | 503   | 37, 38–40         | Yes          |
| Glavind 2013                  | RCT                 | Denmark, multicentric          | 2009–2011         | 1274  | 38, 39            | No           |
| Graziosi et al. 1998 [56]    | Cohort study        | Netherlands, 1 center          | 1990–1995         | 272   | 37, 38, 39, 40, 41| No           |
| Hansen et al. 2008 [57]      | Cohort study        | Denmark, 1 center              | 1998–2006         | 2687  | 37, 38, 39, 40, 41| No           |
| Many et al. 2006 [58]        | Cohort study        | Israel, –                      | –                 | 278   | 38, 39, 40, 41    | No           |
| Matsuo et al. 2008 [59]      | Cohort study        | Japan, 1 center                | 1994–2005         | 364   | 37, 38, 39, 40    | No           |
| McAlister et al. 2013 [45]   | Cohort study        | USA, multicentric              | 2008–2009         | 4125  | 37–38, 39–41      | No           |
| Melamed et al. 2014 [60]     | Cohort study        | Israel, 1 center               | 2010–2011         | 377   | 38, 39            | ≥2           |
| Morrison et al. 1995 [61]    | Cohort study        | England, 1 center              | 1985–1993         | 2341  | 37, 38, 39, 40, 41| No           |
| Nakashima et al. 2014 [41]   | Cohort study        | Japan, 1 center                | 2006–2012         | 684   | 37, 38            | No           |
| Nir et al. 2012 [46]         | Cohort study        | Israel, 1 center               | 2007–2009         | 1050  | 37–38, 39, 40      | No           |
| Parikh et al. 2014 [62]      | Cohort study        | USA, multicentric              | 2008–2011         | 14,613| 37, 38, 39, 40    | No           |
| Resende 2014                  | Cohort study        | Portugal, 1 center             | 2003–2013         | 3123  | 37, 38, 39, 40, 41| No           |
| Terada et al. 2014 [50]      | Cohort study        | Japan, 1 center                | 2006–2013         | 1936  | 37, 38–40         | No           |
| Tita et al. 2009 [38]        | Cohort study        | USA, multicentric, see Chiossi 2013, Brookfield 2017 | 1996–2006 | 13,258 | 37, 38, 39, 40, 41, 42 | Yes          |
| Tracy et al. 2007 [63]       | Cohort study        | Australia, multicentric        | 1999–2002         | 43,059| 37, 38, 39, 40, 41| No           |
| Van den Berg et al. 2001 [64]| Cohort study        | Netherlands, 1 center          | 1994–1998         | 324   | 37, 38, 39, 40    | No           |
| Vidic 2016                    | Cohort study        | Slovenia, multicentric         | 2002–2012         | 7364  | 37, 38, 39, 40, 41, 42 | No           |
| Vilchez et al. 2014 [39]     | Cohort study        | USA, multicentric, see Vilchez 2015 | 2004–2008 | 785,340 | 37, 38, 39, 40, 41 | Yes          |
| Vilchez et al. 2015 [40]     | Cohort study        | USA, multicentric, see Vilchez 2014 | 2004–2008 | 483,052 | 37, 38, 39, 40, 41 | Yes          |
| Wilmink et al. 2010 [65]     | Cohort study        | Netherlands, multicentric      | 2000–2006         | 20,973| 37, 38, 39, 40, 41, 42 | No           |
| Wilmink et al. 2012 [66]     | Cohort study        | Netherlands, multicentric, twins | 2000–2007         | 4557  | 35, 36, 37, 38, 39 | No           |
| Yamazaki et al. 2003 [42]    | Cohort study        | Japan, 1 center               | 1998–2000         | 96    | 37, 38             | No           |
| Zanardo et al. 2004, two publications [48, 49] | Cohort study        | Italy, 1 center               | 1998–2000         | 1280  | 37–38, 39–41      | No           |
| Zanardo et al. 2007 [67]     | Cohort study        | Italy, multicentric           | 2002–2003         | 99888 | 37, 38, 39, 40, 41 + 6 | No           |

≥1 C-Section refers to studies including women who had at least one caesarean section before
not find an indication for selective reporting of the results in any study. Table 2 shows the risk of bias assessment on study and outcome level.

Risk of bias across studies

The overall body of evidence assessment resulted in an assumption of serious or critical risk of bias. Figure 2 shows the risk of bias assessment for the outcome NICU admission. We did not produce graphs for each outcome as there would be nearly no difference in the graphs (Fig. 3).

All meta-analyses except the one for NICU admission included less than ten studies. We were only able to evaluate publication bias for NICU admission, which we did by consulting the funnel plot, which did not suggest publication bias (see Additional file 1). Both, Eggers and Beggs test did not indicate publication bias (Eggers test: p-value: 0.46; Beggs test: p-value: 0.83).

Results of individual studies

Individual study results for NICU admission, neonatal and maternal death can be found in Additional file 1. We only identified one study from Chiossi et al., which analyzed maternal mortality [37]. The cases are very rare (1 in week 38, 4 in week 39) and we calculated a RR of 0.38 (95% CI 0.04 to 3.40, very low quality of evidence) for 37 + 0 to 38 + 6 WG versus ≥39 + 0 WG.

We identified 8 studies which we could not include in any meta-analysis for various reasons. Doan et al., Gawlik et al., McAlister et al., Nir et al., and Zanardo et al. reported outcomes for 37 + (0–6) + 38 + (0–6) WG versus ≥39 + 0 WG and not for individual weeks [44–46, 48, 49]. There were two studies from Japan and one from Germany that compared 37 + (0–6) WG to 38 + (0–6) and 39 + 0 [41] [43]. [42] They all showed similar results like the other studies; less NICU admission in the later WG.

Synthesis of results

We extracted the outcome data for each WG study wise in Excel. We calculated RRs with the reference category 39 + (0–6) WG and created graphs presenting the RRs over time. For each outcome and for each study, graphs were produced in the same manner and we visually inspected if a linear trend could be expected. Figures 4 and 5 show the graphs presenting the development of the primary outcomes NICU admission and neonatal death over time. The curves show the RR of the pooled 14 studies on NICU admission and respectively 4 studies on neonatal death. Both graphs are accompanied by the upper and lower CI. The course of NICU admission is decreasing from 37 + 0 to 39 + 6 WG, while the course of neonatal death shows the u-shape from 37 + 0 to 42 + 6 WG with the lowest at 39 + 0–6 WG. See Additional file 1 for the illustration of individual study results, which are underlying the models chosen.

We performed linear time-response meta-analyses for the outcomes NICU admission, respiratory morbidity, hypoglycemia, Apgar score < 7, jaundice, RDS, TTN, pneumothorax, maternal hysterectomy and maternal blood transfusions. The RR for NICU admission was 0.63 (95% CI 0.56 to 0.71, I² = 95.4% low quality of evidence) (See Fig. 4) for each additional WG. All outcomes except Apgar score < 7, pneumothorax and both maternal outcomes showed a significant higher risk ratio the earlier the CS was performed. Except for sepsis, hypoglycemia, maternal hysterectomy and blood transfusion, all analyses showed high heterogeneity with I² > 30%. See Table 3 for the individual results of the meta-analyses. All studies had a serious or critical risk of bias and therefore we rated the certainty of evidence according as low or very low, see Table 4. Only hypoglycemia was assessed as moderate certainty of evidence. Three other meta-analyses were cubic spline time-response meta-analyses with 39 + (0–6) WG as the reference. Incidence for neonatal death, sepsis and hospitalization ≥5 days all showed U-shaped curves with a minimum at 39 + (0–6) WG, i.e. a decreasing incidence form the 37 + 0 WG to the 39 + (0–6) WG and rising incidence from the 40 + 0 WG. The RR for neonatal death from 37 + 0 to 39 + 6 WG drops to 0.59 (95% CI 0.43 to 0.83, I² = 77.5% low quality of evidence) and after 39 + 6 rises to 2.09 (95% CI 1.18 to 3.70, I² = 77.5% low quality of evidence) (see Fig. 5). Sepsis and hospitalization show
| Study                          | Outcome                  | Bias due to confounding | Bias in selection of participants into the study | Bias in classification of interventions | Bias due to deviations from intended interventions | Bias due to missing data | Bias in measurement of outcomes | Bias in selection of the reported result | Overall bias |
|-------------------------------|--------------------------|-------------------------|-----------------------------------------------|-----------------------------------------|-------------------------------------------------|--------------------------|---------------------------------|------------------------------------------|-------------|
| Alderdice et al. 2005 [51]    | NICU                     | S                       | C                                             | L                                       | L                                               | NI                       | S                              | L                                        | C           |
|                               | Respiratory outcomes     | S                       | C                                             | L                                       | L                                               | NI                       | M                              | L                                        | C           |
| Bailit et al. 2010 [52]       | NICU                     | S                       | S                                             | L                                       | L                                               | NI                       | S                              | L                                        | S           |
|                               | Sepsis                   | S                       | S                                             | L                                       | L                                               | NI                       | M                              | S                                        | L           |
| Balchin et al. 2008 [53]      | Respiratory outcomes     | S                       | C                                             | L                                       | L                                               | NI                       | M                              | L                                        | C           |
| Brookfield et al. 2017 [36]   | Respiratory outcomes     | S                       | S                                             | L                                       | L                                               | NI                       | M                              | L                                        | S           |
| Chiossi et al. 2013 [37]      | NICU, Apgar score        | S                       | S                                             | L                                       | L                                               | NI                       | S                              | L                                        | S           |
|                               | Death                    | S                       | S                                             | L                                       | L                                               | NI                       | L                              | L                                        | S           |
|                               | Respiratory outcomes, sepsis | S                     | S                                             | L                                       | L                                               | NI                       | M                              | L                                        | S           |
|                               | (M) Death, hysterectomy  | S                       | S                                             | L                                       | L                                               | NI                       | L                              | L                                        | S           |
| Clark et al. 2009 [54]        | NICU                     | S                       | S                                             | L                                       | L                                               | NI                       | S                              | L                                        | S           |
| Doan et al. 2014 [44]         | NICU, Apgar Score, jaundice | S                   | S                                             | L                                       | L                                               | NI                       | S                              | L                                        | S           |
|                               | Death, hypoglycemia      | S                       | S                                             | L                                       | L                                               | NI                       | L                              | L                                        | S           |
|                               | Respiratory outcomes     | S                       | S                                             | L                                       | L                                               | NI                       | M                              | L                                        | S           |
| Farchi 2010                   | Respiratory outcomes     | S                       | S                                             | L                                       | L                                               | NI                       | M                              | L                                        | S           |
| Finn et al. 2016 [55]         | NICU                     | S                       | S                                             | L                                       | L                                               | NI                       | S                              | L                                        | S           |
|                               | Respiratory outcomes     | S                       | S                                             | L                                       | L                                               | NI                       | M                              | L                                        | S           |
| Gawlik et al. 2015 [43]       | NICU, Apgar score        | S                       | S                                             | L                                       | L                                               | NI                       | S                              | L                                        | S           |
| Graziosi et al. 1998 [56]     | NICU, jaundice           | S                       | S                                             | L                                       | L                                               | NI                       | S                              | L                                        | S           |
| Hansen et al. 2008 [57]       | Respiratory outcomes     | S                       | S                                             | L                                       | L                                               | NI                       | M                              | L                                        | S           |
| Many et al. 2006 [58]         | Respiratory outcomes     | S                       | C                                             | L                                       | L                                               | NI                       | M                              | L                                        | C           |
| Matsuo et al. 2008 [59]       | Respiratory outcomes     | S                       | C                                             | L                                       | L                                               | NI                       | M                              | L                                        | C           |
| McAlister et al. 2013 [45]    | NICU                     | S                       | C                                             | L                                       | L                                               | NI                       | S                              | L                                        | C           |
| Melamed et al. 2014 [60]      | NICU, Apgar score, jaundice | S                   | S                                             | L                                       | L                                               | NI                       | S                              | L                                        | S           |
|                               | Death, hypoglycemia      | S                       | S                                             | L                                       | L                                               | NI                       | L                              | L                                        | S           |
| Study                          | Outcome                                         | Bias due to confounding | Bias in selection of participants into the study | Bias in classification of interventions | Bias due to deviations from intended interventions | Bias due to missing data | Bias in measurement of outcomes | Bias in selection of the reported result | Overall bias |
|-------------------------------|-------------------------------------------------|-------------------------|------------------------------------------------|----------------------------------------|-------------------------------------------------|--------------------------|--------------------------------------|------------------------------------------|-------------|
| Morrison et al. 1995 [61]     | Respiratory outcomes                            | S                       | S                                               | L                                      | L                                               | NI          | M                                   | L                        | S           |
|                               | (M) Hysterectomy                                | S                       | S                                               | L                                      | L                                               | NI          | L                                   | L                        | S           |
|                               | (M) bleeding                                     | S                       | S                                               | L                                      | L                                               | NI          | S                                   | L                        | S           |
| Nakashima et al. 2014 [41]    | NICU, jaundice                                   | S                       | S                                               | L                                      | L                                               | NI          | S                                   | L                        | S           |
|                               | Respiratory outcomes                            | S                       | S                                               | L                                      | L                                               | NI          | M                                   | L                        | S           |
|                               | Hypoglycemia, sepsis                            | S                       | S                                               | L                                      | L                                               | NI          | L                                   | L                        | S           |
| Nir et al. 2012 [46]          | NICU, Apgar score, jaundice                     | S                       | S                                               | L                                      | L                                               | NI          | S                                   | L                        | S           |
|                               | Respiratory outcomes                            | S                       | S                                               | L                                      | L                                               | NI          | M                                   | L                        | S           |
|                               | Hypoglycemia                                    | S                       | S                                               | L                                      | L                                               | NI          | L                                   | L                        | S           |
| Parikh et al. 2014 [62]       | NICU                                            | S                       | S                                               | L                                      | L                                               | NI          | S                                   | L                        | S           |
|                               | Death                                           | S                       | S                                               | L                                      | L                                               | NI          | L                                   | L                        | S           |
| Resende 2015                  | NICU                                            | S                       | S                                               | L                                      | L                                               | NI          | S                                   | L                        | S           |
|                               | Respiratory outcomes                            | S                       | S                                               | L                                      | L                                               | NI          | M                                   | L                        | S           |
|                               | Hypoglycemia                                    | S                       | S                                               | L                                      | L                                               | NI          | L                                   | L                        | S           |
| Terada et al. 2014 [50]       | Respiratory outcomes                            | S                       | S                                               | L                                      | L                                               | NI          | M                                   | L                        | S           |
| Tita et al. 2009 [38]         | NICU                                            | S                       | S                                               | L                                      | L                                               | NI          | S                                   | L                        | S           |
|                               | Respiratory outcomes                            | S                       | S                                               | L                                      | L                                               | NI          | M                                   | L                        | S           |
|                               | Hypoglycemia, sepsis                            | S                       | S                                               | L                                      | L                                               | NI          | L                                   | L                        | S           |
| Tracy et al. 2007 [63]        | NICU                                            | S                       | S                                               | L                                      | L                                               | NI          | S                                   | L                        | S           |
| Van d. Berg et al. 2001 [64]  | NICU                                            | S                       | C                                               | L                                      | L                                               | NI          | S                                   | L                        | C           |
|                               | Respiratory outcomes                            | S                       | C                                               | L                                      | L                                               | NI          | M                                   | L                        | C           |
| Vidic 2016                    | NICU, Apgar score, jaundice                     | S                       | S                                               | L                                      | L                                               | NI          | S                                   | L                        | S           |
|                               | Respiratory outcomes                            | S                       | S                                               | L                                      | L                                               | NI          | M                                   | L                        | S           |
|                               | Hypoglycemia                                    | S                       | S                                               | L                                      | L                                               | NI          | L                                   | L                        | S           |
| Vilchez et al. 2014 [39]      | NICU, Apgar score                               | S                       | S                                               | L                                      | L                                               | NI          | S                                   | L                        | S           |
| Vilchez et al. 2015 [40]      | Death                                           | S                       | S                                               | L                                      | L                                               | NI          | L                                   | L                        | S           |
| Wilmink et al. 2010 [65]      | NICU, Apgar score, jaundice                     | S                       | S                                               | L                                      | L                                               | NI          | S                                   | L                        | S           |
| Study                      | Outcome                        | Bias due to confounding | Bias in selection of participants into the study | Bias in classification of interventions | Bias due to deviations from intended interventions | Bias due to missing data | Bias in measurement of outcomes | Bias in selection of the reported result | Overall bias |
|---------------------------|--------------------------------|-------------------------|-------------------------------------------------|----------------------------------------|---------------------------------------------------|------------------------|-------------------------------------|------------------------------------------|----------------|
| Wilmink et al. 2012 [66]  | Death, hypoglycemia, sepsis    | S                       | S                                               | L                                      | L                                                 | NI                     | L                                   | L            | S                             |
|                           | Respiratory outcomes           | S                       | S                                               | L                                      | L                                                 | NI                     | M                                   | L            | S                             |
|                           | NICU, Apgar score              | S                       | S                                               | L                                      | L                                                 | NI                     | M                                   | L            | S                             |
| Yamazaki et al. 2003 [42] | Respiratory outcomes           | S                       | S                                               | L                                      | L                                                 | NI                     | M                                   | L            | S                             |
|                           | Hypoglycemia                   | S                       | S                                               | L                                      | L                                                 | NI                     | M                                   | L            | S                             |
| Zanardo et al. 2004, two | Respiratory outcomes           | S                       | S                                               | L                                      | L                                                 | NI                     | M                                   | L            | S                             |
| publications [48, 49]     |                                |                         |                                                  |                                        |                                                   |                        |                                     |                        |                              |
| Zanardo et al. 2007 [67]  | Respiratory outcomes           | S                       | S                                               | L                                      | L                                                 | NI                     | M                                   | L            | S                             |

Risk of bias assessment according to ROBINS-I tool. The seven bias domains are individually assessed for each study. The evaluation options are: L Low; M Moderate; S Serious; C Critical; NI No Information. Respiratory outcomes include all respiratory outcomes measured. Outcomes were summarized according to their risk of bias assessment (M): Maternal outcomes.
Fig. 3 Risk of Bias assessment for NICU admission

Fig. 4 NICU admission
similar significant effects (see Table 3). The display of the GRADE evaluation in Table 4 is insufficient for the reporting the results of the cubic spline model. Therefore we chose to report the results as free text.

**Additional analysis**

We performed subgroup analyses for the primary outcomes NICU admission and neonatal death as we observed very high clinical and statistical heterogeneity. We performed a subgroup analysis with the studies that only include women with repeated CS. For the incidence of NICU admission we found a reduction of 34% in the reference group 39 + (0–6) WG by pooling four studies (RR 0.66 95% CI 0.65 to 0.67, $I^2 = 0$ moderate quality of evidence). The time-response meta-analysis showed a reduction of neonatal mortality until the 39 + (0–6) WG (RR 0.67 95% CI 0.51 to 0.87, $I^2 = 0$ very low quality of evidence) and increasing mortality higher than 39 + 6 WG (RR 1.68 95% CI 1.07 to 2.65, $I^2 = 0$ very low quality of evidence). The individual study results can be found in Additional file 1.
The included studies did not supply enough information on first CS to perform subgroup analysis for first CS.

We identified one study examining twin pregnancies with elective CS from 35 + 0 to 41 + 6 WG [66]. Considering the association pattern we decided to compare 35 + 0 to 37 + 6 WG with 38 + 0 to 41 + 6 week. We calculated a RR of 14.01 (95% CI 0.91 to 17.72) for NICU admission (35 + 0 to 37 + 6 WG n/N = 13/1378; 38 + 0 to 41 + 6 WG n/N = 2/850) and a RR of 0.31 (95% CI 0.03 to 3.40) for neonatal death (35 + 0 to 37 + 6 WG n/N = 1/1378; 38 + 0 to 41 + 6 WG n/N = 2/850).

The sensitivity analyses using univariate analysis for the primary outcomes NICU admission and neonatal death resulted in an RR of 1.67 (95% CI 1.37 to 2.0, I² = 88%) for NICU admission (see Additional file 1) and an OR of 2.24 (95% CI 0.29 to 17.31, I² = 0) for neonatal death, showing higher risks in early term. For the Funnel plot of NICU admission see Additional file 1.

**Comment**

**Main findings**

We found that the rate of NICU admission decreases from 37 + 0 WG to 39 + (0–6) WG for elective CS. Risk of bias was serious in all studies and we even identified some with critical risk. The certainty of the evidence according to GRADE is low. The risk for respiratory morbidity in neonates and other postnatal events (jaundice, hypoglycemia) decrease in the same manner. Assuming a U-shaped pattern with 39 + (0–6) WG at the minimum, we found a decreasing risk of death from 37 + 0 to 39 + (0–6) WG and increasing from then on. The certainty of the evidence is low and a sensitivity analysis showed wide confidence intervals diminishing the robustness of results. Similar results were seen in hospitalization of the neonate for more than 5 days and sepsis. Certainty of evidence is very low and low for respiratory morbidity, hospitalization of the neonate for more than 5 days and jaundice and sepsis. Only hypoglycemia showed moderate certainty of the evidence.

Maternal mortality is a very rare event in countries of WHO stratum A [70]. We only found one study considering maternal death. The other maternal outcomes hysterectomy and blood transfusion showed higher event rates in late term but this only seems to be a hint regarding the statistical uncertainty. All studies considering maternal outcomes had serious risk of bias and certainty of evidence was very low.

We found one study examining twin pregnancies. Elective CS was planned more often preterm and in general earlier than singleton pregnancies. We could not

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**Table 3** Results of primary and subgroup meta-analyses by outcome

| Meta-analyses                  | Studies | References | Patients n | Shape of association | Risk ratio | 95% CI      | I² |
|-------------------------------|---------|------------|------------|----------------------|------------|-------------|----|
| NICU admission all            | 14      | [25, 37, 39, 51, 52, 54–56, 60, 62, 63, 65, 68, 69] | 896,272    | Linear dose-response^a| 0.63       | 0.56–0.71   | 95.4|
| Neonatal death                | 4       | [37, 40, 62, 65] | 533,880    | U-Shaped^b           | <3.95      | 0.43–0.83   | 77.5|
| Respiratory morbidity         | 9       | [51, 53, 55, 57, 61, 64, 65, 68] | 57,693     | Linear dose-response^a| 0.64       | 0.51–0.79   | 95.2|
| Hospitalization ≥5 days       | 5       | [38, 62, 65, 68, 69] | 59,331     | U-Shape^b           | <3.95      | 0.36–0.75   | 96.2|
| Hypoglycemia                  | 6       | [25, 38, 60, 65, 68, 69] | 46,367     | Linear dose-response^a| 0.84       | 0.79–0.91   | 0.0 |
| Apgar Score < 7               | 5       | [39, 56, 60, 65, 69] | 805,274    | Linear dose-response^a| 0.90       | 0.69–1.17   | 65.7|
| Jaundice                      | 5       | [56, 60, 65, 68, 69] | 32,109     | Linear dose-response^a| 0.71       | 0.66–0.77   | 53.7|
| Respiratory distress syndrome | 5       | [37, 59, 60, 65, 69] | 43,888     | Linear dose-response^a| 0.60       | 0.54–0.67   | 45.0|
| Transient tachypnea of the newborn | 5       | [37, 55, 59, 60, 65] | 40,766     | Linear dose-response^a| 0.68       | 0.54–0.86   | 84.1|
| Pneumothorax                   | 4       | [44, 59, 60, 67] | 25,121     | Binary (37 + 38 WG vs. ≥39 WG)^c| 0.99       | 0.03–19.19  | 72.0|
| Maternal hysterectomy          | 2       | [37, 52] | 18,662     | Binary (37 + 38 WG vs. ≥39 WG)^c| 1.10       | 0.03–39.35  | 0.0 |
| Maternal blood transfusion     | 2       | [37, 60] | 15,162     | Binary (37 + 38 WG vs. ≥39 WG)^c| 1.21       | 0.02–65.67  | 30.0|

**Meta-analyses of subgroups**

| NICU admission only ERCS      | 4       | [37, 39, 54, 60] | 792,107    | Linear dose-response^a| 0.66       | 0.65–0.67   | 0.0 |
| NICU death only repeat CS     | 2       | [37, 40] | 497,917    | U-Shape^b           | <3.95      | 0.51–0.87   | 0.0 |

**GRADE** is low. The risk for respiratory morbidity in neonates and other postnatal events (jaundice, hypoglycemia) decrease in the same manner. Assuming a U-shaped pattern with 39 + (0–6) WG at the minimum, we found a decreasing risk of death from 37 + 0 to 39 + (0–6) WG and increasing from then on. The certainty of the evidence is low and a sensitivity analysis showed wide confidence intervals diminishing the robustness of results. Similar results were seen in hospitalization of the neonate for more than 5 days and sepsis. Certainty of evidence is very low and low for respiratory morbidity, hospitalization of the neonate for more than 5 days and jaundice and sepsis. Only hypoglycemia showed moderate certainty of the evidence.

Maternal mortality is a very rare event in countries of WHO stratum A [70]. We only found one study considering maternal death. The other maternal outcomes hysterectomy and blood transfusion showed higher event rates in late term but this only seems to be a hint regarding the statistical uncertainty. All studies considering maternal outcomes had serious risk of bias and certainty of evidence was very low.
pool data with that from singleton pregnancies and cannot draw any conclusion on outcomes from identified data.

For future guidelines and decision making in elective planning of CS there is only sufficient evidence regarding neonatal outcomes. The evidence suggests decreasing NICU admissions in late term, especially in repeated CS. There seems to be a U-shape risk pattern for neonatal death with the minimum at 39 + (0–6) WG. Respiratory morbidity in neonates decreases in late term,

| Table 4: GRADE summary of findings |
|-----------------------------------|
| Outcome                           | Relative effect (95% CI) | Anticipated absolute effects (95% CI) | Certainty |
| NICU admission Nº of participants: 898,272 (1RCT,13 observational studies) | **RR 0.63** (0.56 to 0.71) | **3.3%** | **2.1%** (1.9 to 2.3) | **1.2% fewer** (1.5 fewer to 1 fewer) | **⨁⨁◯◯** LOW |
| Neonatal death Nº of participants: 533,503 (4 observational studies) | n/N IG: 274/25,808 n/N CG: 160/27,542 | < 39 RR 0.59 (0.43 to 0.83) ≥ 39 RR 2.09 (1.18 to 3.70) | **◯◯◯** VERY LOW |
| Respiratory morbidity Nº of participants: 57,693 (9 observational studies) | **RR 0.64** (0.51 to 0.79) | 2.6% | **1.7%** (1.3 to 2.1) | **0.9% fewer** (1.3 fewer to 0.5 fewer) | **◯◯◯** VERY LOW |
| Hospitalization 25 days Nº of participants: 59,331 (5 observational studies) | n/N IG: 2222/24,663 n/N CG: 3289/34,668 | < 39 RR 0.52 (0.36 to 0.75) ≥ 39 RR 2.00 (1.40 to 2.86) | **◯◯◯** VERY LOW |
| Sepsis Nº of participants: 42,381 (4 observational studies) | n/N IG: 366/20,689 n/N CG: 318/21,692 | < 39 RR 0.55 (0.44 to 0.67) ≥ 39 RR 3.57 (1.87 to 6.78) | **◯◯◯** VERY LOW |
| Hypoglycemia Nº of participants: 46,367 (1 RCT, 5 observational studies) | **RR 0.84** (0.79 to 0.91) | 1.2% | **1.0%** (1.0 to 1.1) | **0.2% fewer** (0.3 fewer to 0.1 fewer) | **◯◯◯◯** MODERATE |
| Apgar Score < 7 Nº of participants: 805,274 (5 observational studies) | **RR 0.90** (0.69 to 1.17) | 0.5% | **0.5%** (0.4 to 0.6) | **0.1% fewer** (0.2 fewer to 0.1 more) | **◯◯◯◯** VERY LOW |
| Jaundice Nº of participants: 32,109 (5 observational studies) | **RR 0.71** (0.66 to 0.77) | 2.3% | **1.7%** (1.5 to 1.8) | **0.7% fewer** (0.8 fewer to 0.5 fewer) | **◯◯◯** LOW |
| RDS Nº of participants: 43,888 (5 observational studies) | **RR 0.60** (0.54 to 0.67) | 0.7% | **0.4%** (0.4 to 0.5) | **0.3% fewer** (0.3 fewer to 0.2 fewer) | **◯◯◯** LOW |
| TTN Nº of participants: 40,766 (5 observational studies) | **RR 0.68** (0.54 to 0.86) | 2.5% | **1.7%** (1.4 to 2.2) | **0.8% fewer** (1.2 fewer to 0.4 fewer) | **◯◯◯◯** VERY LOW |
| Pneumothorax Nº of participants: 25,121 (4 observational studies) | **RR 0.99** (0.03 to 39.19) | 0.1% | **0.1%** (0.0 to 4.5) | **0.0% fewer** (0.1 fewer to 4.4 more) | **◯◯◯◯** VERY LOW |
| Maternal death Nº of participants: 14,865 (1 observational studies) | **RR 0.38** (0.04 to 3.40) | 0.0% | **0.0%** (0.0 to 0.2) | **0.0% fewer** (0.0 fewer to 0.1 more) | **◯◯◯◯** VERY LOW |
| Maternal hysterectomy Nº of participants: 18,662 (3 observational studies) | **RR 1.10** (0.03 to 39.35) | 0.2% | **0.2%** (0.0 to 0.79) | **0.0% fewer** (0.2 fewer to 7.7 more) | **◯◯◯◯** VERY LOW |
| Maternal blood transfusion Nº of participants: 15,162 (2 observational studies) | **RR 1.21** (0.02 to 65.67) | 0.8% | **1.0%** (0.0 to 54.0) | **0.2% more** (0.8 fewer to 53.2 more) | **◯◯◯◯** VERY LOW |
| NICU admission only repeat CS Nº of participants: 527,941 (4 observational studies) | **RR 0.66** (0.65 to 0.67) | 3.0% | **2.0%** (2.0 to 2.0) | **1.0% fewer** (1.1 fewer to 1 fewer) | **◯◯◯◯◯** MODERATE |
| NICU death only repeat CS Nº of participants: 497,917 (2 observational studies) | n/N IG: 194/24,1638 n/N CG: 158/25,6234 | < 39 RR 0.67 (0.51 to 0.87) ≥ 39 RR 1.68 (1.07 to 2.65) | **◯◯◯◯◯** VERY LOW |

*time response with reference category 39 week of gestation (RR = 1)
CI Confidence Interval; CG Control group; IG Intervention group; n Number of events; N Number of participants; RCT Randomized controlled trial; RDS Respiratory distress syndrome; RR Relative risk; TTN Transient tachypnea of the newborn
still, evidence is uncertain. We cannot draw any conclusion from the findings regarding maternal outcomes.

**Limitations**

**Certainty of evidence**

We identified serious risk of bias in all included studies due to the main issues of patient selection, confounding and lack of blinding. None of the cohort studies tried to resolve the issue of allocating pregnancies with less complication to late term groups and pregnancies with more complications to early term groups. Nor did any study report the reasons why women were selected for either group. There are diverse possibilities of confounding, for example ante- and postnatal care may not only differ between institutions but also between women considered for early term CS (increased monitoring) and late term. Also NICU admission policies may vary between institutions. Moreover we assume that the knowledge of early term CS is an indicator supporting NICU admission. As we see in Glavind et al., performing an RCT is possible even if randomization must take place in a short period of about two or 3 weeks (e.g. 38 + (0–6) vs 39 + (0–6) WG) [25].

**Limitations in the review process**

Our review has various limitations. We admit methodological limitations by pooling studies with great heterogeneity. We included any study without differentiating inclusion criteria (e.g. elective CS without any medical indication vs. Elective CS with medical indication), which resulted in high heterogeneity.

We could not use any data from the studies that controlled for confounding because the controlling variables were too heterogeneous. Some studies reported the use of ultrasound for an estimation of the gestational age or a combined method with the date of the last menstruation. Others did not report the method.

We did not differentiate or include this information in our analyses and might have missed on relevant issues. Moreover we pooled outcomes like respiratory morbidity which may differ in their definition of measuring. Furthermore, a broader assessment of maternal adverse events might be more relevant than assessing maternal death due to the rarity of events in the countries we considered in our analysis.

Various outcomes can be considered rather surrogates for neonatal morbidity than of direct importance to the patients, such as NICU admission and hypoglycemia [71]. But nevertheless NICU admission may lead to several negative effects on the development of the neonate and the parental relationship, for example the impact on breastfeeding [72, 73]. As NICU admission is always connected with various stressors it may also negatively affect the long term development of the neonate [74, 75]. Moreover the outcome hypoglycemia is a surrogate for neuronal energy and may affect (longterm) neurological development of the neonate [76, 77].

By constructing meta-analyses for NICU admission we summed up data for all WG ≥37 + 0 to 39 + 6 WG because not all included studies specified later WG and also the linear trend showed no change after 39 + 6 WG. For the other outcomes we ignored missing data in > 39 + 6 WG and let the linear trend continue decrease, remain or even change and further on increase (cubic spline models).

We limited our research to high income countries with very low general and child mortality. Those countries have similar rates of elective CS and comparable reasons for CS (e.g. medical, women’s preference, hospitals preference). We excluded lower WHO strata due to various reasons: General and especially child mortality is higher among other due to worse access to health care, and access to health care also indicates the use of CS, for example in central African regions where health care is limited CS rate is lower than 5%. Meanwhile access to health care and elective CS rate vary within one country in rural areas and areas with more infrastructure reflecting prosperity of the people e.g. China, Middle Eastern countries. As women who receive elective CS in low and middle income countries may vary much more regarding the risk and also backgrounds (education, prosperity, access to healthcare and cultural beliefs), this should be covered in a more precise and separate analysis [20].

**Conclusions**

We found that elective CS before the 39 + (0–6) WG lead to more NICU admissions, respiratory morbidity of the neonate and neonatal deaths, though death is rare and increases again after 39 + 6 WG. The decreasing respiratory morbidity is in accordance with the current NICE and RCOG guidelines (refs). Except for repeated CS, evidence is very heterogeneous. Nevertheless one can assume due to the strength of effects performing elective CS in late term is advantageous for neonatal morbidity. Glavind et al. performed a systematic review comparing the 38 + (0–6) and 39 + (0–6) WG for NICU admission, respiratory morbidity and maternal adverse events [78]. They showed similar results in the neonatal outcomes and also did not have enough data on maternal adverse events to make any conclusion. Our results do not differ from the original work for the German ministry of health [16], although our methods differed slightly and we assume a more precise validity of the results owing to the time-response analysis. There is not enough evidence on maternal outcomes to support a decision between early and late term CS. There is a need for more research, especially on maternal outcomes to provide a balanced decision between neonatal and
maternal health. Moreover it would be desirable to know more about the reasons that can cause heterogeneity to support patient individual decisions based on pregnancy characteristics, morbidities or maternal characteristics.

Deviations from the protocol
We deviated from the protocol in the extraction of two outcomes. First we did not extract birth weight of the neonate, as we came to the decision, that early term births have naturally lower birth weight than full term neonates. We neither extracted the outcome maternal adverse events, as they were defined so differently and heterogenic, that we could not see any coherence. e did not request study protocols directly from the authors, as we assumed that the probability that protocols for registry studies were developed is low. As we did not pool maternal mortality we end up not using any beta binomial model for pooling data at all. Furthermore we did not pool adjusted data as adjustment factors were too heterogeneous.

Supplementary information
Supplementary information accompanies this paper at https://doi.org/10.1186/s12884-020-03036-1.

Abbreviations
CI: Confidence interval; CS: Caesarean section; NICU: Neonatal intensive care unit; RCT: Randomized controlled trial; RDS: Respiratory distress syndrome; TTN: Transient tachypnea of the neonate; VBAC: Vaginal birth after caesarean section; WHO: World health organization; WG: Week of gestation

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Authors’ contributions
BP, TM and DP designed the study. BP wrote the first draft of the manuscript. DP developed the search strategy draft. BP and SP screened the titles and abstracts and full text independently. AG and BP screened literature of other sources than databases. BP, SP and TM extracted the data and performed risk of bias and GRADE assessment. TM developed and performed the data synthesis. SS is the clinical expert. SP, SB and EN helped to draft the manuscript. All authors have been involved in revising the manuscript. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted. All authors have read and approved the manuscript.

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Availability of data and materials
The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

Author details
1 Institute for Research in Operative Medicine, Witten/Herdecke University, Othmerheimer Str. 200, 51109 Cologne, Germany. 2 Department of Obstetrics and Gynecology, Witten/Herdecke University, Marien Hospital Witten, Marienplatz 2, 58452 Witten, Germany. Brandenburg Medical School - Theodor Fontane, Faculty of Health, Campus Neuruppin, Fehrbelliner Str. 38, 16816 Neuruppin, Germany. Interdisciplinary Centre for Health Services Research, Witten/Herdecke University, Alfred-Herrhausen-Straße 50, 58448 Witten, Germany.

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