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CHAPTER 2

Impact of obstetric history on the risk of spontaneous preterm birth in singleton and multiple pregnancies: a systematic review

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For EBM CONNECT

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ABSTRACT

Background

Information about the recurrence of spontaneous preterm birth in subsequent twin/singleton pregnancies is scattered.

Objective

To quantify the risk of recurrence of spontaneous preterm birth in different subtypes of subsequent pregnancies.

Search strategy

An electronic literature search in OVID MEDLINE and EMBASE complemented by PubMed, to find recent studies.

Selection criteria

Studies comparing the risk of spontaneous preterm birth after a previous preterm and previous term pregnancy.

Data collection and analysis

The absolute risk of recurrence with a 95% confidence interval and the absolute risk of preterm birth after a term delivery were calculated. Data from studies were pooled using the Mantel–Haenszel method.

Main results

We detected 13 relevant studies. The risk of recurrence of preterm birth was significantly increased in all preterm pregnancy subtypes, compared with their term counterparts. Women pregnant with twins after a previous preterm singleton had the highest absolute risk of recurrence (57%, 95%CI 52–62) and after a previous term singleton their absolute risk was 25% (95%CI 24–27). Women pregnant with a singleton after a previous preterm twin pregnancy have an absolute recurrence risk of 10% (95%CI 8.2–12) whereas a singleton pregnancy after delivering a previous twin up to term yields a low absolute risk of only 1.3% (95%CI 0.8–2.2). Women pregnant with a singleton after a previous preterm singleton have an absolute recurrence risk of 20% (95%CI 20–21).

Authors' conclusions

The risk of recurrence of preterm birth is influenced by the singleton/twin order in both pregnancies, and varies between 10% for a singleton after previous preterm twin to 57% for a twin after a previous preterm singleton.

INTRODUCTION

Preterm birth is one of the most widespread problems in obstetrics. In 2010, an estimated 14.9 million babies were born preterm, which was 11% of all live births worldwide.[1] Preterm birth and its complications are responsible for most neonatal deaths in otherwise healthy infants, and can lead to lifelong complications such as cerebral palsy, visual disorders and chronic diseases in adulthood.[2;3]

Recurrent spontaneous preterm birth is defined as more than one preterm birth related to the spontaneous onset of labour with intact membranes or preterm rupture of membranes.[4] Information about the risk of recurrence of preterm birth is important for women considering a subsequent pregnancy. In addition, obstetricians need these data to counsel women and to assess and apply preventive strategies.

Women with a twin pregnancy are known to be at increased risk of preterm birth, as around 40% will deliver spontaneously before 37 weeks of gestation.[3] Although systematic reviews have been published on the biological background and treatment of recurrent preterm birth,[4;5] a clear overview of the magnitude of the risk of recurrent spontaneous preterm birth has so far not been available. We therefore decided to perform a systematic review of the risk of recurrence of spontaneous preterm birth in different subsequent pregnancy subtypes; women with a singleton pregnancy after a preterm singleton birth; women with a twin after a preterm singleton birth; and women with a singleton after a preterm twin birth. We also collected data on the course of pregnancy after a previous term delivery of singletons and twins.

METHODS

Literature search

A medical librarian (JL) performed a comprehensive literature search of the electronic databases MEDLINE (OVID, from 1948) and EMBASE (OVID, from 1980) to identify publications on the risk of recurrence of preterm birth in singleton and multiple pregnancies. In addition, PubMed was searched for publications ahead of print not yet included in OVID MEDLINE, using only text words and the command “publisher[sb]”. The latest search date update was 8 January 2013. An initial pilot search in PubMed established that some relevant papers were missed if we searched for *all* concepts simultaneously. We therefore constructed a rather complex search as follows. The basis was: (A) a broad search for preterm birth combined with (B) a methodological filter (for clinical trials, observational and epidemiological studies, registries, medical history, etc), using a strategy incorporating subject headings (e.g. MeSH terms in MEDLINE) and text words, in the title and abstract. (A) plus (B) were successively combined with (C), a text word search for risk of recurrence of preterm birth, OR (D), a text word search for prediction/risk of

preterm birth (without recurrence), OR (E) a broad search (using both subject heading and text words) for singletons or multiple pregnancies combined with a search for recurrence or prediction/risks. (E) had little added value over (C) and (D). Thus the final search had the structure (A and B) and (C or D or E). (see Appendix S1 in Supporting Information for the entire MEDLINE search). A similar search was constructed for EMBASE. No language restrictions were applied. We excluded animal studies by using double negation (i.e. in MEDLINE not animals/not humans/). The search included an iterative process to refine the search strategy through adding search terms as new relevant citations were identified (i.e. by checking the reference lists of relevant papers). The bibliographic records retrieved were downloaded and imported into Reference Manager® software (version 12.0) to remove duplicates, and store and analyse the search results.

Criteria for inclusion

Study design

We considered all cohort studies concerning recurrence of spontaneous preterm birth for inclusion. Study size was not used as a limiting criterion for inclusion.

Study population

To be included, studies were required to contain women with at least one spontaneous preterm birth at <37 weeks of gestation in their history or women with at least one term birth in their history. No limitations in relation to age, race, parity, the number of fetuses per pregnancy or other baseline characteristics were set. Study populations consisting of only women with iatrogenic preterm birth or studies mixing both populations were excluded. Also study populations consisting of other groups at high risk of preterm birth such as women with uterine anomalies and those who had had a previous abortion or cervical surgery without a previous preterm birth were excluded.

Outcome measures

Any of the following outcome measures were accepted for inclusion:

1. risk of spontaneous preterm singleton delivery before 37 weeks of gestation after a preterm or term singleton delivery
2. risk of spontaneous preterm singleton delivery before 37 weeks of gestation after a preterm or term twin delivery
3. risk of spontaneous preterm twin delivery before 37 weeks of gestation after a preterm or term singleton delivery.

Data extraction and quality assessment

Two authors (BK and PB) independently screened the titles and abstracts of identified studies. Relevant articles were selected and full texts were studied. Studies were selected by inclusion criteria and data extraction. Disagreements were resolved by consensus. Studies with data on the recurrence risk of preterm birth in a subsequent delivery were selected for further reading.

Data extraction was completed by BK and PB using a data extraction form. We did not contact authors for additional data. We determined the strength of the evidence using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system.[6]

Data analysis

The primary outcome was a recurrence of spontaneous preterm birth in a singleton birth after a previous singleton birth, a twin birth after a previous singleton birth or a singleton birth after a previous twin birth before 37 weeks of gestation. A secondary outcome was the recurrence of preterm birth below other gestational age cut-offs. For each study, we constructed a table with the numbers of preterm and term births in the index pregnancy and the numbers of preterm and term births in subsequent pregnancies. For each study, we calculated the absolute risk of recurrence with a 95% confidence interval (95% CI) for the proportion of preterm births and the absolute risk of preterm birth after a term delivery, with a 95% CI.

Subsequently, data from the studies were pooled using the Mantel–Haenszel method. We converted odds ratios (OR) or risk ratios (RR) using the generic inverse variance method when no absolute numbers were available.[7] We chose to use a random-effects model because of the heterogeneity between included studies. All analyses were performed with Review Manager (RevMan) version 5.1 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2011).

RESULTS

The results of the search are shown in Figure 1. Our search identified 9104 publications (Appendix S1). Among these were 2547 duplicates. We screened abstracts of the 6557 unique titles; 6519 of these were excluded because they did not match the inclusion criteria whereas 39 articles were potentially relevant and therefore full texts of these articles were screened. Checking of cross-references did not reveal further studies. We excluded 26 further articles mainly because of the inability to extract absolute numbers, the lack of a control term group or because they used (partly) the same population (see Appendix S2). When two articles described (partly) the same population, the largest most relevant publication was included in our systematic review.

Thirteen articles were relevant and included in this review. Six studies on the risk of singleton–singleton subsequent births, four on twin–singleton and three on singleton–twin subsequent births.

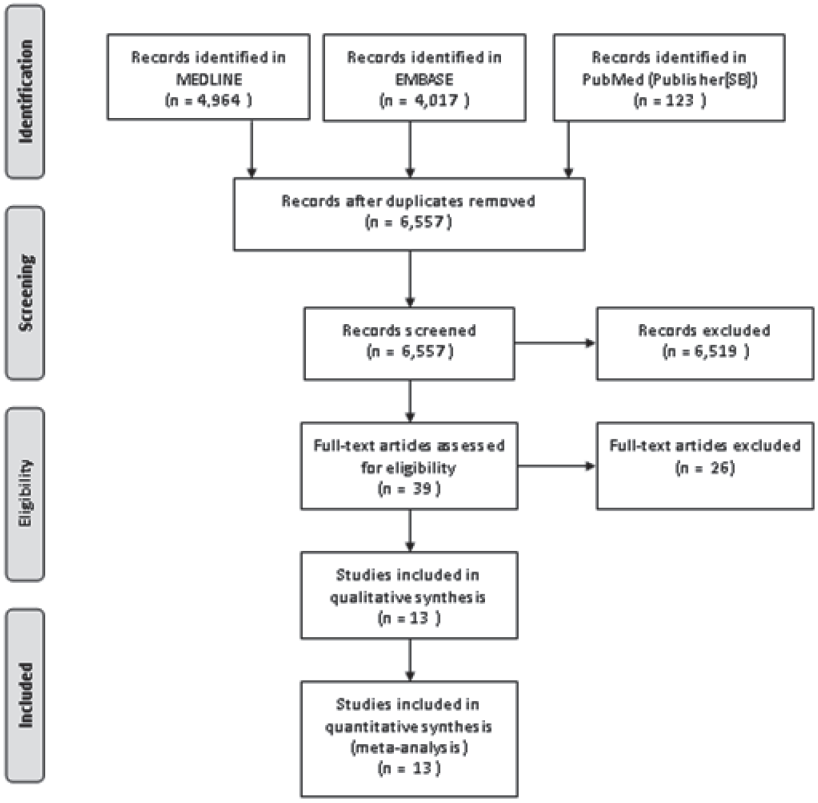

Figure 1 | Prisma flow diagram of included studies

First singleton, second singleton

After application of inclusion and exclusion criteria six studies remained that described the risk of a spontaneous preterm singleton after a previous singleton pregnancy.[8-13] Table 1 shows the characteristics of the included studies. The sample size of the included studies ranged from 1257 women (Mercer et al.[12]) to 452 680 women (Lykke et al.[11]) We found that 22.1% [8056/(28 373 + 8056)] of all singleton preterm births in the second pregnancy were in women with a previous preterm singleton birth. The absolute risk of recurrence of a delivery before 37 weeks of gestation ranged in the individual studies from 15.8% (Lykke et al.[11]) to 30.2% (Laughon et al.[13]) (Figure 2). The pooled estimate of the absolute recurrence risk was 20.2% (95%CI 19.9–20.6). The risk of a preterm singleton delivery before 37 weeks of gestation after a term singleton pregnancy ranged from 2.7% in Lykke et al.[11] to 7.6% in Mercer et al.[12] (pooled estimate 4.0%, 95%CI 3.9–4.0) (Figure 2).

Women with a previous singleton birth at < 37 weeks of gestation were at a statistically significant increased risk for recurrent preterm birth compared with women with a previous term birth (pooled OR 5.43, 95%CI 4.03–7.31) (Figure S1). Although three studies also did a subgroup analysis in groups delivering at other gestational ages, they all used different cut-off points. As a consequence, their results could not be pooled. They all individually showed an increasing risk of preterm birth with decreasing gestational age at first delivery.

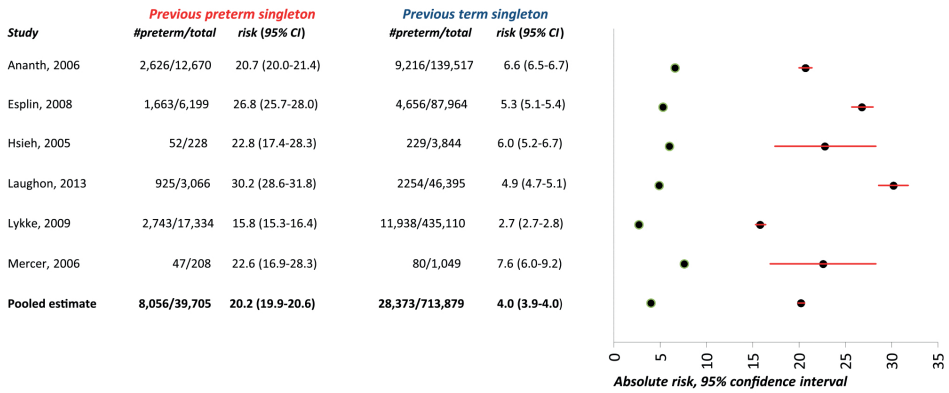

Figure 2 | Absolute risk of singleton preterm birth after previous term or preterm singleton birth.

First twin, second singleton

Four studies were identified that described the risk of a spontaneous preterm singleton after a previous twin pregnancy (Table 2).[14–17] We found that 84.4% [81/(81 + 15)] of all singleton preterm births in the second pregnancy were in women with a previous preterm twin birth. Both Rafael et al.[14] and Facco et al.[15] also included women with a term birth before the twin pregnancy. The study of Menard et al.[16] in contrast to the other studies included mostly black women.

Table 1 | Characteristics of included studies: singleton–singleton

First author	Year	Study type	Inclusion period	Setting	No. in study	Loss to follow up/ incomplete records	Lower limit PTD[$]	Stillbirths in definition PTD
Ananth[8]	2006	Cohort	1989–97	Retrospective cohort of births Missouri, USA	154 809	NA	NA	NA
Esplin[9]	2008	Cohort	1989-2001	Population database of births in Utah, USA	98 724	3,50%	20 weeks	No
Hsieh[10]	2005	Cohort	1991–97	Chang Gung Memorial hospital computerized obstetric database, Taiwan	4072	NA	NA	No
Mercer[12]	2006	Cohort	1992–94	Preterm prediction study, 10 perinatal centers, USA	1257	NA	20 weeks	No
Laughon[13]	2013	Cohort	2002–10	20 hospitals, Utah, USA	49 395	NA	20 weeks	Yes
Lykke[11]	2009	Cohort	1978-2007	National perinatal registry, Denmark	452 680	NA	20 weeks	No

PTD, preterm delivery; NA, not available; PT, preterm singleton group; T, term singleton group.

Table 2 | Characteristics of included studies: twin–singleton

First author	Year	Study type	Inclusion period	Setting	No. in study	Lost to follow-up/ incomplete records	Lower limit PTD	Stillbirths in definition PTD
Facco[14]	2007	Cohort	1995-2005	Northwestern Memorial Hospital, Chicago, USA	167	9 (5%)	20 weeks	No
Rafael[16]	2012	Cohort	1996-2010	Christiana Care Health Systems, Newark, USA	255	0%	18 weeks	No
Schaaf[17]	2012	Cohort	1999–2007	National Perinatal Registry, The Netherlands	1957	NA	22 weeks	No
Menard[15]	1995	Cohort	1981–93	Medical University of South Carolina, USA	144	NA	500 g	NA

PTD, preterm delivery; NA, not available; PT, preterm twin group; T, term twin group.

Inclusion criteria	Exclusion criteria	Mean age (years)	Race	Parity	Interpregnancy interval (months)
Women with first and second singleton birth	NA	20–34, PT 74.4%, T 81.2%	White, PT 65.8%, T 83.4%	nulliparous with 2 subsequent births	PT 27.8, T30.7
Women with first and second spontaneous singleton birth	NA	PT 24.2. T 24.9	White, PT 30.1%, T 33.6%	nulliparous with 2 subsequent births	NA
Women with two consecutive births at 20 weeks or more	Multiple pregnancies, fetal anomalies, cervical incompetence, stillbirth, indicated preterm deliveries	PT 30.7, T 30.6	NA	NA	<12months PT 48%, T 39.7%
Gravid women with two singleton pregnancies	Placenta previa, major anomalies, poly-oligohydramnios, HIV, cerclage, symptoms of preterm birth at 24 weeks	PT 24.6, T 24.8	Black, PT 67.5%, T 62%	nulliparous PT 67.5% T 67.4%	NA
Women with two consecutive births at 20 weeks or more	Multiple pregnancies	25.6	White 86.5%, black 0.4%, Hispanic 10.6%	Nulliparous 59.5%	18.5
Women with first and second delivery in this timeframe	Cardiovascular diagnosis, diabetes, women moving	29.5	NA	nulliparous with 2 subsequent births	NA

Inclusion criteria	Exclusion criteria	Mean age (years)	Race	Parity	Interpregnancy interval (months)
Women with a twin followed by a singleton pregnancy	Intrauterine death, major congenital anomalies, iatrogenic preterm births in either pregnancy, preterm delivery in history	PT 30.9, T 30.0	PT 69.7% white, T 70.6% white	PT 28.3%, T 30.9%, previous term birth	NA
Women with a twin with a subsequent delivery in same hospital	Intrauterine death, major congenital anomalies, iatrogenic preterm births in either pregnancy, preterm delivery in history	PT 30.4, T 30.8	PT 68.1% white, T 61.3% white	PT 39.6%, T 41.4%, previous term birth	PT 24.3%, T 15.3%, <6 or >60
Women with a first twin birth followed by a singleton pregnancy	Intrauterine death, major congenital anomalies, iatrogenic preterm births in the singleton pregnancy	PT 29.1, T 29.2	PT 88.7% white, T 91.4% white	Nulliparous women with two subsequent births	PT 33, T 36
Women delivering twins followed by a singleton pregnancy with prenatal care at university	Maternal transports, births < 500 g	25.2	85.4% black	NA	NA

The risk of recurrent preterm birth ranged from 7.3% (Schaaf et al. [17]) to 19.8% (Menard et al [16] ;pooled estimate 10.0%, 95%CI 8.2–12.3; Figure 3). The risk of a preterm singleton after a term twin ranged from 0.8% (Schaaf et al. [17]) to 6.9% (Menard et al. [16]; pooled estimate 1.3%, 95%CI 0.8–2.2; Figure 3). Delivery of a preterm twin at < 37 weeks of gestation was associated with a significantly increased risk of a spontaneous preterm birth in a subsequent singleton pregnancy compared with delivery of a previous term twin (pooled OR 6.7, 95% CI 2.3–19.1; Figure S2).

Three studies also described the risk of a subsequent preterm birth in a subgroup of twins delivered between 34 and 37 weeks of gestation[14;16;17]. They did not describe the absolute numbers of term and preterm births so the absolute risk of recurrence could not be calculated. However, we were able to pool the risk ratios and odds ratios described in the individual studies. Delivery of a preterm twin between 34 + 0 and 36 + 6 weeks of gestation is associated with a significantly increased risk of a spontaneous preterm birth in a subsequent singleton pregnancy compared with women who had delivered a previous twin at term (pooled OR 2.6, 95% CI 1.2–5.7; Figure S2).

Two studies also described the risk of a subsequent preterm birth for subgroups of a previous twin delivery between 30 and 34 weeks of gestation and below 30 weeks of gestation[16;17]. Rafael et al.[14] also subdivided data at lower gestational ages, but because they used different cut-off points their results could not be used in these pooled estimates. Delivery of a preterm twin between 30 + 0 and 33 + 6 weeks of gestation was associated with a significantly increased risk of spontaneous preterm birth in a subsequent singleton pregnancy (pooled OR 6.7, 95%CI 2.3–19.1; Figure S2). Delivery of a preterm twin at < 30 weeks of gestation was associated with a significantly increased risk of spontaneous preterm birth in a subsequent singleton pregnancy (pooled OR 10.9, 95%CI 3.8–31.0; Figure S2).

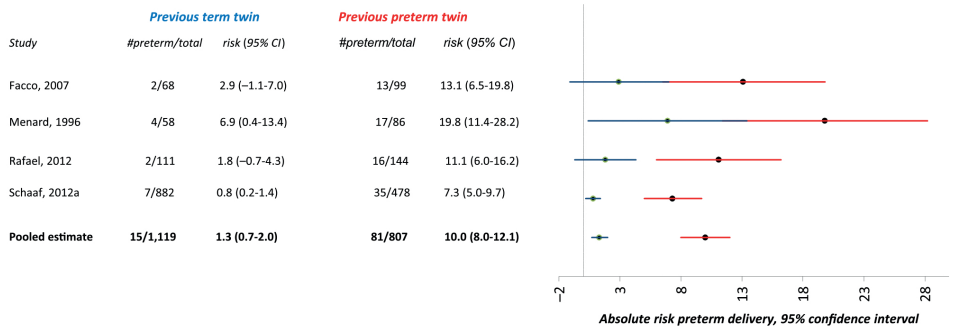

Figure 3 | Absolute risk of singleton preterm birth after a previous term or preterm twin birth.

First singleton, second twin

We identified three eligible studies that estimated the risk of a spontaneous preterm twin after a singleton pregnancy[18-20] (Table 3). We found that 11.9% of preterm twins in the second pregnancy were in women with a previous preterm singleton.

The absolute risk of recurrence of spontaneous birth < 37 weeks of gestation varies within the studies from 47.5 to 73.9% (pooled estimate 57.0%, 95%CI 51.9–61.9; Figure 4). The risk of a preterm twin after a term singleton pregnancy was 20.4% (Schaaf et al. [20]) , 31.2% (Ananth et al. [18]) and 44.4% (Facco et al. [19]; pooled estimate 25.4%, 95%CI 24.3–26.5; Figure 4). A previous preterm singleton is associated with a significantly increased risk of a spontaneous preterm twin in a subsequent pregnancy compared with a term singleton (pooled OR 3.8 95% CI 1.4–10.7; Figure S3).

Although two studies (Ananth et al. [18] and Schaaf et al. [20]) performed subgroup analysis based on gestational age, they could not be pooled because of the different gestational age cut-offs used. Both studies found an increasing risk of preterm birth with a decreasing gestational age in the previous pregnancy.

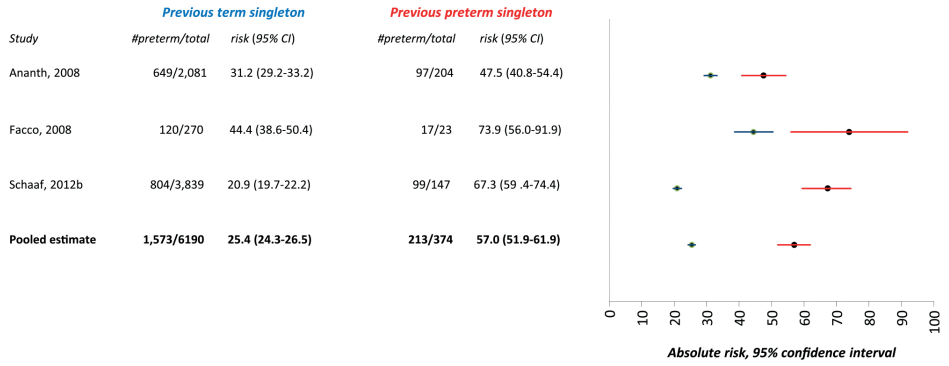

Figure 4 | Absolute risk of twin preterm birth after a previous term or preterm singleton birth.

Quality of evidence

Study limitations

A majority of studies did not report on the completeness of data or loss to follow up[8;10-12;16-18;20] or did not even describe exclusion criteria.[8;9] Also some important baseline characteristics were not reported in studies, such as the race[10;11] or parity[10;16] of the women.

The lower limit for the definition of preterm birth differed between the included studies. Although most studies used 20 weeks of gestation as a lower limit,[9;11-13;13;15;18;19] 18 weeks of gestation [14] or 22 weeks of gestation,[17;20] or a weight cut-off[16] were also used as lower limits. Two studies did not mention a lower limit for preterm birth.[8;10] None of the studies including twins provided information about chorionicity.

Table 3 | Characteristics of included studies: singleton–twin

First author	Year	Study type	Inclusion period	Setting	No. in study	Lost to follow-up/ incomplete records	Lower limit PTD	Stillbirths in definition PTD
Ananth[18]	2008	Cohort	1989–97	Retrospective cohort of births Missouri, USA	2329	NA	20 weeks	No
Facco[19]	2008	Cohort	1995-2005	Northwestern Memorial Hospital, Chicago, USA	293	14 (4%)	20 weeks	No
Schaaf[17]	2012	Cohort	1999–2007	National Perinatal Registry, The Netherlands	4071	NA	22 weeks	No

PTD, preterm delivery; NA, not available; GA, gestational age; PT, preterm singleton group; T, term singleton group

Consistency

Inconsistencies were found in the comparison between singleton–singleton and singleton–twin, with I^2 values of 99% ($P < 0.001$) and 94% ($P < 0.001$), respectively. These inconsistencies may be based on differences in baseline characteristics or the exclusion criteria of individual studies, but because of the lack of reporting in some studies this could not be proven. As a consequence, evidence was downgraded in these comparisons.

Directness

Most studies used women's first and second pregnancies to estimate the risks; however, some studies also included women with a previous term birth before the index pregnancy,[12;14;15;19] or any previous birth.[13] As a consequence, evidence was downgraded in these comparisons.

Precision

No important imprecision could be detected. Most studies were quite large with narrow confidence intervals.

Publication bias

Publication bias cannot be completely ruled out, although both small and large studies were identified and included.

	Inclusion criteria	Exclusion criteria	Mean age (years)	Race	Parity	Interpregnancy interval (months)
	First singleton live birth followed by a gestation resulting in a twin live birth	Intrauterine death, no GA, or < 20 week GA	32% 25–29	76.3% white	Nullipara with two subsequent pregnancies	30.6
	Singleton followed by a twin > 20 weeks	Iatrogenic PTD in singleton or twin, major anomaly, intrauterine death, prophylactic cerclage, women with prior preterm deliveries before study period	PT 32.2, T 31.5	PT 47.8% white, T 70.7% white	Prior term birth, PT 26.1%, T 21.8%	NA
	First two pregnancies, singleton followed by a twin	Iatrogenic PTD in subsequent twin pregnancy, major anomaly, intrauterine death	PT: 29.8, T 29.4	PT 94.4% white, T 91.9% white	Nullipara with two subsequent pregnancies	PT 28, T 28m

GRADE system

The quality of evidence according to the GRADE system is summarised in Tables S1–S3. As a consequence of downgrading for inconsistency and directness and upgrading for dose–response gradient, the overall quality of evidence for the singleton–singleton recurrence risk was judged to be very low (Table S1).

The overall quality for the twin–singleton recurrence risk and the subgroup 34 + 0 to 36 + 6 was judged to be low due to downgrading for directness and upgrading for dose–response gradient. The quality for the subgroups 30 + 0 to 33 + 6 and < 30 weeks was judged to be moderate due to upgrading for dose–response gradient (Table S2).

The singleton–twin comparison had some inconsistencies and problems with directness, leading to a very low overall quality (Table S3).

DISCUSSION

Main findings

This systematic review provides an overview of the risk of recurrence of spontaneous preterm birth in different types of subsequent pregnancies. Recurrent preterm birth makes a substantial contribution to the total preterm birth count, with 22.1% of preterm singletons births occurring in women with a previous preterm singleton, 84.4% of preterm singleton births in women with a previous preterm twin and 11.9% of preterm twin births in women with a previous preterm singleton. The risk of recurrence of spontaneous preterm birth is significantly increased in all pregnancy subtypes compared with their term counterparts. The strength of this evidence is low to moderate for the twin–singleton comparison and very low for the singleton–singleton and singleton–twin comparisons. Women pregnant with a twin after a previous preterm singleton have the highest absolute risk of recurrence (57.0%), but even after a previous term singleton the absolute risk of preterm birth is still high (25.4%). Women pregnant with a singleton after a previous preterm twin have the lowest risk of recurrence (10.0%) and a pregnancy after delivering a previous twin up to term yields the lowest absolute risk of preterm birth, only 1.3%. Women pregnant with a singleton after a previous preterm singleton have an absolute risk of recurrence of 20.3%.

Strengths and limitations:

The strength of this systematic review is the relatively large sample sizes of the pooled estimates. The overall quality of the included studies was quite good; however, they were observational studies and as such are prone to several forms of bias. Limitations of the study design were taken into account in the assessment of the overall quality of evidence.

Misclassification of preterm birth is an issue in all the studies included in this review. If mentioned in the original publication, gestational age estimate was based on last menstrual period or on best clinical estimates. Ultrasound was only used in the more recent years of the cohorts. Estimates of last menstrual period are known to be rather imprecise [21]and could have led to misclassification of preterm birth.[21] This could have led to women being classified as having had a previous preterm birth when it actually was a term birth and women being classified as having had a term birth when it was actually a preterm birth.[22;23] The direction of this misclassification could be either way.

In addition, the lower limit for the definition of preterm birth differed between the included studies or was not even reported, making comparison difficult. Also, in the studies that reported on twins, no information about chorionicity was available. Finally, preterm stillbirths were excluded in almost all studies. Misclassification between stillbirth and live birth in very preterm babies is possible which could also have influenced our results.

Although we were able to identify a lot of studies, various studies used different cut-offs for subgroup analyses at lower gestational ages. As a consequence these data could

not be pooled and not all existing evidence could be summarised in this review. Besides, some studies grouped spontaneous with indicated preterm birth which meant that they were excluded from this review. Some studies on the subject were only published as conference abstracts so more evidence is expected to be published in the future.

This systematic review was only limited to the risk of recurrence of spontaneous preterm birth because we think that the indications for iatrogenic preterm birth and the possible interchange between hypertensive disorders and growth restriction are very important for the specific risk of recurrence and also for counselling parents. That information is already available[24;25] and is therefore outside the scope of this particular review. This decision could be doubted because there is evidence that women with a previous iatrogenic preterm birth are also at increased risk of a subsequent spontaneous preterm delivery.[8;17;20;26] In addition, most guidelines advise induction of twins before 37 weeks depending on the chorionicity of the twins. Those women with an iatrogenic preterm birth might have delivered prematurely on their own for other reasons if there was no intervention. Excluding these women might have led to selection bias.

It is important to realise that the estimates in this review are only crude measures. Confounding factors may be responsible for some of the observed results. We were unable to correct for the confounding factors in each individual study. Furthermore, this review focused on only two successive pregnancies. The risk of recurrence might be different in women with more than one previous preterm birth.

Finally, information about possible treatments for the prevention of recurrent preterm birth was not available in the selected studies. It is possible that women with a previous preterm birth received treatment to prevent recurrence, such as progesterone, pessary or cerclage. Treatment could have led to an underestimation of the absolute risk of recurrence.

Interpretation

We now know that the risk of preterm birth is dependent not only on the gestational age of the previous pregnancy but also on the type of the previous and current pregnancy (twin or singleton). We can provide doctors and patients with more specific risks of recurrence based on specific obstetric history and the type of the current pregnancy.

We realise, however, that obstetric history in itself is not totally predictive of recurrent spontaneous preterm birth, but it is one of the factors available to counsel women before they start their second pregnancy. Once women are pregnant, we can further define their personal risk profile by adding cervical length measurement or certain biomarkers.[27]

CONCLUSION

Although our review provides an overview, more detailed information is necessary for a better prediction of risk for individuals and better allocation of resources. We were unable to stratify on maternal race, for example, although differences in preterm birth rates between races have been shown before.[1;28] We therefore think that subdivision at the level of maternal race will be valuable. Similarly, stratification for the start of delivery (spontaneous labour versus premature rupture of membranes) and subdivisions for different weeks of gestation could be helpful, since decreasing gestational age is associated with increasing mortality, morbidity and increased neonatal care and costs.[1]

In order to obtain these more individualised risk scores, other studies should be carried out. We did not attempt to obtain the original data from each study, although meta-analysis with individual patient data would be more accurate and would allow the creation of prediction models. We think that a global collaborative approach could be the solution to obtaining a more detailed risk scale, stratified for race, gender and gestational age of delivery in first and second pregnancies.

Our results underline the impact of recurrent preterm birth on the total preterm birth count and indicate which women are most and which are least at risk of preterm birth based on their obstetric history. It is clear that the risks of recurrence differ between different pregnancy subtypes. These risk estimations can be used to adjust the care for each specific risk group, evaluate innovative strategies for the prevention of recurrence or inform women about their risks in a subsequent pregnancy.

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SUPPORTING INFORMATION

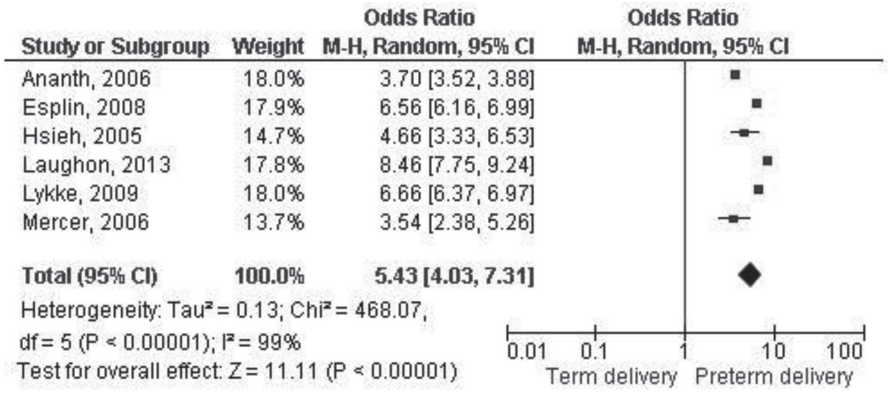

Figure S1 | Risk of preterm singleton < 37 weeks after previous spontaneous preterm singleton delivery < 37 weeks

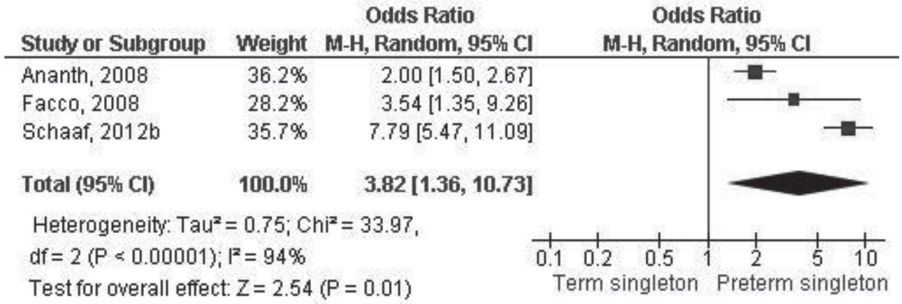

Figure S3 | Risk of preterm singleton delivery < 37 weeks after a previous preterm twin < 37 wee

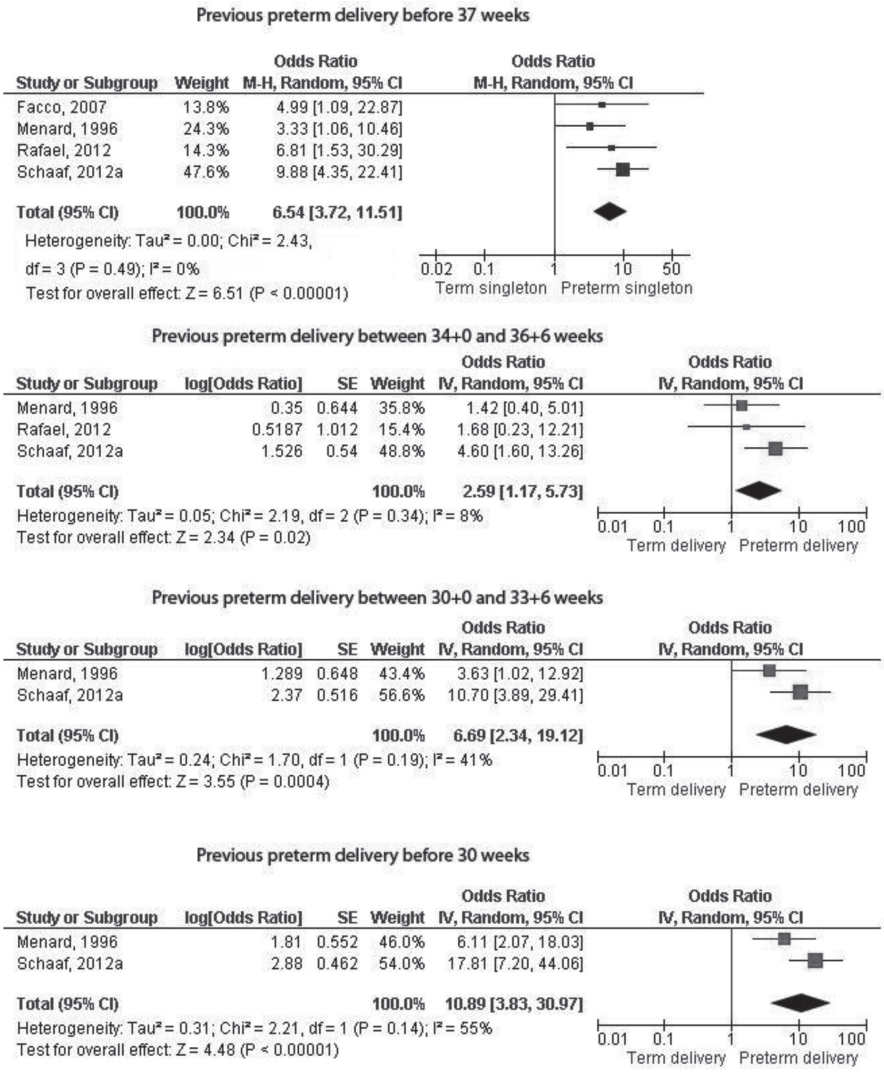

Figure S2 | Risk of preterm singleton delivery < 37 weeks after a previous spontaneous preterm twin < 37 weeks, between 34+0 an 36+6, between 30+0 and 33+6 and <30 weeks

Table S1 | Grade evidence profile table for women pregnant with a singleton pregnancy after a preterm singleton delivery

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Previous preterm singleton delivery	Previous term singleton delivery	Relative (95% CI)	Absolute	Quality	Importance
Risk of a spontaneous preterm singleton birth <37 weeks after a previous preterm singleton birth <37 weeks												
6	Observational studies	No serious risk of bias	Serious[1]	Serious[2]	No serious imprecision	Dose response gradient[3]	8056/39705 (20.3%)	28373/713879 (4%)	OR 5.43 (4.03 to 7.31)	144 more per 1000 (from 103 more to 193 more)	⨁OOO VERY LOW	CRITICAL

1. Point estimates of individual studies differ without great differences in population
2. Inclusion of preganancies with a previous term or previous preterm pregnancy before the index pregnancy
3. The earlier the gestational age in the first preganancy the higher the recurrance risk.

Table S2 | Grade evidence profile table for women pregnant with a singleton pregnancy after a preterm twin delivery

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Previous preterm twin delivery	Previous term twin delivery	Relative (95% CI)	Absolute	Quality	Importance
Risk of spontaneous preterm singleton birth <37 weeks after previous preterm twin <37 weeks												
4	Observational studies	No serious risk of bias	No serious inconsistency	Serious	No serious imprecision	Dose response gradient[2]	102/1404 (7.3%)	15.1119 (1.3%)	OR 5.71 (3.29 to 9.92)	59 more per 1000 (from 29 more to 105 more)	⊕⊕OO LOW	CRITICAL
Risk of spontaneous preterm birth <37 weeks after a previous preterm twin birth between 34+0-36+6												
3	Observational studies	No serious risk of bias	No serious inconsistency	Serious	No serious imprecision	Dose response gradient[2]	0/2356 (0%)	0%	OR 2.63 (1.24 to 5.56)	-[3]	⊕⊕OO LOW	IMPORTANT
Risk of spontaneous preterm birth <37 weeks after a previous preterm twin birth between 30+0 to 33+6												
2	Observational studies	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	Dose response gradient[2]	0/2101 (0%)	0%	OR 7.03 (3.19 to 15.51)	-[3]	⊕⊕⊕O MODERATE	IMPORTANT
Risk of spontaneous preterm singleton birth <37 weeks after a previous preterm twin birth between <30 weeks												
2	Observational studies	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	Dose response gradient[2]	0/2101 (0%)	0%	OR 11.46 (5.72 to 22.96)	-[3]	⊕⊕⊕O MODERATE	IMPORTANT

1. Inclusion of pregnancies with a previous term pregnancy before the index pregnancy
2. The earlier the gestational age in the first pregnancy the ghigher the recurrance risk
3. No numbers of individual participants were available for these subgroups

Table S3 | Grade evidence profile table for women pregnant with a twin pregnancy after a preterm singleton delivery

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Previous preterm twin delivery	Previous term twin delivery	Relative (95% CI)	Absolute	Quality	Importance
Risk of spontaneous preterm twin birth <37 weeks after previous preterm singleton birth <37 weeks												
3	Observational studies	No serious risk of bias	Serious[1]	Serious[2]	No serious imprecision	Dose response gradient[2]	213/374 (57%)	1573/6190 (25.4%)	OR 3.41 (2.75 to 4.21)	283 more per 1000 (from 230 more to 335 more)	⊕OOO VERY LOW	CRITICAL

1. Point estimates of individual studies differ without greater differences in population
2. Inclusion of pregnancies with a previous term pregnancy before the index pregnancy
3. The earlier the gestational age in the first pregnancy the higher the recurrance risk