**Human Reproduction, Vol.28, No.7 pp. 1943–1952, 2013**
Advanced Access publication on May 3, 2013 doi:10.1093/humrep/det130

human reproduction

**META-ANALYSIS** ***Reproductive epidemiology***

# Impact of Caesarean section on subsequent fertility: a systematic review and meta-analysis

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*Submitted on March 26, 2013; resubmitted on March 26, 2013; accepted on April 8, 2013*

**STUDY QUESTION:** Is there an association between a Caesarean section and subsequent fertility?

**SUMMARY ANSWER:** Most studies report that fertility is reduced after Caesarean section compared with vaginal delivery. However, studies with a more robust design show smaller effects and it is uncertain whether the association is causal.

**WHAT IS KNOWN ALREADY:** A previous systematic review published in 1996 summarizing six studies including 85 728 women suggested that Caesarean section reduces subsequent fertility. The included studies suffer from severe methodological limitations.

**STUDY DESIGN, SIZE, DURATION:** Systematic review and meta-analysis of cohort studies comparing subsequent reproductive outcomes of women who had a Caesarean section with those who delivered vaginally.

**PARTICIPANTS/MATERIALS, SETTING, METHODS:** Searches of Cochrane Library, Medline, Embase, CINAHL Plus and Maternity and Infant Care databases were conducted in December 2011 to identify randomized and non-randomized studies that compared the subsequent fertility outcomes after a Caesarean section and after a vaginal delivery. Eighteen cohort studies including 591 850 women matched the inclusion criteria. Risk of bias was assessed by the Newcastle–Ottawa scale (NOS). Data extraction was done independently by two reviewers. The meta-analysis was based on a random-effects model. Subgroup analyses were performed to assess whether the estimated effect was influenced by parity, risk adjustment, maternal choice, cohort period, and study quality and size.

**MAIN RESULTS AND THE ROLE OF CHANCE:** The impact of Caesarean section on subsequent pregnancies could be analysed in 10 studies and on subsequent births in 16 studies. A meta-analysis suggests that patients who had undergone a Caesarean section had a 9% lower subsequent pregnancy rate [risk ratio (RR) 0.91, 95% confidence interval (CI) (0.87, 0.95)] and 11% lower birth rate [RR 0.89, 95% CI (0.87, 0.92)], compared with patients who had delivered vaginally. Studies that controlled for maternal age or specifically analysed primary elective Caesarean section for breech delivery, and those that were least prone to bias according to the NOS reported smaller effects.

**LIMITATIONS, REASONS FOR CAUTION:** There is significant variation in the design and methods of included studies. Residual bias in the adjusted results is likely as no study was able to control for a number of important maternal characteristics, such as a history of infertility or maternal obesity.

**WIDER IMPLICATIONS OF THE FINDINGS:** Further research is needed to reduce the impact of selection bias by indication through creating more comparable patient groups and applying risk adjustment.

**STUDY FUNDING/COMPETING INTEREST(S):** None.

**TRIAL REGISTRATION NUMBER:** n/a.

**Key words:** meta-analysis / Caesarean section / fertility

† Equal contribution.

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# Introduction

Caesarean sections may lead to reduced fertility. A systematic review published in 1996 and summarizing clinical evidence up to late 1980s found that Caesarean sections were associated with fewer subsequent pregnancies and longer inter-pregnancy intervals than vaginal deliveries (Hemminki, 1996). Various explanations have been proposed, ranging from placental bed disruption or pelvic adhesions (Murphy et al., 2002) to women's reproductive choices (Porter et al., 2003; Oral and Elter, 2007).

The possible adverse association between Caesarean delivery and subsequent fertility is a growing concern, not least because Caesarean section rates have continued to rise (Lancet, 2000; OECD, 2011). Factors driving this increase include increasing maternal age, changes in accepted indications for elective Caesarean section and changes in women's choices about how they want to give birth (Leitch and Walker, 1998; Anderson, 2004; Churchill et al., 2006). The fact that these factors themselves are also likely to influence fertility directly adds to the difficulty of establishing causal relationships.

The systematic review noted methodological weaknesses in many of the included studies (Hemminki, 1996). A particular problem was 'selection bias by indication'. For example, Smith et al. (2006) noted that twin pregnancies, which are likely to be delivered by a Caesarean section, would probably influence future decisions about conception, and that the fertility of women who deliver preterm, which again is likely to involve a Caesarean delivery, may differ from women who deliver at term.

More recent studies have aimed to overcome these methodological weaknesses. Some studies have used national administrative datasets (Hemminki et al., 2005; Smith et al., 2006; Tollanes et al., 2007). These datasets provide a rich description of patient characteristics, which can support more adequate selection of comparative populations and better risk adjustment. For example, they restricted enrolled populations to low-risk singleton primiparous deliveries (Smith et al., 2006; Tollanes et al., 2007) or adjusted for confounding factors such as maternal age (Hemminki et al., 2005; Smith et al., 2006).

In this paper, we describe a systematic review including the most recent evidence on the impact of a Caesarean section on the occurrence and timing of subsequent pregnancies and births. We performed a meta-analysis to derive an overall estimate of effect and evaluated whether this was influenced by the quality of the study methods.

# Materials and Methods

The review was conducted in accordance with the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) guidelines (Stroup et al., 2000) and Cochrane recommendations on systematically reviewing non-randomized studies (Reeves et al., 2011). The protocol for this review is available from the authors upon request.

## Search methods for identification of studies

One reviewer (I.G.-U.) performed an electronic search of the Cochrane Library, Medline, Embase, CINAHL Plus and Maternity and Infant Care database on 16 December 2011. There were no language or publication date restrictions. The search strings used for electronic searches were based on MeSH terms and keywords related to fertility and Caesarean section, and were developed with the help of a librarian experienced in assisting systematic reviews of maternity care. The search strategy used for Medline is given in Supplementary data S1. We also checked the reference lists of included studies and used the citation tracking ('relevant articles') tool in Pubmed to identify any additional studies not captured by the electronic search.

## Eligibility criteria

Studies which compared the fertility outcomes for women after a previous Caesarean section versus previous vaginal delivery were eligible for inclusion. The primary outcomes of interest were rates of subsequent pregnancy or birth. Inter-pregnancy interval after the index delivery was defined as a secondary outcome.

The review allowed the inclusion of randomized and non-randomized studies. We excluded studies in which the calculation of the pregnancy rate for the population was not possible due to the study design (e.g. case–control studies), and studies that were conducted in low-income countries because the access to and indications for a Caesarean section delivery differ substantially from middle- or high-income settings (Dumont et al., 2001; Buekens et al., 2003; Collin et al., 2006).

## Study selection

Two reviewers (S.B.-A. and C.P.L.) independently assessed the potential relevance of all titles and abstracts identified from the electronic searches, and in the second stage reviewed the full texts of the potentially relevant articles for inclusion. A study published as an abstract was included only if it contained sufficient information to demonstrate that the study met the review's inclusion criteria and was of an acceptable methodological standard. A third reviewer (I.G.-U.) checked the final list of included and excluded studies, and any disagreements about including particular studies were resolved by discussion.

## Data extraction

Data were always extracted independently by two reviewers (I.G.-U., S.B.-A. or C.P.L.) and disagreements were resolved by discussions with the third reviewer. A standard form, which was modified from the Cochrane Pregnancy and Childbirth Group's data extraction template, was used to extract data on study characteristics, methods and study results. If two or more articles used the same data source in overlapping years, we selected the study that had the larger sample size. If the duplicate articles considered different outcomes, both articles were included. All data on study results were entered into Review Manager software (2011).

## Assessment of risk of bias

We used the eight-item Newcastle–Ottawa scale (NOS) to assess the risk of bias within included studies (Wells et al., 2008). In the NOS, a study can be awarded a maximum of nine 'stars' on items related to the selection of the study groups (four stars), the comparability of the groups (two stars) and the ascertainment of outcome of interest (three stars). The instrument and the coding manual were tailored by the review team to capture key confounding factors, the adequacy of the follow-up duration, and the criteria to judge the representativeness of the study population (see Supplementary data S2 for further details).

## Data synthesis

For the rate of subsequent pregnancy or birth after the index delivery, log risk ratios (RRs) and standard errors of RRs were calculated from the raw data presented in the included papers. Odds ratios were converted to RRs using the method described in Zhang and Yu (1998). The meta-analysis was performed using a random-effects model (DerSimonian and Laird, 1986) as this model takes account of the variability of the effect that a Caesarean section has on subsequent fertility across the underlying studies. The degree of variability across the studies was summarized using the $I^2$

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measure that represents the percentage of total variation across the studies that is due to heterogeneity rather than chance (Higgins and Thompson, 2002).

Subgroup analyses were performed to assess whether the mode of delivery on subsequent birth reported by the studies was influenced by inclusion criteria (primiparous or all women), adjustment for maternal age, maternal choice (planned pregnancies only or not specified), cohort period (pre-1985 or post-1985), total NOS star rating ($>6$ stars or $\leq 6$) and size ($<1000$, between 1000 and 50 000 and $>50\,000$ index pregnancies). We did not pool the estimates of inter-birth or inter-pregnancy intervals in a meta-analysis because few studies contained this information and those studies that did had adopted different methodologies.

# Results

Electronic searches provided 4626 unique citations. Of these, 4591 were excluded based on the title or abstract because they were not relevant to the review or did not meet the stated study design criteria. We reviewed the full text of the remaining 35 citations, and rejected 15 citations for failing to meet the inclusion criteria and 2 further studies because they used the same data source as a larger or a more recent study (Supplementary data S3). Overall, 18 studies with a total number of 591 850 women were included in the review (Fig. 1).

## Study characteristics

The characteristics of included studies are summarized in Table I. All included studies were cohort studies with varying follow-up durations, spanning almost 50 years of practice. Thirteen studies were conducted in European countries, four in the USA and one in Brazil. Eight studies were hospital-based and enrolled between 106 and 1152 women. The population-based studies included at least 10 000 women with the exception of Hemminki *et al*. (1985), which utilized survey data from a representative sample of 812 women. The largest study included in the review had a population size of 362 473.

The patient cohorts varied from being all inclusive to being restricted to primiparous women who delivered a live singleton baby with cephalic presentation at term. None of the studies explicitly excluded women who may have had infertility treatment or subfertility prior to the index delivery. However, four studies attempted to reduce the impact of confounding by restricting the cohort either to 'healthy' women (defined broadly as having no major non-pregnancy-related chronic conditions; Hemminki, 1987; Hemminki *et al*., 2005) or to women with uncomplicated pregnancies (Tollanes *et al*., 2007; Eijsink *et al*., 2008). Two studies reported separately outcomes for women who had a Caesarean section for breech presentation to women who delivered vaginally, arguing that these cohorts are more comparable than cohorts that included women with other indications for a Caesarean section because breech presentation at term is determined mostly by chance (Smith *et al*., 2006; Eijsink *et al*., 2008). One study compared the subsequent fertility outcomes of women who needed operative delivery in theatre at second stage of labour with those who had an instrumental delivery (Bahl *et al*., 2004).

The NOS star ratings are shown in Table II. The studies that attempted to reduce confounding with restrictive inclusion criteria were awarded higher rates on the NOS selection domain. For the comparability domain, four studies were awarded one star because maternal age and parity was controlled for either in study designs with matched controls or in the statistical analysis. Five studies were awarded one star as they excluded women that had stillbirths in the index delivery. Six studies were awarded two stars as they satisfied both comparability criteria. For the outcome assessment domain, seven studies lost stars for not adequately presenting loss to follow-up, and seven studies lost stars as they had used either self-reported patient data or poor descriptions of the outcome assessment process.

## Estimated effect of a Caesarean section on subsequent fertility

Subsequent fertility outcome was measured as the next pregnancy following the index delivery in two studies, and the next birth in eight studies. Eight studies measured both outcomes. The subsequent pregnancy and birth rates varied greatly between studies (Table II). Pregnancy rates ranged from under 50% to over 90%, while birth rates ranged from under 30% to over 75%. These differences reflect predominantly the different lengths of time over which subsequent events were measured. The shortest maximum follow-up time was 3 years, while the longest maximum was 21 years. However, the rates will also have been influenced by varying fertility rates among the countries during the period in which the cohorts were enrolled.

Results from the meta-analysis show that a Caesarean section, on average, reduced the likelihood of a subsequent pregnancy [RR 0.91, 95% confidence interval (CI) (0.87–0.95), Fig. 2a] and birth [RR 0.89, 95% CI (0.87–0.92), Fig. 2b] compared with a vaginal delivery. The spread of the RRs across the studies was larger than can be expected by chance alone ($I^2 = 86\%$ for pregnancies and $I^2 = 81\%$ for births).

Subgroup analysis showed that the pooled estimates of the impact of a Caesarean section on subsequent births were comparable across subgroups of studies stratified by maternal choice, cohort period and study size (Table III). However, in the nine studies with the highest study quality (NOS score $>$ 6), the pooled effect on the subsequent birth rate [RR 0.91, 95% CI (0.89–0.92)] was smaller than in the other studies [RR 0.86, 95% CI (0.77–0.94)]. Risk adjustment also reduced the estimated impact of a Caesarean section on fertility. Studies that controlled for maternal age showed a smaller effect [RR 0.92, 95% CI (0.87–0.97)] than studies with no adjustment [RR 0.88, 95% CI (0.86–0.91)].

Only two studies reported the fertility outcomes for women who had a primary, elective Caesarean section (Table III). The outcomes after elective Caesarean section for breech presentation were comparable with unassisted vaginal delivery in both studies, and the pooled effect of a Caesarean section on subsequent birth was not statistically significant [RR 0.94, 95% CI (0.88–1.01); Smith *et al*., 2006; Eijsink *et al*., 2008].

Time to subsequent fertility was defined as time from index birth to last menstrual period in subsequent pregnancy (inter-pregnancy interval) in five studies and time from index birth to subsequent birth (inter-birth interval) in three studies (Table IV). Median inter-pregnancy intervals after a Caesarean section were 2–6 months longer than intervals after vaginal delivery. The difference was statistically significant in two studies (Mollison *et al*., 2005; Smith *et al*., 2006). Median inter-birth intervals were up to 3 months longer after a Caesarean section. The difference was significant in one study (Tollanes *et al*., 2007).

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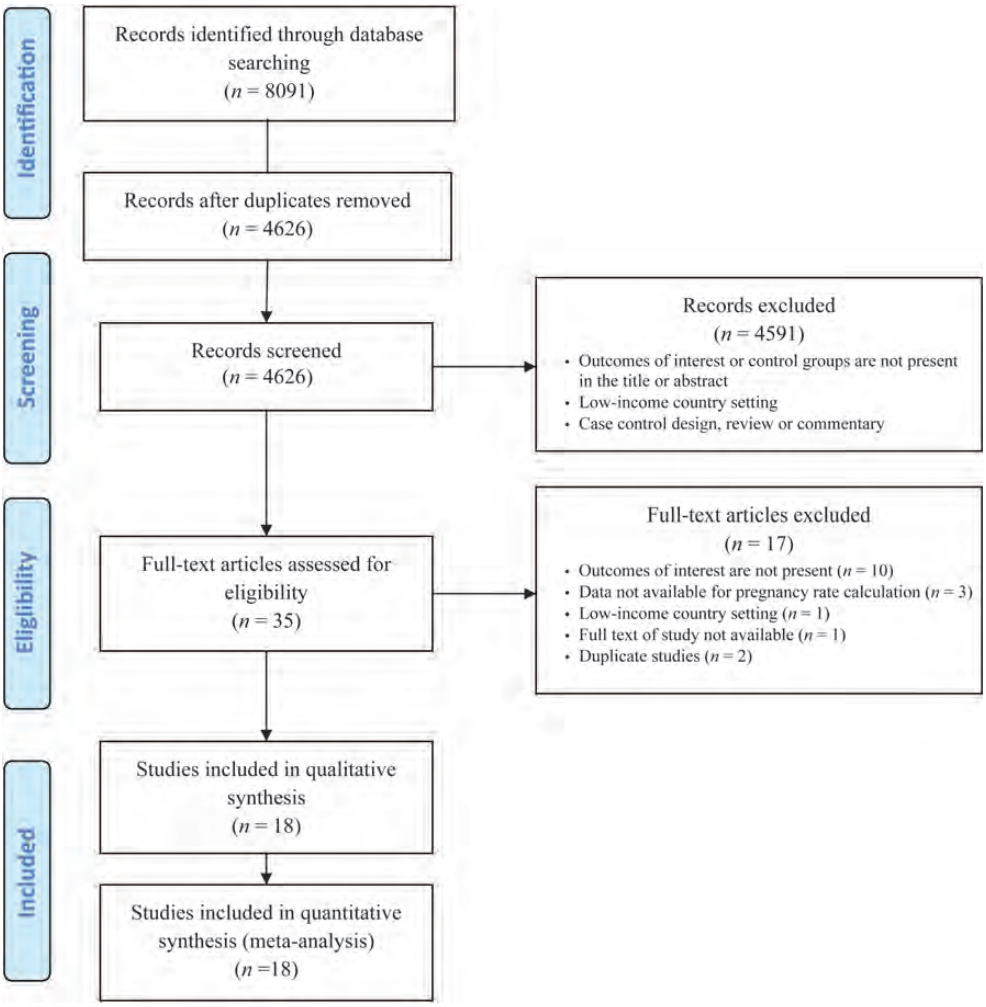


**Figure 1** Flow chart of identification and selection of studies for inclusion in the systematic review.

# Discussion

Most of the 16 studies in this systematic review found that fertility is reduced after a Caesarean section compared with vaginal delivery. The meta-analysis suggests that the pregnancy and birth rate in women who had a Caesarean section was ~10% lower than in women who had delivered vaginally. However, there was considerable heterogeneity across the studies in terms of their design and quality. Studies that controlled for maternal age or those that were least prone to bias found smaller effects. Moreover, the two studies that compared fertility after a Caesarean section for breech presentation with spontaneous vaginal vertex delivery, which can be argued represents a comparison that is similar to a randomized comparison, reported a small effect that was not statistically significant (Smith *et al.*, 2006; Eijsink *et al.*, 2008). This highlights that the observed reduction in subsequent fertility after a Caesarean section may not be causal but a result of study limitations. Our systematic review supersedes the previous review published in 1996. We identified an additional 13 studies increasing the total number of women who could be included from 85 728 to 591 850. Furthermore, we used validated methods to search, select and appraise all relevant studies. We searched a range of sources, adopted broad inclusion criteria and the search and data extraction were performed by two people independently. Nevertheless, the results of our systematic review broadly agreed with those described before.

The studies included in the review spanned a long time period and differed with respect to various study characteristics, such as country of origin, length to follow-up, and data sources. There was considerable diversity of scores on the NOS risk of bias assessment. Two-thirds of the included studies did not attempt to control for selection bias by indication or other confounding factors. Only three studies analysed data for women whose preferences on subsequent pregnancies were known. The heterogeneity across the included studies is a reason that the pooled estimates from the meta-analysis need to be interpreted with caution.

Careful control for selection by indication is important as there is a complex relationship between factors influencing Caesarean section rates and subsequent fertility. Women who are subfertile or who have had infertility treatment are more likely to have a Caesarean section at index delivery (LaSala and Berkeley, 1987; Pandian *et al.*, 2001; Murphy *et al.*, 2002). Also, maternal age (Rosenthal and Paterson-Brown, 1998;

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**Table I Characteristics of included studies.**

| Study ID | Country | Setting | Cohort period | Inclusion criteria[a] | Intervention | Control[b] | Outcome[c] | Risk adjustment |
|---|---|---|---|---|---|---|---|---|
| Hemminki *et al.* (1985) | USA | Population | 1957–1982 | P S L | CS | VD | P B | Matched: Age, race, marital status, date |
| Hall *et al.* (1989) | Scotland | Population | 1964–1983 | P S L | CS | SVD, IVD | P B | Unadjusted |
| Tollanes *et al.* (2007) | Norway | Population | 1967–1996 | P S L + U | CS | VD | B | Unadjusted |
| Hemminki (1987) | Sweden | Population | 1973, 1976 | P S L + H | CS | VD | B | Matched: Age, baby gender |
| Zdeb *et al.* (1984) | USA | Population | 1975 | P L | CS | SVD | P B | Matched: age, education, race |
| LaSala and Berkeley (1987) | USA | Hospital | 1978 | All | CS | VD | P B (Planned) | Matched: Age, parity, date |
| Smith *et al.* (2006) | Scotland | Population | 1980–1984 | P S L T | Emergency CS, Elective CS for breech | SVD | B | Age, marital status, deprivation, birthweight, baby gender, maternal height and induction |
| Mollison *et al.* (2005) | Scotland | Population | 1980–1997 | P S L | CS | SVD, IVD | P B | P: Age, gravida, socioeconomic status, gestation; B: Unadjusted |
| Huttly *et al.* (1990) | Brazil | Population | 1982 | All | CS | VD | P | Age, income, parity, education |
| Hemminki (1996) | Finland | Population | 1987–1988 | P | CS | VD | P B | Matched: Age, hospital, date |
| Hemminki *et al.* (2005) | Finland | Population | 1987–1989 | P + H | CS | SVD, IVD | B | Unadjusted |
| Gottvall and Waldenstrom (2002) | Sweden | Hospital | 1989–1992 | P | CS | VD | B | Unadjusted |
| Jolly *et al.* (1999) | England | Hospital | 1991 | P S L | CS | SVD, IVD | B (Planned) | Random selection |
| Tower *et al.* (2000) | England | Hospital | 1992–1993 | P | CS | SVD | P | Matched: Age, date |
| Salem *et al.* (2011) | USA | Hospital | 1994–2006 | All | CS | VD | B | Age, gestation, birthweight, Somalian women only. |
| Six *et al.* (2005) | Austria | Hospital | 1998 | P S L | CS | VD | B | Random selection |
| Eijsink *et al.* (2008) | Netherlands | Hospital | 1998–2002 | P S L T + U | CS for breech | SVD | P B | Unadjusted |
| Bahl *et al.* (2004) | England | Hospital | 1999–2000 | S L T C | Emergency CS | IVD | P B (Planned) | P: Age, parity, social class, neonatal trauma, prolonged hospital stay; B: Unadjusted |

[a]P(rimip) S(ingleton) L(ive) T(erm) C(ephalic) H(ealthy mother) or U(ncomplicated pregnancy).
[b]IVD (Instrumental delivery), SVD (non-instrumental vaginal delivery), VD (vaginal delivery, unspecified).
[c]P(regnancy) B(irth), (Planned) pregnancies only.



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**Table II** Risk of bias in included studies and summary data on subsequent fertility events.[a]

| Study ID | Patient selection | Comparability of groups | Ascertainment of outcome | Total NOS star rating | Country | Number of index deliveries[b] | Follow-up[c] | Pregnancy rate | | Birth rate | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | CS (%) | VD (%) | CS (%) | VD (%) |
| Hemminki *et al.* (1985) | 4 | 2 | 2 | 8 | USA | 812 | * | 63.1 | 62.1 | 53.0 | 53.0 |
| Hall *et al.* (1989) | 3 | 1 | 2 | 6 | Scotland | 22 948 | * (1 to 19) | 47.2 | 60.1 | 39.8 | 52.2 |
| Tollanes *et al.* (2007) | 4 | 1 | 3 | 7 | Norway | 362 473 | * (7 to 21) | | | 75.4 | 83.5 |
| Hemminki (1987) | 4 | 2 | 3 | 9 | Sweden | 12 918 | 5.5 (5 to 6) | | | 54.1 | 59.5 |
| Zdeb *et al.* (1984) | 3 | 2 | 2 | 7 | USA | 11 026 | 5 (5 to 5) | 56.5 | 59.8 | 50.9 | 53.6 |
| LaSala and Berkeley (1987) | 2 | 1 | 2 | 5 | USA | 444 | * (3 to 6) | 92.7 | 98.2 | 77.7 | 81.7 |
| Smith *et al.* (2006) | 4 | 2 | 3 | 9 | Scotland | 69 069 | 15 (15 to 15) | | | 69.4 | 74.8 |
| Mollison *et al.* (2005) | 3 | 2 | 3 | 8 | Scotland | 25 371 | * (5 to 17) | 66.9 | 73.2 | 55.7 | 60.9 |
| Huttly *et al.* (1990) | 2 | 1 | 1 | 4 | Brazil | 4240 | 3.6 (3 to 4) | 38.0 | 44.0 | | |
| Hemminki (1996) | 3 | 1 | 3 | 7 | Finland | 16 500 | * (* to 6) | 62.7 | 71.9 | 51.6 | 61.3 |
| Hemminki *et al.* (2005) | 4 | 0 | 3 | 7 | Finland | 62 325 | * (9 to 12) | | | 70.9 | 79.0 |
| Gottvall and Waldenstrom (2002) | 2 | 0 | 3 | 5 | Sweden | 617 | * (8 to 10) | | | 74.6 | 81.0 |
| Jolly *et al.* (1999) | 2 | 1 | 1 | 4 | England | 435 | 5 (5 to 5) | | | 61.7 | 75.1 |
| Tower *et al.* (2000) | 2 | 1 | 2 | 5 | England | 1152 | 5 (5 to 5) | 58.7 | 61.8 | | |
| Salem *et al.* (2011) | 2 | 0 | 0 | 2 | USA | 106 | * (1 to 13) | | | 63.2 | 64.7 |
| Six *et al.* (2005) | 2 | 1 | 1 | 4 | Austria | 908 | 5 (5 to 5) | | | 24.4 | 27.9 |
| Eijsink *et al.* (2008) | 3 | 1 | 3 | 7 | Netherlands | 314 | 3.4 (5 to 8) | 80.4 | 77.6 | 63.0 | 61.6 |
| Bahl *et al.* (2004) | 2 | 2 | 1 | 5 | England | 192 | 3 (3 to 3) | 67.0 | 79.3 | 55.0 | 60.9 |

*Indicates not specified.

[a]The Newcastle–Ottawa scale (NOS) was used to produce a star rating of the risk of bias related to patient selection, comparability of study groups and ascertainment of outcome. Higher rates represent lower risk of bias. See text and Supplementary data S2 for further information.

[b]Number of deliveries included in the meta-analysis. In included studies, if the results were stratified by characteristics of index delivery (such as parity), only the results of the subgroup with better adjustment for confounders was included in the meta-analysis. Therefore, the numbers in this column may be different to the total number of deliveries reported in the individual studies.

[c]Median (minimum to maximum) follow-up in years.



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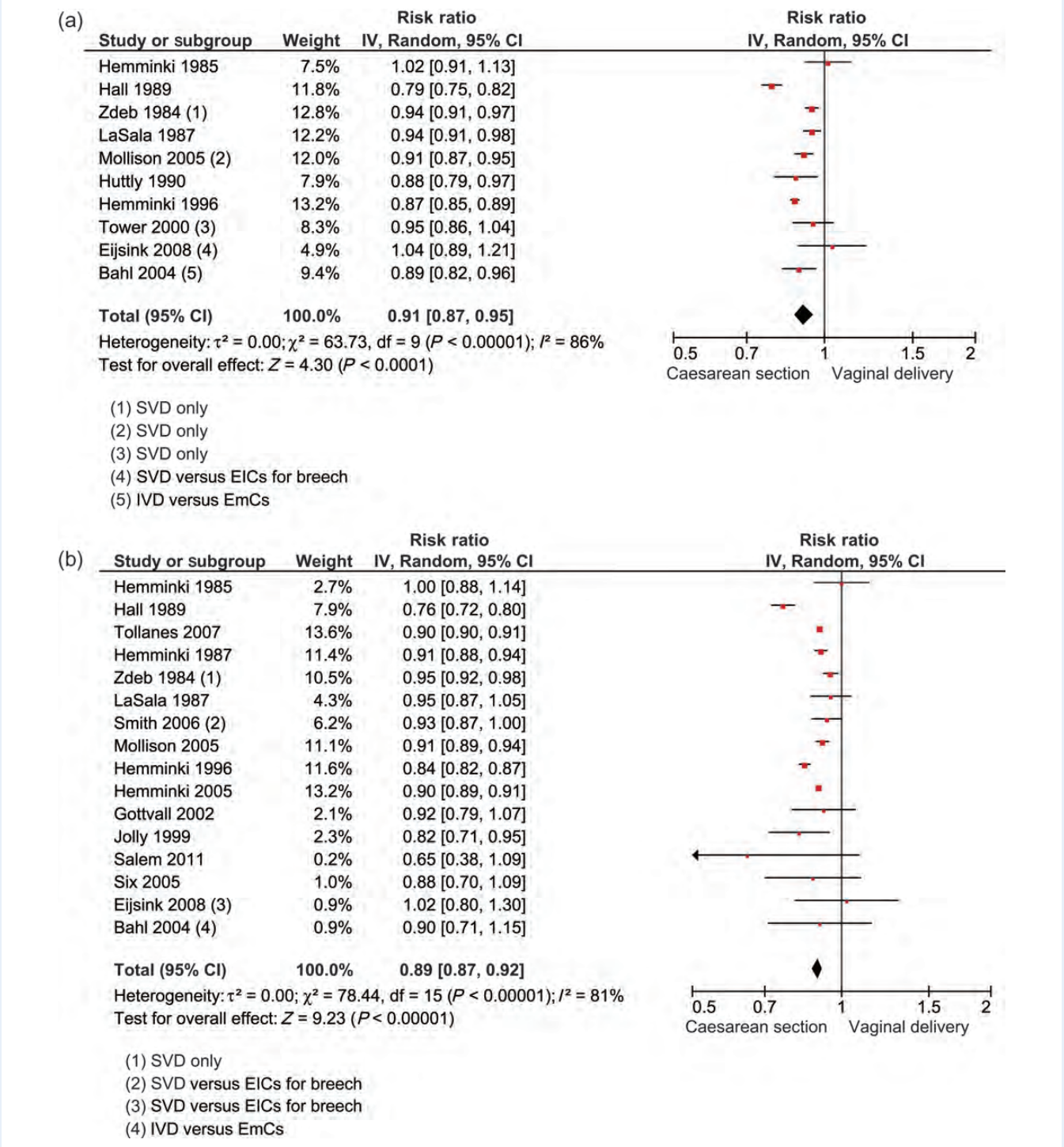


**Figure 2** (**a**) Impact of Caesarean section on subsequent pregnancies. (**b**): Impact of Caesarean section on subsequent births.

Dunson *et al.*, 2004) and obesity (Crane *et al.*, 1997; Rich-Edwards *et al.*, 2002), and various conditions that make a pregnancy high-risk (Pandian *et al.*, 2001) influence both Caesarean rates and fertility.

A further limitation of the studies included in our review is that they do not capture spontaneous or induced abortions or ectopic pregnancies. However, this is likely to have only small effects on the studies' results as abortion and ectopic pregnancy rates are similar for different modes of delivery at the preceding births (Smith *et al.*, 2006).

It has been argued that the absence of conception after a Caesarean section is mainly voluntary (Jolly *et al.*, 1999; Porter *et al.*, 2003; Bhattacharya *et al.*, 2006). For example, negative experiences around the time of the delivery may affect future fertility decisions. Three small studies—with a combined size of 1071—limited enrolment to women who had

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**Table III Subgroup analysis of the impact of Caesarean section on subsequent birth rates according to study characteristics.**

| | *n* | RR (95% CI) | $I^2$ (%) |
|---|---|---|---|
| All | 16 | 0.89 (0.87, 0.92) | 81 |
| By inclusion criteria | | | |
| Primiparous women only | 13 | 0.89 (0.87, 0.92) | 84.1 |
| Not limited to primiparous women | 3 | 0.93 (0.84, 1.03) | 6.9 |
| By mode of delivery | | | |
| Elective Caesarean section for breech | 2 | 0.94 (0.88, 1.01) | 0 |
| Not specified | 14 | 0.89 (0.87, 0.91) | 83 |
| By risk adjustment | | | |
| Adjusted for maternal age | 9 | 0.92 (0.87, 0.97) | 84.2 |
| Not adjusted for maternal age | 7 | 0.88 (0.86, 0.91) | 80.0 |
| By maternal choice | | | |
| Planned pregnancies only | 3 | 0.90 (0.82, 0.99) | 30.7 |
| Not specified | 13 | 0.89 (0.87, 0.92) | 84.1 |
| By cohort period[a] | | | |
| Pre-1985 | 10 | 0.90 (0.88, 0.92) | 87.2 |
| Post-1985 | 8 | 0.89 (0.87, 0.92) | 74.4 |
| By study quality | | | |
| NOS Score $>6$ | 9 | 0.91 (0.89, 0.92) | 79.0 |
| NOS Score $\leq 6$ | 7 | 0.86 (0.77, 0.94) | 70.8 |
| By study size | | | |
| Less than 1000 index pregnancies | 8 | 0.93 (0.87, 0.98) | 3.5 |
| Between 1000 and 50 000 | 5 | 0.88 (0.82, 0.93) | 93.7 |
| More than 50 000 | 3 | 0.90 (0.90, 0.91) | 0.0 |

[a]Two studies contributed both to the pre-1985 and post-1985 cohorts (Mollison *et al.*, 2005; Tollanes *et al.*, 2007).

**Table IV Inter-pregnancy or inter-birth intervals in months.**

| Study | Comparison | Method | Measure | Interval after CS | Interval after VD |
|---|---|---|---|---|---|
| Date of index birth to date of last menstrual period of subsequent pregnancy | | | | | |
| Eijsink *et al.* (2008) | CS Breech versus VD | Crude | Median (IQR) | 20 (n/a) | 18 (n/a) |
| Mollison *et al.* (2005) | CS versus SVD | Kaplan–Meier | Median (95% CI) | 36.3 (34.4, 38.2) | 30.4 (29.7, 31.0)* |
| Smith *et al.* (2006) | EICS Breech versus SVD | Crude | Median (IQR) | 25.7 (16.1, 38.5) | 23.4 (14.2, 38.0)* |
| Tower *et al.* (2000) | CS versus SVD | Crude | Median (IQR) | 31 (23, 44) | 29 (22, 39) |
| Zdeb *et al.* (1984) | CS versus VD | Crude | Median | 21.8 | |
| Date of index birth to date of subsequent birth | | | | | |
| Tollanes *et al.* (2007)[1967–1981] | CS versus VD | Crude | Median (IQR) | 38.1 (27.5, 52.5) | 35.0 (24.6, 48.8)* |
| Tollanes *et al.* (2007)[1982–1996] | CS versus VD | Crude | Median (IQR) | 35.9 (26.3, 49.8) | 34.8 (25.8, 47.6) |
| Hemminki *et al.* (1985) | CS versus VD | Kaplan–Meier | Median (95% CI) | 44.4 (n/a) | 45.6 (n/a) |
| Tower *et al.* (2000) | CS versus SVD | Crude | Median (IQR) | 33 (24, 46) | 32 (23, 44) |

*Indicates significance at $P < 0.01$.

aimed for another pregnancy in order to eliminate influences related to women's choices as much as possible. However, they still reported that fertility rates in women who had a Caesarean section were decreased by 10%.

The pathophysiological reasons why a Caesarean section may lead to a reduction in fertility are unclear, although incomplete uterine healing and post-operative infection have been suggested. Hurry *et al.* reported in 1984 that while post-Caesarean section endometritis or pelvic cellulitis did not have an adverse effect on subsequent reproductive outcomes, pelvic abscess was associated with a significant reduction in fertility (Hurry *et al.*, 1984). However, more recent studies suggest that there is no evidence that women with a prior Caesarean section are at increased

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risk of tubal factor infertility (Wolf *et al.*, 1990; Bider *et al.*, 1998; Saraswat *et al.*, 2008), abnormal hysterosalpingograms (Lash *et al.*, 2008) or poor reproductive outcomes due to increased adhesion formation (Kendrick *et al.*, 1996; Nather *et al.*, 2002; Barnhart *et al.*, 2006).

In conclusion, recent studies into the relationship between a Caesarean section and subsequent fertility continue to find that a Caesarean delivery is associated with reduced rates of subsequent fertility compared with vaginal delivery. This suggests that the impact of a Caesarean section is likely to be small if there is an effect at all. To explore the remaining uncertainty about the observed association between a Caesarean section and subsequent fertility, there is a need for greater attention to achieving comparable patient groups through selection criteria and further developing risk adjustment. Future work may consider the exclusion of certain groups such as multigravida with a history of poor reproductive outcomes, subfertility treatment and other risks to fertility (such as advanced age or obesity). The main focus should be on the likelihood and timing of a subsequent pregnancy after planned elective Caesarean section when compared with normal delivery with no serious adverse maternal or neonatal outcomes, in order to be clearer about the effects of the Caesarean section itself, as opposed to the women's social and clinical circumstances.

## Supplementary data

Supplementary data are available at http://humrep.oxfordjournals.org/.

## Acknowledgements

We thank Ms Elaine Garrett and Ms Lisa Xue, RCOG librarians, for their contribution in building the search strategies used in the review and Dr Oliver Groene for the data extraction and assessment of risk of bias of one included study that was published in German.

## Authors' roles

All authors have fulfilled all conditions required for authorship. I.G.-U., D.A.C., A.T., T.A.M. and J.M. conceived and designed the study; S.B.-A., C.P.L. and I.G.-U. conducted the search, selection, risk of bias assessment and data extraction; I.G.-U. analysed the data with support from D.A.C.; I.G.-U. and D.A.C. wrote the manuscript; S.B.-A., C.P.L., T.A.M., A.T. and J.M. commented on drafts. I.G.-U. is guarantor.

## Funding

I.G.-U. is supported by the Royal College of Obstetricians and Gynaecologists.

## Conflict of interest

None declared.

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