Gurol-Urganci, I.; Cromwell, DA; Mahmood, TA; van der Meulen, JH; Templeton, A (2014) A population-based cohort study of the effect of Caesarean section on subsequent fertility. Human reproduction (Oxford, England). ISSN 0268-1161 DOI: https://doi.org/10.1093/humrep/deu057

DOI: 10.1093/humrep/deu057

A population-based cohort study of the effect of caesarean section on subsequent fertility

Running title: Impact of caesarean delivery on fertility

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Abstract

Study question: Is there an association between caesarean section and subsequent fertility?

Summary answer: There is no or only a slight effect of caesarean section on future fertility.

What is known already: Previous studies have reported that delivery by a caesarean section is associated with fewer subsequent pregnancies and longer inter-pregnancy intervals. The interpretation of these findings is difficult because of significant weaknesses in study designs and analytical methods, notably the potential effect of the indication for caesarean section on subsequent delivery.

Study design, size, duration: Retrospective cohort study of 1,047,644 first births to low-risk women using routinely collected, national administrative data of deliveries in English maternity units between 1st April 2000 and 31st March 2012.

Participants/materials, setting, methods: Primiparous women aged 15 to 40 years who had a singleton, term, live birth in the English National Health Service were included. Women with high-risk pregnancies involving placenta praevia, pre-eclampsia, eclampsia, (gestational or pre-existing) hypertension or diabetes were excluded from the main analysis. Kaplan-Meier analyses and Cox proportional hazard models were used to assess the effect of mode of delivery on time to subsequent birth, adjusted for age, ethnicity, socioeconomic deprivation and year of index delivery.

Main results and the role of chance: Among low-risk primiparous women, 224,024 (21.4%) were delivered by caesarean section. The Kaplan-Meier estimate of the subsequent birth rate at 10 years for the cohort was 74.7%. Compared to vaginal delivery, subsequent birth rates were marginally lower after elective caesarean for breech (adjusted hazard ratio, HR 0.96, 95% CI 0.94 to 0.98). Larger effects were observed after elective caesarean for other indications (adjusted HR 0.81, 95% CI 0.78 to 0.83), and emergency caesarean (adjusted HR 0.91, 95% CI 0.90 to 0.93). The effect was smallest for elective caesarean for breech, and this was not statistically significant in women younger than 30 years of age (adjusted HR 0.98, 95% CI 0.96 to 1.01).

Limitations, reasons for caution: We used birth cohorts from maternity units with good quality parity information. The data are likely to be nationally representative because the characteristics of the deliveries in included and omitted units were similar. There may be residual bias in our adjusted results due to unmeasured maternal factors such as obesity and voluntary absence of conception. Any residual bias would lead to an overestimate of the effect of caesarean section on fertility, and the true effect is therefore likely to be smaller than the effect reported in our study.

Wider implications of the findings: Our results provide strong evidence that there is no or only a slight effect of caesarean section on future fertility. The clinical and social circumstances leading to the caesarean section have a greater effect on future fertility than the caesarean section itself. This finding is important in light of rising caesarean section rates.

Study funding/competing interest(s): IG-U is supported by the Lindsay Stewart R&D Centre, Royal College of Obstetricians and Gynaecologists, UK. The authors have no conflicts of interest to declare.

Trial registration number: n/a

Keywords: administrative data, caesarean section, fertility

Introduction

The possible adverse association between caesarean delivery and subsequent fertility is of concern because both caesarean section rates and the age of first time mothers continue to rise (Lancet, 2000, Murphy et al., 2002, OECD, 2013). Various studies have reported that delivery by caesarean section is associated with fewer subsequent pregnancies and longer inter-pregnancy intervals (Hall et al., 1989, Hemminki, 1987, Hemminki et al., 1996, Hemminki et al., 2005, Mollison et al., 2005, Smith et al., 2006, Tollanes et al., 2007). However, recent systematic reviews have demonstrated that the results are inconsistent, associated with significant weaknesses in study designs and analytical methods (Gurol-Urganci et al., 2013, Hemminki, 1996).

A major limitation of previous studies has been inadequate adjustment for “bias by indication”. Birth rates following caesarean section are influenced by the mother’s experience of caesarean delivery as well as by the clinical circumstances that are linked to the indication for a caesarean section. For example, women who have had infertility treatment are more likely to have a caesarean delivery, particularly if they are older (LaSala et al., 1987, Murphy et al., 2002, Pandian et al., 2001), while women suffering from medical conditions such diabetes, hypertension and auto immune disease may be advised against further childbearing. In response, some investigators have argued that fertility outcomes in women who had caesarean section for breech presentation are most comparable to women who delivered vaginally because breech presentation at term is largely determined by chance (Smith et al., 2006).

A further limitation is that obstetric practice has changed significantly with lower thresholds for caesarean delivery (Churchill et al., 2006) and the results of previous studies may not be representative of current obstetric practice, as even the most recent cohorts captured deliveries from the early 1990s.

In this study, we evaluated the extent to which the caesarean section procedure itself is associated with subsequent fertility by using a large national dataset with detailed information on maternal characteristics and pregnancy outcomes. We aimed to determine the effect of accompanying clinical and social circumstances, and in turn minimise the effect of bias by indication.

Materials and Methods

We used the Hospital Episode Statistics (HES) – a data warehouse that includes records of all inpatient admissions and day cases in the English NHS trusts (acute hospital organizations) – to identify all deliveries that took place between April 2000 and March 2012. The records are extracted from local patient administration systems and undergo a series of validation and cleaning processes before being made available for analysis (HSCIC).

The HES database contains patient demographics, administrative data, and clinical information for each episode of inpatient care. Diagnostic information is coded using the International Classification of Diseases 10^{th} revision (ICD10) (WHO, 2012) and operative procedures are coded using the UK Office for Population Censuses and Surveys classification, 4^{th} revision (OPCS4) (2012). For maternity episodes, the HES database has supplementary fields known as the 'maternity tail' which capture parity, birth weight, gestational age, method of delivery, and pregnancy outcome. The accuracy and completeness of diagnostic and procedures data is high (Burns et al., 2012). The maternity tail is not compulsory and the level of data completeness varies across NHS Trusts.

We studied primiparous women aged 15 to 40 years, who had a singleton, live, term birth. We confined the analysis to NHS trusts that had parity information recorded in at least half of the deliveries, and had a proportion of primiparous women between 25% and 55% (overall about

40% of women giving birth in England and Wales are primiparous)(ONS, 2007). The quality of parity data was evaluated for each year of the study.

To minimise the risk of bias by indication, the main analysis was focused on women with low risk pregnancies. First, we excluded all women who had inpatient fertility treatments before the index delivery, and those reported to have had a history of infertility. Second, we labelled a pregnancy as high risk if the woman was recorded as having placenta praevia, pre-eclampsia or eclampsia, hypertension (pre-existing or gestational) or diabetes. Women with high-risk pregnancies were analysed separately.

Mode of delivery was defined using information in the OPCS4 procedure codes, or if this was unavailable, by the delivery method specified in the maternity tail. We distinguished between vaginal delivery, instrumental delivery, elective caesarean for breech and transverse lie, elective caesarean for other indications and emergency caesarean section. Maternal demographic risk factors were age (15 to 29, 30 to 34, 35 to 40 years), ethnicity (white, asian, black, other), and socio-economic deprivation of the mother's area of residence using the Index of Multiple Deprivation (IMD), a measure that combines economic, social and housing indicators)(ODPM, 2004). In HES, "Asian" category includes women of Indian, Bangladeshi and Pakistani ethnicity, women of Chinese ethnicity were included in the "Other" category. Deprivation is based on the quintiles of 32,480 areas in England ranked according to IMD score. The OPCS4 and ICD10 codes used to identify the risk factors are provided in Appendix 1.

Statistical Analysis

We used survival analysis methods to estimate the crude and adjusted effect of the mode of delivery on the time to subsequent birth for women with low-risk pregnancies. The Cox regression models adjusted for maternal age, ethnicity, socioeconomic deprivation and year of index delivery. Time to subsequent birth was defined from the start date of index delivery episode to the date of the subsequent birth. Reaching a maternal age of 45 years or the end of study period (31 March 2012), whatever came first, were handled as censoring events. To account for a lack of independence in the data of women treated in the same NHS trust, the standard errors of the model coefficients were calculated using a clustered sandwich estimator.

We further examined the association between mode of delivery and time to subsequent birth, stratified by age at the time of pregnancy among women with low-risk pregnancies and by the different clinical conditions that defined high-risk pregnancies.

We compared the distributions of maternal age, pregnancy complications and mode of delivery in NHS trusts with good quality data to those hospitals with poor quality data to explore the extent to which bias might be introduced by the omission of hospitals with incomplete data. All analyses were done in Stata/IC version 12.1.

Ethical approval

This study is exempt from UK National Research Ethics Service approval because it involved analysis of an existing data set of anonymised data for service evaluation. Approval for the use of HES data was obtained as part of the standard Hospitals Episode Statistics approval process.

Results

There were 6,449,593 singleton, live, term deliveries in 139 English NHS trusts between April 2000 and March 2012. Among these, 39.0% took place in NHS trusts that had poor quality parity data, and the records for these NHS trusts were omitted. The median number of NHS trusts included in each year was 81 (Inter-quartile range: 78 to 86). Omitting episodes with missing parity data left 3,936,215 deliveries of which 1,325,773 (33.7%) were first births. This group of first births included 125,036 (9.4%) women who had a high-risk pregnancy, 7,440

(0.5%) women with a recorded history of infertility, and a further 145,653 (11.0%) records missing information on ethnicity or social deprivation. Excluding these records left 1,047,644 primiparous deliveries for analysis.

The characteristics of included women at first birth, and the rates of subsequent birth at 3, 5 and 10 years are presented in Table 1. Complete 10-year follow up was available for only two years of the study cohort, for index deliveries in 2000 and 2001. Over two-thirds of the women were less than 30 years of age when they gave birth. The overall caesarean section rate for the cohort was 21.4%, with less than 4% of women having an elective caesarean section.

The unadjusted Kaplan-Meier estimate of the subsequent birth rate at 10 years for the cohort was 74.7%. The 10-year birth rate decreased with advancing age. Women aged 30 to 34 years, on average, had their second baby earlier than women younger than 30. The subsequent birth rate was highest for Asian women, with a 10-year birth rate of 81.7% as compared with 74.8% for white women. Women who had an elective caesarean section for an indication other than a breech baby were least likely to have a subsequent birth (64.4%). There were only small differences in the birth rates between women who had vaginal and instrumental deliveries.

All types of caesarean section were associated with a reduced subsequent birth rate (Table 2 and Figure 1). The adjusted effect size was smallest for elective caesarean section for breech (adjusted HR 0.96, 95% CI 0.94 to 0.98) and largest for women who had an elective caesarean section for other indications (adjusted HR 0.81, 95% CI 0.78 to 0.83). The impact of different caesarean delivery categories by age groups is given in Table 3. The adjusted effect size for women under 30 years old having elective caesarean section for breech was not statistically significant (adjusted HR 0.98, 95% CI 0.96 to 1.01), while elective caesarean section for breech was associated with 5% to 10% reduction in the subsequent birth rate for older women. Results from a Cox regression model with age category and mode of delivery interaction terms demonstrated that subsequent fertility declines with age, regardless of mode of delivery ($p<0.001$ for each pairwise comparison, data not shown).

For women with high-risk pregnancies, all types of caesarean section were again associated with a reduced subsequent birth rate compared to women who had a vaginal delivery (Table 4). Elective caesarean section was associated with 15 to 26% reduction in subsequent birth rates as compared with vaginal delivery, while emergency caesarean section was associated with a 13 to 16% reduction in subsequent birth rates for women with high-risk pregnancies.

Discussion

Among primiparous women with a low-risk pregnancy, the rates of subsequent birth are lower among women who deliver by caesarean section compared to those who had vaginal deliveries. The size of the effect depends on the type and indication for caesarean section. The effect of elective caesarean section for breech on subsequent fertility is very small irrespective of age and was not significant for women younger than 30 years. This suggests that the impact of the caesarean procedure itself on subsequent fertility is minimal. The biggest effect was observed with elective caesarean section for other indications. Together, these results suggest that unmeasured clinical and social factors during pregnancy and the intrapartum period which led to the decision to perform a caesarean section might explain the apparent effect of caesarean section on future fertility.

Strengths and limitations of study

This is the largest cohort study to date analysing the association between mode of delivery and fertility. It includes over one million primiparous low-risk women, almost double the total number of women included in the most recent systematic review (Gurol-Urganci et al., 2013).

The use of HES data has several advantages. First, over 96% of all deliveries in England occur in NHS trusts and are therefore captured by HES (Birthplace in England Collaborative et al., 2011). Second, the availability of data since 1997 allowed for a sufficiently long follow-up period to observe subsequent fertility patterns. Finally, the HES data provides a rich description of patient case-mix as it captures multiple procedures and diagnoses at an individual level. In this study, we used various data items available within the HES records to define comparable populations, and perform risk adjustment. This was necessary because the relationship between caesarean section and fertility is complex. Advancing maternal age (Dunson et al., 2004, Rosenthal et al., 1998), various conditions that make a pregnancy high-risk including pre-existing infertility (Pandian et al., 2001), and pregnancy outcomes such as multiple or preterm births (Smith et al., 2006) influence both caesarean rates and subsequent reproductive decisions. HES data allowed the analysis to include demographic characteristics and the socio-economic status of the mother as well as obstetric outcomes.

Further strengths of this study are that it more accurately represents current attitudes and practice than previous studies. Most previous large studies with careful designs (Hemminki et al., 2005, Mollison et al., 2005, Smith et al., 2006, Tollanes et al., 2007) had cohorts established before 1995. Since then, the possible indications for caesarean section have widened. Changes have included: the recommendation that breech presentation be delivered by a caesarean section in preference to a trial of vaginal birth; increasing emphasis on the identification of intra-uterine growth restriction and delivery by a caesarean section in fetal interest; and lower thresholds for the caesarean delivery of preterm babies. There has also been a shift towards an earlier resort to caesarean section in the second stage of labour in preference to difficult instrumental delivery and increased use of caesarean following failed induction of labour (Churchill et al., 2006, Leitch et al., 1998, Loudon et al., 2010, MacKenzie et al., 2003, Penn et al., 2001).

In HES, as in other administrative databases, the coding of the diagnoses and procedures could be potentially inaccurate. A recent systematic review assessing the published accuracy of routinely collected data in the UK concluded that, since the introduction of Payment by Results in 2002, the coding accuracy in HES has been increasingly robust to support its use in research and decision-making (Burns et al., 2012). Majority of NHS Trusts submit good quality of data to HES (Kirkman et al., 2009), and when data completeness, consistency and accuracy are analysed carefully (Cromwell et al., 2014, Knight et al., 2013), HES is a valuable source of data for epidemiological as well as longitudinal studies related to maternity care in England (Bragg et al., 2010, Gurol-Urganci et al., 2011, Pradhan et al., 2013).

A further weakness is that this study included only 61% of all singleton, live, term births to women who delivered in an NHS hospital over a 12-year period. Excluding NHS trusts with poor data quality may have introduced bias, but the distributions of maternal age, pregnancy complications and mode of delivery were comparable to hospitals with good quality data (Appendix 2). A recent study also concluded that birth cohorts from hospitals with high completeness of recording for key fields in HES may be generalizable and representative of all hospitals nationally (Murray et al., 2013).

There may be residual bias in our adjusted results because we were not able to adjust for maternal factors such as obesity (Crane et al., 1997, Rich-Edwards et al., 2002) and voluntary absence of conception (Bhattacharya et al., 2006, Jolly et al., 1999, Porter et al., 2003), or completely account for history of infertility (Murphy et al., 2002, Pandian et al., 2001). Any residual bias due to unmeasured confounding factors would lead to an overestimate of the effect of caesarean section on fertility. Consequently, we would expect the unbiased effect to be smaller than those reported in our study.

Subsequent fertility outcomes should ideally be measured as the next pregnancy following the index delivery, but HES data does not capture spontaneous or induced abortions or ectopic pregnancies. However, the effect of this is likely to be small as the rate of early spontaneous pregnancy losses and ectopic pregnancies were found to be similar by mode of delivery at first birth (O'Neill et al., 2013, Smith et al., 2006).

Comparison with previous work

A recent systematic review identified eighteen cohort studies on this topic (Gurol-Urganci et al., 2013). Pooling the results from these studies suggested that caesarean section, on average, reduced the likelihood of a subsequent birth compared with a vaginal delivery (RR=0.89, 95% CI=0.87 to 0.92). However, these previous studies varied in important ways. The enrolled population ranged from being all inclusive to being restricted to primiparous women who delivered a live singleton baby at term. Only four studies limited the cohort to low-risk pregnancies (Eijsink et al., 2008, Hemminki, 1987, Hemminki et al., 2005, Tollanes et al., 2007). Two studies reported separately the outcomes for women who had caesarean section for breech presentation (Eijsink et al., 2008, Smith et al., 2006). Both concluded that there was no strong association between caesarean section for breech presentation and subsequent fertility, which is confirmed by the results of our much larger study.

Conclusions

Over the past 15 years, there have been significant changes in the practice of obstetrics as well as the characteristics of the obstetric population. On average, women are delaying their child bearing (Smith et al., 2008) and, with advances in medical care, more women with complex medical problems are becoming pregnant. These factors, as well as the possibility of litigation (Habiba et al., 2006), are leading to a change in the proportion of primiparous women likely to undergo caesarean section.

Previous studies have suggested that caesarean section may reduce subsequent fertility rates. However, the results from many studies could be biased due to weaknesses in their study designs and analytical methods. By carefully defining patient groups and adjusting for case-mix, we reduced the risk of bias by indication and found that the effect on fertility from a caesarean section is likely to be very small. The medical and social circumstances leading to the decision to carry out a caesarean section may contribute more to the observed reduction in fertility than the caesarean section itself.

Author's roles: All authors have fulfilled all conditions required for authorship. All authors conceived the study. IG-U and DAC contributed to its design and conducted the analyses. IG-U wrote the manuscript, and DAC, TAM, JHvdM and AT commented on drafts. All authors approved the final version for publication. IG-U is guarantor.

Acknowledgements: We thank the Health and Social Care Information Centre for providing the Hospital Episode Statistics data used in this study.

Funding: IG-U is supported by the Lindsay Stewart R&D Centre, Royal College of Obstetricians and Gynaecologists, UK.

Conflict of interest: None.

References

Bhattacharya S, Porter M, Harrild K, Naji A, Mollison J, van Teijlingen E, Campbell DM, Hall MH and Templeton A. Absence of conception after caesarean section: voluntary or involuntary? *BJOG: An International Journal of Obstetrics and Gynaecology* 2006; **113**:268-275.

Birthplace in England Collaborative G, Brocklehurst P, Hardy P, Hollowell J, Linsell L, Macfarlane A, McCourt C, Marlow N, Miller A, Newburn M et al. Perinatal and maternal outcomes by planned place of birth for healthy women with low risk pregnancies: the Birthplace in England national prospective cohort study. *BMJ* 2011; **343**:d7400.

Bragg F, Cromwell DA, Edozien LC, Gurol-Urganci I, Mahmood TA, Templeton A and van der Meulen JH. Variation in rates of caesarean section among English NHS trusts after accounting for maternal and clinical risk: cross sectional study. *BMJ* 2010; **341**:c5065.

Burns EM, Rigby E, Mamidanna R, Bottle A, Aylin P, Ziprin P and Faiz OD. Systematic review of discharge coding accuracy. *Journal of public health (Oxford, England)* 2012; **34**:138-148.

Churchill H, Savage W and Francome C. Caesarean birth in Britain. 2nd ed. edn, 2006. Middlesex University Press.

Crane SS, Wojtowycz MA, Dye TD, Aubry RH and Artal R. Association between pre-pregnancy obesity and the risk of cesarean delivery. *Obstetrics and Gynecology* 1997; **89**:213-216.

Cromwell DA, Knight HE and Gurol-Urganci I. Parity derived for pregnant women using historical administrative hospital data: Accuracy varied among patient groups. *Journal of clinical epidemiology* 2014.

Dunson DB, Baird DD and Colombo B. Increased infertility with age in men and women. *Obstetrics and Gynecology* 2004; **103**:51-56.

Eijsink JJ, van der Leeuw-Harmsen L and van der Linden PJ. Pregnancy after Caesarean section: fewer or later? *Human Reproduction* 2008; **23**:543-547.

Gurol-Urganci I, Bou-Antoun S, Lim C, Cromwell D, Mahmood T, Templeton A and van der Meulen J. Impact of caesarean section on subsequent fertility: a systematic review and meta-analysis. *Hum Reprod* 2013; **28**:1943-1952.

Gurol-Urganci I, Cromwell DA, Edozien LC, Onwere C, Mahmood TA and van der Meulen JH. The timing of elective caesarean delivery between 2000 and 2009 in England. *BMC Pregnancy Childbirth* 2011; **11**:43.

Habiba M, Kaminski M, Da Fre M, Marsal K, Bleker O, Librero J, Grandjean H, Gratia P, Guaschino S, Heyl W et al. Caesarean section on request: a comparison of obstetricians' attitudes in eight European countries. *BJOG : an international journal of obstetrics and gynaecology* 2006; **113**:647-656.

Hall MH, Campbell DM, Fraser C and Lemon J. Mode of delivery and future fertility. *British Journal of Obstetrics and Gynaecology* 1989; **96**:1297-1303.

Hemminki E. Pregnancy and birth after cesarean section: a survey based on the Swedish birth register. *Birth* 1987; **14**:12-17.

Hemminki E. Impact of Caesarean section on future pregnancy - A review of cohort studies. *Paediatric and Perinatal Epidemiology* 1996; **10**:366-379.

Hemminki E and Merilainen J. Long-term effects of cesarean sections: ectopic pregnancies and placental problems. *American Journal of Obstetrics and Gynecology* 1996; **174**:1569-1574.

Hemminki E, Shelley J and Gissler M. Mode of delivery and problems in subsequent births: a register-based study from Finland. *American Journal of Obstetrics and Gynecology* 2005; **193**:169-177.

HSCIC. The processing cycle and HES data quality. http://www.hscic.gov.uk/article/1825/The-processing-cycle-and-HES-data-quality. Date accessed: 04/02/2014. 2013.

Jolly J, Walker J and Bhabra K. Subsequent obstetric performance related to primary mode of delivery. *British Journal of Obstetrics and Gynaecology* 1999; **106**:227-232.

Kirkman MA, Mahattanakul W, Gregson BA and Mendelow AD. The accuracy of hospital discharge coding for hemorrhagic stroke. *Acta neurologica Belgica* 2009; **109**:114-119.

Knight HE, Gurol-Urganci I, Mahmood TA, Templeton A, Richmond D, van der Meulen JH and Cromwell DA. Evaluating maternity care using national administrative health datasets: how are statistics affected by the quality of data on method of delivery? *BMC health services research* 2013; **13**:200.

Lancet. Caesarean section on the rise. *Lancet* 2000; **356**:1697.

LaSala AP and Berkeley AS. Primary cesarean section and subsequent fertility. *American Journal of Obstetrics and Gynecology* 1987; **157**:379-383.

Leitch CR and Walker JJ. The rise in caesarean section rate: the same indications but a lower threshold. *British Journal of Obstetrics and Gynaecology* 1998; **105**:621-626.

Loudon JA, Groom KM, Hinkson L, Harrington D and Paterson-Brown S. Changing trends in operative delivery performed at full dilatation over a 10-year period. *Journal of obstetrics and gynaecology : the journal of the Institute of Obstetrics and Gynaecology* 2010; **30**:370-375.

MacKenzie IZ, Cooke I and Annan B. Indications for caesarean section in a consultant obstetric unit over three decades. *Journal of obstetrics and gynaecology : the journal of the Institute of Obstetrics and Gynaecology* 2003; **23**:233-238.

Mollison J, Porter M, Campbell D and et al. Primary mode of delivery and subsequent pregnancy. *BJOG: An International Journal of Obstetrics and Gynaecology* 2005; **112**:1061-1065.

Murphy DJ, Stirrat GM, Heron J and Team AS. The relationship between Caesarean section and subfertility in a population-based sample of 14 541 pregnancies. *Human Reproduction* 2002; **17**:1914-1917.

Murray J, Saxena S, Modi N, Majeed A, Aylin P and Bottle A. Quality of routine hospital birth records and the feasibility of their use for creating birth cohorts. *Journal of public health (Oxford, England)* 2013; **35**:298-307.

O'Neill S, Khashan A, Kenny L, Greene R, Henriksen T, Lutomski J and Kearney P. Caesarean section and subsequent ectopic pregnancy: a systematic review and meta-analysis. *BJOG : an international journal of obstetrics and gynaecology* 2013.

ODPM. Office of the Deputy Prime Minister: The English indices of deprivation 2004: summary (revised). http://webarchive.nationalarchives.gov.uk/20120919132719/www.communities.gov.uk/documents/communities/pdf/131206.pdf**.** Date accessed: 04/02/2014. 2004.

OECD. Health at a Glance 2013: OECD Indicators. http://www.oecd.org/els/health-systems/Health-at-a-Glance-2013.pdf Date accessed: 04/02/2013. 2013.

ONS. Birth statistics: Births and patterns of family building England and Wales (FM1) FM1 No. 36. Table 1.9 Components of total fertility rates1: occurrence within/outside England and Wales marriage, birth order and age of mother, 1997-2007. http://www.official-documents.gov.uk/document/other/9787777148210/9787777148210.pdf Date accessed 04/02/2014. 2007.

OPCS. OPCS-4 Classification. http://www.connectingforhealth.nhs.uk/systemsandservices/data/clinicalcoding/codingstandards/opcs4. Date accessed: 04/09/2013. 2012.

Pandian Z, Bhattacharya S and Templeton A. Review of unexplained infertility and obstetric outcome: a 10 year review. *Human Reproduction* 2001; **16**:2593-2597.

Penn Z and Ghaem-Maghami S. Indications for caesarean section. *Best practice & research Clinical obstetrics & gynaecology* 2001; **15**:1-15.

Porter M, Bhattacharya S, van Teijlingen E and et al. Does Caesarean section cause infertility? *Human Reproduction* 2003; **18**:1983-1986.

Pradhan A, Tincello DG and Kearney R. Childbirth after pelvic floor surgery: analysis of Hospital Episode Statistics in England, 2002-2008. *BJOG : an international journal of obstetrics and gynaecology* 2013; **120**:200-204.

Rich-Edwards JW, Spiegelman D, Garland M, Hertzmark E, Hunter DJ, Colditz GA, Willett WC, Wand H and Manson JE. Physical activity, body mass index, and ovulatory disorder infertility. *Epidemiology* 2002; **13**:184-190.

Rosenthal AN and Paterson-Brown S. Is there an incremental rise in the risk of obstetric intervention with increasing maternal age? *British Journal of Obstetrics and Gynaecology* 1998; **105**:1064-1069.

Smith GC, Cordeaux Y, White IR, Pasupathy D, Missfelder-Lobos H, Pell JP, Charnock-Jones DS and Fleming M. The effect of delaying childbirth on primary cesarean section rates. *PLoS medicine* 2008; **5**:e144.

Smith GCS, Wood AM, Pell JP and Dobbie R. First cesarean birth and subsequent fertility. *Fertility and Sterility* 2006; **85**:90-95.

Tollanes MC, Melve KK, Irgens LM and Skjaerven R. Reduced fertility after cesarean delivery: a maternal choice. *Obstetrics and Gynecology* 2007; **110**:1256-1263.

WHO. International Classification of Diseases (ICDs). http://www.who.int/classifications/icd/en/ Date accessed 04/02/2014. 2012.

Figure Legends

Figure 1: Kaplan-Meier estimates of the proportion of women having a subsequent birth, stratified by mode of delivery at index birth, unadjusted

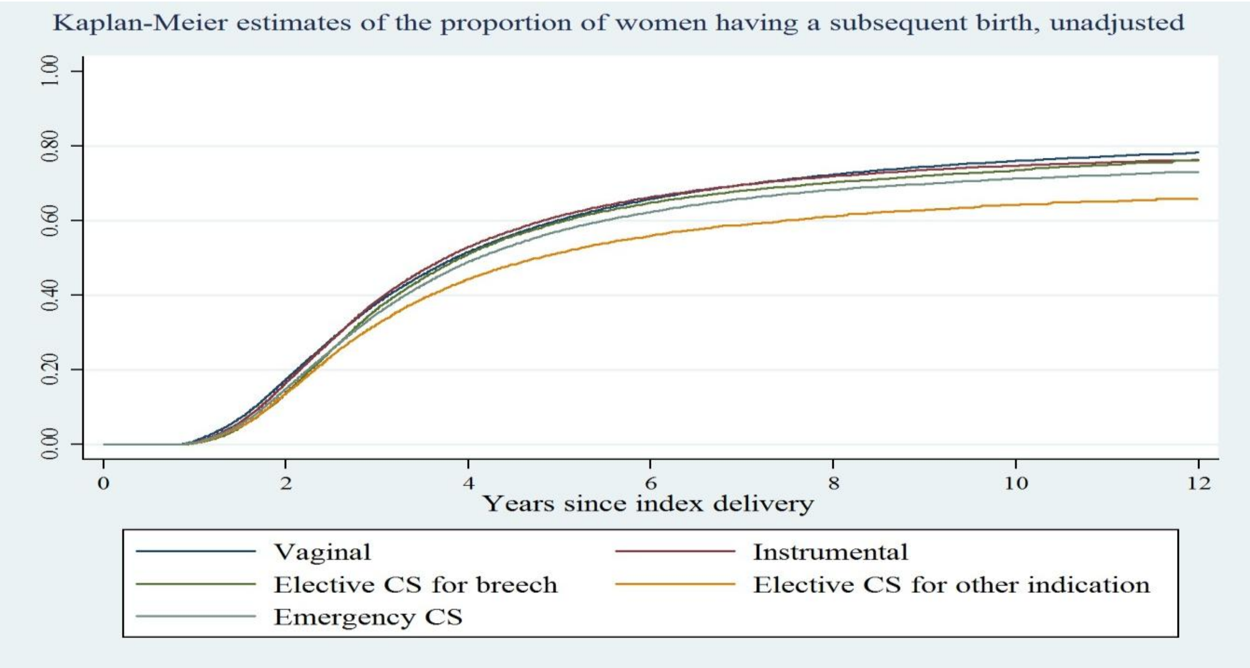

Table 1: Kaplan-Meier estimates of the proportion of women having a subsequent birth at selected years following index delivery, by maternal demographic factors and outcomes of delivery.

	Number of deliveries	Percent of deliveries	Percent of women having a subsequent birth at		
			3 years	5 years	10 years
All	1,047,644	100	37.5	59.8	74.7
Maternal age (years)					
15-29	713,403	68.1	36.7	60.4	78.2
30-34	244,112	23.3	41.8	63.0	70.8
35-40	90,129	8.6	32.5	45.9	n/a
Ethnicity					
White	844,341	80.6	37.2	59.7	74.8
Asian	108,943	10.4	43.6	67.9	81.7
Black	40,619	3.9	33.3	50.5	66.1
Other	53,741	5.1	33.8	52.5	65.5
Deprivation (quintiles)					
Least deprived	167,318	16.0	42.4	64.9	75.6
Q2	174,453	16.7	39.4	61.9	74.6
Q3	194,984	18.6	37.0	59.6	73.7
Q4	230,451	22.0	34.6	56.9	73.4
Most deprived	280,438	26.8	36.1	57.9	75.8
Mode of delivery					
Vaginal	596,902	57.0	38.0	60.3	76.0
Instrumental	226,718	21.6	38.7	61.3	74.8
Elective CS for breech	24,905	2.4	36.4	59.7	73.5
Elective CS for other indication	16,182	1.5	32.2	51.4	64.4
Emergency CS	182,937	17.5	35.1	57.3	71.3

Table 2: Association between the risk of a subsequent pregnancy and characteristics of index delivery. Hazard ratios (HR) were estimated using Cox proportional hazards regression. Multivariate regression model adjusts for maternal age, ethnicity, deprivation and year of index delivery.

	Unadjusted HR* (95% CI)	Adjusted HR* (95% CI)
Maternal age (years)		
15-29	1	1
30-34	0.99 (0.96,1.03)	0.98 (0.95,1.01)
35-40	0.64 (0.60,0.67)	0.63 (0.60,0.67)
Ethnicity		
White	1	1
Asian	1.28 (1.19,1.37)	1.28 (1.20,1.37)
Black	0.82 (0.78,0.87)	0.85 (0.81,0.90)
Other	0.84 (0.80,0.87)	0.85 (0.82,0.88)
Deprivation (quintiles)		
Least deprived	1	1
Q2	0.94 (0.92,0.96)	0.92 (0.90,0.95)
Q3	0.89 (0.86,0.91)	0.86 (0.84,0.89)
Q4	0.85 (0.82,0.87)	0.81 (0.79,0.84)
Most deprived	0.90 (0.86,0.95)	0.85 (0.82,0.88)
Mode of delivery		
Vaginal	1	1
Instrumental	1.00 (0.99,1.01)	1.00 (0.99,1.01)
Elective CS for breech	0.94 (0.92,0.96)	0.96 (0.94,0.98)
Elective CS for other indication	0.76 (0.74,0.79)	0.81 (0.78,0.83)
Emergency CS	0.90 (0.88,0.91)	0.91 (0.90,0.93)
Year of index delivery		
2000	1	1
Change per year	1.01 (1.00, 1.01)	1.01 (1.01, 1.02)

* All associations were statistically significant at p<0.001

Table 3: Association between the rate of subsequent births and the mode of index delivery by age group for primiparous women with low-risk pregnancies.

The mode of delivery for women with low-risk pregnancies by age group (n(%))

	Age: 15-29	**Age: 30-34**	**Age: 35-40**
Vaginal delivery	447,451 (62.7)	114,418 (46.9)	35,033 (38.9)
Instrumental delivery	139,070 (19.5)	63,413 (26.0)	24,235 (26.9)
Elective CS for breech	13,385 (1.9)	7,981 (3.3)	3,539 (3.9)
Elective CS for other	7,585 (1.1)	5,209 (2.1)	3,388 (3.8)
Emergency CS	105,912 (14.8)	53,091 (21.7)	23,934 (26.6)
Total	713,403 (100)	244,112 (100)	90,129 (100)

The effect of mode of delivery on subsequent birth rates by age group (Adjusted HR (95% CI)[1])

	Age: 15-29	**Age: 30-34**	**Age: 35-40**
Vaginal delivery	1	1	1
Instrumental delivery	1.00 (0.99,1.01)	1.02 (1.01,1.04)	1.00 (0.98,1.03)
Elective CS for breech	0.98 (0.96,1.01)	0.95 (0.92,0.98)	0.90 (0.85,0.96)
Elective CS for other indication	0.85 (0.81,0.89)	0.78 (0.74,0.82)	0.77 (0.73,0.82)
Emergency CS	0.93 (0.92,0.94)	0.91 (0.90,0.93)	0.89 (0.86,0.92)

[1] Hazard ratios (HR) were estimated using Cox proportional hazards regression, and adjusted for ethnicity, deprivation and year of index delivery.

Table 4: Association between the rate of subsequent births and mode of index delivery by obstetric condition among women with high risk pregnancies.

Mode of delivery for women with high risk pregnancies by obstetric condition (n(%))

	Placenta Praevia	Eclampsia / Preeclampsia	Hypertension Pre-existing or gestational	Diabetes Pre-existing or gestational
Vaginal delivery	249 (6.2)	8945 (35.6)	30712 (47)	6737 (34.9)
Instrumental delivery	130 (3.3)	5331 (21.2)	15566 (23.8)	3949 (20.4)
Elective CS	2610 (65.4)	1178 (4.7)	2078 (3.2)	2011 (10.4)
Emergency CS	1002 (25.1)	9662 (38.5)	16997 (26)	6618 (34.3)
Total	3991 (100)	25116 (100)	65353 (100)	19315 (100)

The effect mode of delivery on subsequent birth rates by obstetric condition (Adjusted HR (95% CI)[1])

	Placenta Praevia[2] n=3,612[3]	Eclampsia / Preeclampsia n=25,116	Hypertension Pre-existing or gestational n=65,353	Diabetes Pre-existing or gestational n=19,315
Vaginal delivery	-	1	1	1
Instrumental delivery	-	1.00 (0.95,1.05)	0.99 (0.97,1.02)	0.97 (0.91,1.04)
Elective CS	1	0.78 (0.70,0.86)	0.85 (0.78,0.92)	0.74 (0.68,0.81)
Emergency CS	0.98 (0.87,1.10)	0.87 (0.83,0.92)	0.87 (0.85,0.90)	0.84 (0.80,0.89)

[1] Hazard ratios (HR) were estimated using Cox proportional hazards regression, and adjusted for age, ethnicity, deprivation and year of index birth.
[2] Women with vaginal / instrumental birth excluded as the number of women in these categories are very low. The comparison is between emergency versus elective caesarean section.
[3] Row total exceeds total number of women excluded from the main analysis (n=110,342): 3,433 women had multiple pregnancy risks.

Supplementary table 1: Coding of variables in the analysis

Diagnosis	ICD-10 Code
Placenta praevia	O44
Eclampsia / preeclampsia	O14-5
Pre-existing hypertension	O10-11; I10
Gestational hypertension	O13; O16
Pre-existing diabetes	O240-3; E10-11
Gestational diabetes	O244; O249
History of infertility	Z35.0

Preterm deliveries <37 weeks were defined as delivery episodes with an ICD-10 code for preterm delivery (O60).

Stillbirths were defined as delivery episodes with a maternity tail code for stillbirth (birthstat 2-4;9). If this field was missing in the maternity tail, ICD-10 codes for stillbirth were used (Z371; Z373-4; Z376-7).

Multiple deliveries were defined as delivery episodes with an ICD-code for a multiple birth (Z37.2–7) OR strong evidence of a multiple birth in the maternity tail (>1 valid date of birth [dobbaby], birthweight [birweit], birth order [birord] AND >1 in the number of babies [numbaby] field).

Mode of delivery was defined using OPCS4 codes: vaginal delivery (R23, R24), instrumental delivery (R21, R22), elective caesarean section (R17) and emergency caesarean section (R18; R251).

Supplementary table 2: Comparison of maternal characteristics and outcomes of delivery in omitted and included episodes (n(%))

	Included episodes	Omitted episodes
	3,936,215	2,513,378
Maternal age (years)		
15-29	2,132,642 (54.2)	1,319,747 (52.5)
30-34	1,143,301 (29.1)	744,627 (29.6)
35-40	660,272 (16.8)	449,004 (17.9)
Mode of delivery		
Vaginal	2,607,115 (66.2)	1,640,469 (65.3)
Instrumental	472,649 (12.0)	301,911 (12.0)
Elective CS	350,031 (8.9)	235,188 (9.4)
Emergency CS	506,420 (12.9)	335,810 (13.4)
Pregnancy complications		
Placenta praevia	17,882 (0.5)	11,650 (0.5)
Preeclampsia / eclampsia	54,173 (1.4)	39,039 (1.5)
Diabetes mellitus (pre-existing or gestational)	83,426 (2.1)	49,058 (2.0)
Hypertension (pre-existing or gestational)	159,764 (4.1)	94,898 (3.8)

[All comparisons showed a statistically significant difference with $p<0.001$, except for placenta praevia where the difference was not statistically significant $p=0.17$]