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Title page

Severe maternal morbidities in women with a prior caesarean delivery planning vaginal birth or elective repeat caesarean section: a retrospective cohort analysis using data from the UK Obstetric Surveillance System

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ABSTRACT

Objective: To conduct a secondary analysis of data from the UK Obstetric Surveillance System (UKOSS) to estimate the rates of specific maternal risks associated with planned Vaginal Birth after Caesarean (VBAC) and Elective Repeat Caesarean Section (ERCS).

Design: A retrospective cohort analysis using UKOSS data.

Setting: All hospitals with consultant led maternity units in the UK.

Population: Pregnant women who had a previous caesarean section.

Method: Women who had undergone a previous caesarean section were divided into two exposure groups: planned VBAC and ERCS. We calculated the incidence of each of the four outcomes of interest with 95% confidence intervals (CI) for the two exposure groups using proxy denominators (total estimated VBAC and ERCS maternities in a given year). Incidences were compared between groups using chi squared or Fisher's exact tests and risk ratios with exact 95% CI.

Main outcome measures: Severe maternal morbidities: peripartum hysterectomy, severe sepsis, peripartum haemorrhage and failed tracheal intubation.

Results: The risks of all complications examined in both groups were low. The rates of peripartum hysterectomy, severe sepsis, peripartum haemorrhage and failed tracheal intubation were not significantly different between the two groups in absolute or relative terms.

Conclusion: While the risk of uterine rupture in VBAC and ERCS groups is well understood, this national study did not demonstrate any other clear differences in the outcomes we examined. The absolute and relative risks of maternal complications were small in both groups. Large epidemiological studies could further help to assess whether the incidence of these rare outcomes would significantly differ between VBAC and ERCS groups if a larger number of cases were to be examined. In the interim, this study provides important information to help pregnant women in their decision making process.

ARTICLE SUMMARY

Strengths and limitations of the study

- While the risk of uterine rupture associated with VBAC is known, this study estimated the rates of other specific maternal risks (peripartum hysterectomy, severe sepsis, peripartum haemorrhage and failed tracheal intubation) associated with VBAC and ERCS using existing national data from the UK Obstetrics Surveillance System (UKOSS).
- Low incidence of severe maternal morbidities in the UK makes it difficult to compare their risks between VBAC and ERCS groups. The UKOSS database of research data on rare and potentially life threatening conditions in pregnancy provided a unique opportunity to estimate the risk of the four adverse maternal outcomes between the two groups in a cost-effective manner.

- The method used to generate the exposure groups (planned VBAC and ERCS) could have misclassified some women who were planning ERCS, but went into spontaneous labour and were thus included under the VBAC group. However, we do not anticipate a large proportion of such women.
- Cases which could not be grouped into VBAC or ERCS due to missing information could have biased the study results, mainly for the sepsis group. We have thus reported the results of a sensitivity analysis.
- A large epidemiological study with a greater number of cases would improve the power and possibly show significant differences in the outcomes, however, this study intended to take advantage of existing secondary data and the results could pave way for further studies.

Key words: Vaginal Birth after Caesarean, Elective Repeat Caesarean Section, peripartum hysterectomy, severe sepsis, peripartum haemorrhage, failed tracheal intubation.

Word count: 2250

INTRODUCTION

Current UK guidelines^{1 2} advise that women who have undergone a prior delivery by caesarean section should be informed of the risks and benefits of Elective Repeat Caesarean Section (ERCS) as well as the risks and benefits of planned Vaginal Birth after Caesarean (VBAC). Such a discussion requires comprehensive evidence of the risks associated with ERCS compared to VBAC. Several studies have examined the risk of uterine rupture following VBAC,³⁻⁵ but robust data comparing a wider range of complications of VBAC and ERCS are limited and the few randomised controlled studies^{6 7} have limitations.

A previous study in the UK demonstrated uterine rupture to be associated with VBAC.⁸ Uterine rupture is a rare and serious complication of VBAC, but when comparing ERCS and VBAC it is important to consider other maternal complications. The aim of this study was therefore to estimate the rates of other specific maternal risks associated with VBAC and ERCS using available national data from the UK Obstetric Surveillance System (UKOSS).

METHODS

Study Design

We conducted a retrospective cohort analysis using data from the UKOSS. Details of the UKOSS methodology are described elsewhere.^{9 10} UKOSS was set up in 2005 to investigate uncommon disorders of pregnancy and 'near-miss' conditions.¹⁰ Case notification cards are sent to all consultant-led obstetric units in the UK every month. An approach of 'nil-reporting' together with rigorous follow-up of non-responders ensures good case ascertainment. For every case reported, details are completed in a data collection form by the clinician responsible for managing the case. Further details of the UKOSS methodology are provided elsewhere.^{9 10}

Exposure groups were planned vaginal birth after caesarean (VBAC) and elective repeat caesarean section (ERCS). Women who had a history of caesarean section and underwent elective caesarean section during the current pregnancy were included in the ERCS group. Women who had a previous caesarean section, but planned vaginal delivery during current pregnancy were included in the planned VBAC group irrespective of whether they actually had a vaginal delivery.

Outcomes of interest were the maternal complications peripartum hysterectomy, severe sepsis, peripartum haemorrhage and failed tracheal intubation, which are suggested to be related to VBAC or ERCS in other studies.^{6 11 12} We had national datasets within UKOSS for the outcomes (peripartum hysterectomy,¹³ severe sepsis,¹⁴ peripartum haemorrhage,^{15 16} and failed tracheal intubation¹⁷) and thus case definitions were based on the standard case definitions used in the UKOSS (provided in Table-1).

Table-1: Definitions of outcomes included from the UKOSS national studies

Condition	Definition
Peripartum hysterectomy	Any woman giving birth to an infant and having a hysterectomy during the same clinical episode.
Peripartum haemorrhage	Cases were pregnant women of 20 weeks gestation or more identified as having ≥ 8 units of red blood cell transfusion within a 24 hour period.
Failed tracheal intubation	A case of failed intubation was defined as failure to achieve tracheal intubation during a rapid sequence induction for obstetric anaesthesia, thereby initiating a failed intubation drill.
Severe sepsis	Any pregnant woman (up to six weeks postpartum) diagnosed with severe sepsis (irrespective of the source of infection). A severe sepsis case would be expected to include women in one of the following groups: <ol style="list-style-type: none"> 1. Death related to infection or suspected infection 2. Any women requiring level 2 or level 3 critical care (or obstetric HDU type care) due to severe sepsis or suspected severe sepsis 3. A clinical diagnosis of severe sepsis – based on 2 or more the following – <ol style="list-style-type: none"> a. Temperature $> 38^{\circ}\text{C}$ or $< 36^{\circ}\text{C}$ measured on 2 occasions at least 4 hours apart b. Heart rate > 100 beats/minute measured on 2 occasions at least 4 hours apart c. Respiratory rate > 20/minute measured on 2 occasions at least 4 hours apart d. White cell count $> 17 \times 10^9/\text{L}$ or $< 4 \times 10^9/\text{L}$ or with $> 10\%$ immature band forms, measured on 2 occasions

Study sample

For each of the four maternal outcomes, for which a national dataset was available, we used the total reported cases. Among the cases, those without a previous history of caesarean section were excluded. We also excluded women with placenta praevia/accreta/percreta diagnosed before delivery to exclude known confounding due to these conditions which would be regarded as an absolute indication for ERCS. The final sample of cases that remained was divided into planned VBAC and ERCS groups based on planned mode of delivery. If a dataset did not include information on 'planned mode of delivery', we investigated two other variables – 'woman underwent induction of labour with or without prostaglandins and/or oxytocin' and 'woman went into labour'. If either of these were 'true', we categorised the woman as planned VBAC (irrespective of her actual mode of delivery - vaginal or caesarean), otherwise ERCS. If information on any of these criteria was not available, we grouped the cases into a missing category. A schematic diagram of the process of derivation of the study samples for peripartum hysterectomy, severe sepsis, peripartum haemorrhage and failed intubation is provided in figure-1.

Statistical analyses

We calculated the incidence of each of the outcomes of interest with 95% confidence intervals (CI) for the two exposure groups, VBAC and ERCS, using the denominators - total expected VBAC and ERCS maternities in a given year. The method of calculating proxy denominators was similar to that used by Fitzpatrick et al. to report the incidence of uterine rupture in VBAC and ERCS groups.⁸ Total

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3 maternities for the UK in the study period for each of the outcomes were calculated from the
4 annually reported birth data for England and Wales,¹⁸ Scotland¹⁹ and Northern Ireland.²⁰ From
5 these, we calculated the estimated number of maternities likely to have undergone previous
6 caesarean section, which was 13% of the total maternities, derived from a group of population
7 based controls comprised of women giving birth in the UK in 2012-13. Based on proportions
8 observed in the control group of the UKOSS uterine rupture study,⁸ we further divided the
9 maternities with previous caesarean section into women undergoing planned VBAC (44% of the
10 total maternities with previous caesarean section) and women undergoing planned ERCS (56% of
11 the total maternities with previous caesarean section) which gave the required proxy denominators.
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18 In addition, we also tested whether the calculated rates in the exposure groups were significantly
19 different from each other using chi square test or Fisher's exact test. We estimated the risk ratios
20 and exact 95% confidence intervals (CI) to ascertain the relative risk of severe maternal morbidities
21 in the planned VBAC compared to ERCS group. We also used descriptive statistics to compare the
22 two exposures groups. In order to account for any differences in known and potential confounding
23 factors, we conducted multivariable logistic regression analyses for the outcomes for which we had
24 a control group: peripartum hysterectomy, sepsis and failed intubation. The multivariable logistic
25 regression analysis results for uterine rupture have been published previously.⁸
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31 In the sample for sepsis, 11 cases could not be classified into VBAC or ERCS due to missing
32 information, and peripartum haemorrhage and hysterectomy each had one case with missing
33 information (Figure-1). We conducted a sensitivity analysis by calculating incidence rates assuming
34 extreme scenarios and accordingly including the missing numbers under each of the two exposure
35 groups.
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38 RESULTS

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40 A total of 83 confirmed cases of peripartum haemorrhage, 66 cases of hysterectomy, 49 cases of
41 severe sepsis and 7 cases of failed tracheal intubation were included in the study (Figure-1). The
42 exposure groups, ERCS and planned VBAC, for each of the outcomes were not significantly
43 different in terms of maternal age, body mass index (BMI), parity, history of previous pregnancy
44 problems and socioeconomic status. The calculated incidence rates of the maternal complications
45 were low and were not found to be significantly different between the two groups (Table-2). The
46 relative risk of the severe maternal morbidities was not different between the VBAC and ERCS
47 groups (Table-2).
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Table-2: Rate of severe maternal morbidities in VBAC and ERCS groups

Conditions	Study period	Total Maternities for the study period	Maternities with previous Caesarean deliveries*	VBAC			ERCS			P-value of χ^2 test* for outcome difference between VBAC & ERCS	Risk ratios (VBAC to ERCS) (Exact 95% CI)
				Maternities with previous CS with VBAC [†]	Cases	Estimated rate per 100,000 maternities (95% CI)	Maternities with previous CS with ERCS [‡]	Cases	Estimated rate per 100,000 maternities (95% CI)		
Uterine rupture [§]	01/04/2009 to 30/04/2010	852206	127831	56246	116	206.7 (170.5 - 247.3)	71585	20	27.9 (17.1 - 43.2)	<0.001	7.39 (4.58 - 12.55)
Peripartum hysterectomy	01/02/2005 to 29/02/2006	839785	109172	48036	35	72.9 (50.8 - 101.3)	61136	30	49.1 (33.1 - 70.0)	0.110	1.49 (0.89 - 2.50)
Sepsis	01/06/2011 to 31/05/2012	801770	104231	45861	23	50.1 (31.7 - 75.2)	58370	18	30.8 (18.3 - 48.7)	0.119	1.63 (0.84 - 3.19)
Peripartum haemorrhage	01/09/2007 to 31/03/2009 [§]	1176025	152884	67269	31	46.0 (31.3 - 65.4)	85616	51	59.5 (44.3 - 78.3)	0.259	0.77 (0.48 - 1.23)
Failed intubation	01/04/2008 to 31/03/2010	1504593	195597	86062	2	2.3 (0.2 - 8.3)	109535	5	4.5 (1.4 - 10.6)	0.476	0.51 (0.05 - 3.11)

*Proportion of maternities likely to have undergone previous caesarean section (based on 13% calculated from the Sepsis controls, 2012-13, drawn from the general population); [†] Proportion of maternities with previous caesarean section (CS) likely to undergo VBAC (based on 44% calculated from UKOSS-uterine rupture controls as was done by Fitzpatrick et al (8)); [‡] Proportion of maternities with previous caesarean section (CS) likely to undergo ERCS (based on 56% calculated from UKOSS-uterine rupture controls as was done by Fitzpatrick et al (8)); VBAC – Vaginal birth after caesarean; ERCS – Elective Repeat Caesarean section; CI – Confidence Interval; [§] For counts <5 Fisher's Exact test was done instead of Pearson's chi squared test, [§] The total maternities for this 18 month study were calculated as: Total maternities in 2008 + half of the maternities in 2009, as the number of maternities found for 2007 (from the same sources) did not appear to be in complete agreement with the 2005-2012 trend. Owing to this uncertainty in the 2007 numbers, the 2008 and 2009 maternities have been used here.

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3 The unadjusted odds ratios for the adverse outcomes, for which we had a control group, were not
4 significantly different between the VBAC and ERCS groups (data not shown). The odds of
5 peripartum hysterectomy (adjusted odds ratio=0.92; 95%CI=0.45 to 1.91) and sepsis (adjusted odds
6 ratio =0.51; 95% CI=0.22 to 1.19) in the ERCS group were not significantly different from that of the
7 VBAC group after controlling for current and previous pregnancy problems, number of previous
8 caesarean sections, pre-existing medical problems, parity, smoking status, socioeconomic status,
9 ethnic background, marital status, BMI and maternal age. The adjusted odds ratio was not
10 meaningful for failed intubation which had a total sample size of 15.

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16 Sensitivity analysis for cases with missing information showed that although the rates changed
17 slightly in the planned VBAC and ERCS groups for peripartum haemorrhage and hysterectomy, it
18 did not result in a significant difference in the risk of the adverse outcome between the two exposure
19 groups in either scenario. However, for severe sepsis, when all the 11 cases with missing
20 information were included in the planned VBAC group, the rate in the VBAC group was found to be
21 significantly higher than the rate in the ERCS group (p-value for chi square test=0.002). When these
22 cases were included in the ERCS group, the rates of sepsis in the two exposure groups were equal
23 (50 per 100,000 maternities).

24 25 26 27 28 29 **DISCUSSION**

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31 This study using the UKOSS data and a nested retrospective cohort design did not find a significant
32 difference in the incidence and relative risk of adverse maternal outcomes between the VBAC and
33 ERCS groups. However, the incidence rates of these outcomes were low.

34 35 36 37 **Strengths and Limitations**

38 Low incidence of severe maternal morbidities in the UK makes it difficult to compare their risks
39 between VBAC and ERCS groups. The UKOSS database of research data on rare and potentially
40 life threatening conditions in pregnancy provided a unique opportunity to estimate the risk of four
41 adverse maternal outcomes between the two groups in a cost-effective manner. The method used to
42 generate the exposure groups (planned VBAC and ERCS) could have misclassified some women
43 who were planning ERCS, but went into spontaneous labour and were thus included under the
44 VBAC group. However, we do not anticipate a large proportion of such women. Cases which could
45 not be grouped into VBAC or ERCS due to missing information could have biased the study results,
46 mainly for the sepsis group. We have thus reported the results of a sensitivity analysis. Although we
47 accounted for known confounders for each outcome in the multivariable logistic regression analyses,
48 the results cannot be interpreted with certainty due to the small sample sizes. A longer term study
49 with a greater number of cases would improve the power and possibly show significant differences
50 in the outcomes, however, this study intended to take advantage of existing secondary data and the
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3 results could pave the way for further studies. Furthermore, the adverse outcomes presented in this
4 study are immediate risks associated with the current pregnancy in the ERCS and VBAC groups
5 and we cannot comment on the risk of morbidity in future pregnancies.
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8 While the higher risk of uterine rupture associated with planned VBAC is known,^{4 8 21 22} studies from
9 different parts of the world have reported variable relative and absolute risks of other maternal
10 complications in ERCS versus VBAC groups. Similar to the findings of this study, a multicentre
11 prospective cohort study in the USA,⁴ a Canadian study¹¹ and a meta-analysis of literature published
12 between 2000 and 2007²² did not find any difference in the risk of hysterectomy between those that
13 underwent a trial of labour and those that had an elective caesarean section. However, a decision
14 model analysis conducted by Paré et al. suggested that the decision to undergo VBAC or ERCS
15 among women with one prior caesarean section should be guided by the number of planned
16 subsequent pregnancies.²³ Based on an analysis of risk of hysterectomy, the authors suggested that
17 ERCS should be the strategy of choice for women planning one additional pregnancy, but for
18 women who desire two or more subsequent pregnancies VBAC should be attempted to minimise
19 morbidity associated with multiple caesarean sections.²³
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28 In contrast to our findings, a study in Australia found a 63% lower risk of peripartum haemorrhage in
29 the planned ERCS compared to planned VBAC group⁶ and the multicentre study from the USA
30 demonstrated a higher odds of transfusion in the VBAC group compared with the ERCS.⁴ However,
31 a meta-analysis suggested a lower risk of peripartum haemorrhage in the VBAC group²¹ and other
32 studies did not show any difference.^{11 22} A prospective cohort study of obese women using data
33 collected through the UKOSS did not find any difference in anaesthetic complications between
34 ERCS and planned VBAC groups,²⁴ but this finding cannot be generalised to non-obese women.
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39 **Conclusion**

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41 While the risk of uterine rupture in VBAC and ERCS groups is well understood, this national study
42 did not demonstrate any other clear differences in the outcomes we examined. The absolute and
43 relative risks of maternal complications were small in both groups which is important information to
44 help pregnant women in their decision making process. Large epidemiological studies with a longer
45 time-period for data collection are required to assess whether the incidence of these rare outcomes
46 would significantly differ between VBAC and ERCS groups if a larger number of cases were to be
47 examined. In the interim, this study contributes additional information to the process of individualised
48 decision-making about mode of delivery by women who have had a previous delivery by caesarean
49 section, as recommended in current guidance.
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REFERENCES

1. Royal College of Obstetricians and Gynaecologists. Birth After Previous Caesarean Birth (Green-top 45): RGOG, 2007.
2. National Institute for Health and Care Excellence. Caesarean section (CG132): NICE, 2011.
3. Guise J-M, McDonagh MS, Osterweil P, Nygren P, Chan BK, Helfand M. Systematic review of the incidence and consequences of uterine rupture in women with previous caesarean section. *BMJ: British Medical Journal* 2004;329(7456):19-25.
4. Landon MB, Hauth JC, Leveno KJ, Spong CY, Leindecker S, Varner MW, et al. Maternal and perinatal outcomes associated with a trial of labor after prior cesarean delivery. *New England Journal of Medicine* 2004;351(25):2581-89.
5. Odibo AO, Macones GA. Current concepts regarding vaginal birth after cesarean delivery. *Current opinion in obstetrics & gynecology* 2003;15(6):479-82.
6. Crowther CA, Dodd JM, Hiller JE, Haslam RR, Robinson JS, on behalf of the Birth After Caesarean Study Group. Planned Vaginal Birth or Elective Repeat Caesarean: Patient Preference Restricted Cohort with Nested Randomised Trial. *PLoS Med* 2012;9(3):e1001192.
7. Law LW, Pang MW, Chung TK-H, Lao TT-H, Lee DT-S, Leung TY, et al. Randomised trial of assigned mode of delivery after a previous cesarean section-Impact on maternal psychological dynamics. *Journal of Maternal-Fetal and Neonatal Medicine* 2010;23(10):1106-13.
8. Fitzpatrick KE, Kurinczuk JJ, Alfirevic Z, Spark P, Brocklehurst P, Knight M. Uterine Rupture by Intended Mode of Delivery in the UK: A National Case-Control Study. *PLoS Med* 2012;9(3):e1001184.
9. Knight M, Lindquist A. The UK Obstetric Surveillance System: Impact on patient safety. *Best Practice & Research Clinical Obstetrics & Gynaecology* 2013;27(4):621-30.
10. Knight M, Kurinczuk JJ, Tuffnell D, Brocklehurst P. The UK Obstetric Surveillance System for rare disorders of pregnancy. *BJOG: An International Journal of Obstetrics & Gynaecology* 2005;112(3):263-65.
11. McMahon MJ, Luther ER, Bowes WA, Olshan AF. Comparison of a Trial of Labor with an Elective Second Cesarean Section. *New England Journal of Medicine* 1996;335(10):689-95.
12. van Ham MAPC, van Dongen PWJ, Mulder J. Maternal consequences of caesarean section. A retrospective study of intra-operative and postoperative maternal complications of caesarean section during a 10-year period. *European Journal of Obstetrics & Gynecology and Reproductive Biology* 1997;74(1):1-6.
13. Knight M, on behalf of UKOSS. Peripartum hysterectomy in the UK: management and outcomes of the associated haemorrhage. *BJOG: An International Journal of Obstetrics & Gynaecology* 2007;114(11):1380-87.
14. Acosta CD, Knight M, Lee HC, Kurinczuk JJ, Gould JB, Lyndon A. The Continuum of Maternal Sepsis Severity: Incidence and Risk Factors in a Population-Based Cohort Study. *PloS one* 2013;8(7):e67175.
15. Kayem G, Kurinczuk JJ, Alfirevic Z, Spark P, Brocklehurst P, Knight M. Uterine compression sutures for the management of severe postpartum hemorrhage. *Obstetrics & Gynecology* 2011;117(1):14-20.
16. Kayem G, Kurinczuk JJ, Alfirevic Z, Spark P, Brocklehurst P, Knight M. Specific second-line therapies for postpartum haemorrhage: a national cohort study. *BJOG: An International Journal of Obstetrics & Gynaecology* 2011;118(7):856-64.
17. Quinn AC, Milne D, Columb M, Gorton H, Knight M. Failed tracheal intubation in obstetric anaesthesia: 2 yr national case-control study in the UK. *British Journal of Anaesthesia* 2013;110(1):74-80.
18. Office for National Statistics. Birth summary tables, England and Wales. Newport: Office for National Statistics.
19. General Register Office for Scotland. Vital Events Reference Tables. Edinburgh: General Register Office for Scotland.
20. Northern Ireland Statistics and Research Agency. Registrar General Annual Reports Belfast: NISRA.
21. Mozurkewich EL, Hutton EK. Elective repeat cesarean delivery versus trial of labor: a meta-analysis of the literature from 1989 to 1999. *American Journal of Obstetrics and Gynecology* 2000;183(5):1187-97.

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2
3 22. Rossi AC, D'Addario V. Maternal morbidity following a trial of labor after cesarean section vs elective
4 repeat cesarean delivery: a systematic review with metaanalysis. *American journal of obstetrics and*
5 *gynecology* 2008;199(3):224-31.
6
7 23. Paré E, Quinones JN, Macones GA. Vaginal birth after cesarean section versus elective repeat cesarean
8 section: assessment of maternal downstream health outcomes. *BJOG-an International Journal of*
9 *Obstetrics and Gynaecology* 2006;113(1):75-85.
10
11 24. Homer CSE, Kurinczuk JJ, Spark P, Brocklehurst P, Knight M. Planned vaginal delivery or planned
12 caesarean delivery in women with extreme obesity. *BJOG: An International Journal of Obstetrics &*
13 *Gynaecology* 2011;118(4):480-87.

Caption for the figure

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17 Figure 1: Schematic diagram of derivation of study sample
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24 **Competing interest:** The authors declare that they have no competing interests.
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26 **Ethics statement:** The London Multi-centre Research Ethics Committee approved the UK Obstetric
27 Surveillance System (UKOSS) general methodology (04/MRE02/45) and the surveillance of
28 individual near-miss maternal morbidities using UKOSS (04/MRE02/73, 10/H0717/20, 08/H0781/1,
29 07/MRE02/24).
30

31 **Contributions to authorship:** MN coded the data, carried out the analysis, and wrote the first draft
32 of the article. KS contributed to the writing of the article. NN contributed to the analysis. MK
33 designed the study, supervised the data collection and analysis, and contributed to writing the
34 article. MG developed the research question, contributed to the design of the study and writing the
35 article.
36
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47 **Data sharing statement:** Data sharing is governed by the National Perinatal Epidemiology Unit
48 Data Sharing policy, available on request from Prof. Marian Knight.
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Figure 1: Schematic diagram of derivation of study sample

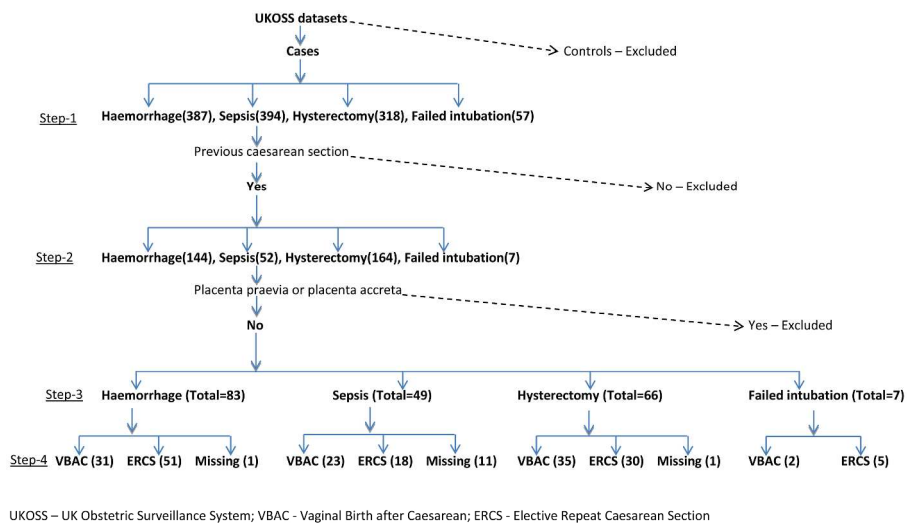


Figure 1: Schematic diagram of derivation of study sample
275x181mm (300 x 300 DPI)

Review only

STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

	Item No	Recommendation	Page number/s
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1 & 2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4 & 5
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5 (methods of follow-up – not applicable because it is a retrospective cohort analysis)
		(b) For matched studies, give matching criteria and number of exposed and unexposed	Not applicable
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4 & 5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4 & 5
Bias	9	Describe any efforts to address potential sources of bias	5 & 6
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5 & 6
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	5 & 6
		(b) Describe any methods used to examine subgroups and interactions	Not applicable
		(c) Explain how missing data were addressed	6
		(d) If applicable, explain how loss to follow-up was addressed	Not applicable
		(e) Describe any sensitivity analyses	6
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5 & Figure-1
		(b) Give reasons for non-participation at each stage	Not applicable
		(c) Consider use of a flow diagram	Figure-1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential	6

		confounders	
		(b) Indicate number of participants with missing data for each variable of interest	6, 7, 8 & Figure-1
		(c) Summarise follow-up time (eg, average and total amount)	Not applicable
Outcome data	15*	Report numbers of outcome events or summary measures over time	6, 7 & 8
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8
		(b) Report category boundaries when continuous variables were categorized	Not applicable
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8
Discussion			
Key results	18	Summarise key results with reference to study objectives	8
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	8 & 9
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9
Generalisability	21	Discuss the generalisability (external validity) of the study results	9
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	11

*Give information separately for exposed and unexposed groups.

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Selected maternal morbidities in women with a prior caesarean delivery planning vaginal birth or elective repeat caesarean section: a retrospective cohort analysis using data from the UK Obstetric Surveillance System

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1 **Title page**

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3 Selected maternal morbidities in women with a prior caesarean delivery planning
4 vaginal birth or elective repeat caesarean section: a retrospective cohort analysis using
5 data from the UK Obstetric Surveillance System

6
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3738 **ABSTRACT**

39 **Objective:** To conduct a secondary analysis of data from the UK Obstetric Surveillance
40 System (UKOSS) to estimate the rates of specific maternal risks associated with planned
41 Vaginal Birth after Caesarean (VBAC) and Elective Repeat Caesarean Section (ERCS).

42 **Design:** A retrospective cohort analysis using UKOSS data from four studies conducted
43 between 2005 and 2012.

44 **Setting:** All hospitals with consultant led maternity units in the UK.

45 **Population:** Pregnant women who had a previous caesarean section.

46 **Method:** Women who had undergone a previous caesarean section were divided into two
47 exposure groups: planned VBAC and ERCS. We calculated the incidence of each of the four
48 outcomes of interest with 95% confidence intervals (CI) for the two exposure groups using
49 proxy denominators (total estimated VBAC and ERCS maternities in a given year).
50 Incidences were compared between groups using chi squared or Fisher's exact tests and
51 risk ratios with exact 95% CI.

52 **Main outcome measures:** Severe maternal morbidities: peripartum hysterectomy, severe
53 sepsis, peripartum haemorrhage and failed tracheal intubation.

54 **Results:** The risks of all complications examined in both groups were low. The rates of
55 peripartum hysterectomy, severe sepsis, peripartum haemorrhage and failed tracheal
56 intubation were not significantly different between the two groups in absolute or relative
57 terms.

58 **Conclusion:** While the risk of uterine rupture in VBAC and ERCS groups is well understood,
59 this national study did not demonstrate any other clear differences in the outcomes we
60 examined. The absolute and relative risks of maternal complications were small in both
61 groups. Large epidemiological studies could further help to assess whether the incidence of
62 these rare outcomes would significantly differ between VBAC and ERCS groups if a larger
63 number of cases were to be examined. In the interim, this study provides important
64 information to help pregnant women in their decision making process.

65 **ARTICLE SUMMARY**66 **Strengths and limitations of the study**

- 67 • While the risk of uterine rupture associated with VBAC is known, this study estimated the
68 rates of other specific maternal risks (peripartum hysterectomy, severe sepsis, peripartum
69 haemorrhage and failed tracheal intubation) associated with VBAC and ERCS using
70 existing national data from the UK Obstetrics Surveillance System (UKOSS).
- 71 • Low incidence of severe maternal morbidities in the UK makes it difficult to compare their
72 risks between VBAC and ERCS groups. The UKOSS database of research data on rare
73 and potentially life threatening conditions in pregnancy provided a unique opportunity to

1
2 74 estimate the risk of the four adverse maternal outcomes between the two groups in a
3 75 cost-effective manner.

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5 76 • The method used to generate the exposure groups (planned VBAC and ERCS) could
6 77 have misclassified some women who were planning ERCS, but went into spontaneous
7 78 labour and were thus included under the VBAC group. However, we do not anticipate a
8 79 large proportion of such women.

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11 80 • Cases which could not be grouped into VBAC or ERCS due to missing information could
12 81 have biased the study results, mainly for the sepsis group. We have thus reported the
13 82 results of a sensitivity analysis.

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15 83 • A large epidemiological study with a greater number of cases would improve the power
16 84 and possibly show significant differences in the outcomes, however, this study intended
17 85 to take advantage of existing secondary data and the results could pave way for further
18 86 studies.

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23 88 **Key words:** Vaginal Birth after Caesarean, Elective Repeat Caesarean Section, peripartum
24 89 hysterectomy, severe sepsis, peripartum haemorrhage, failed tracheal intubation.

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26 90 **Word count:** 2413

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92 INTRODUCTION

93 Current UK guidelines^{1 2} advise that women who have undergone a prior delivery by caesarean
94 section should be informed of the risks and benefits of Elective Repeat Caesarean Section (ERCS)
95 as well as the risks and benefits of planned Vaginal Birth after Caesarean (VBAC). Such a
96 discussion requires comprehensive evidence of the risks associated with ERCS compared to VBAC.
97 Several studies have examined the risk of uterine rupture following VBAC,³⁻⁵ but robust data
98 comparing a wider range of complications of VBAC and ERCS are limited and the few randomised
99 controlled studies^{6 7} have limitations.

100 A previous study in the UK demonstrated uterine rupture to be associated with VBAC.⁸ Uterine
101 rupture is a rare and serious complication of VBAC, but when comparing ERCS and VBAC it is
102 important to consider other maternal complications. The aim of this study was therefore to estimate
103 the rates of other specific maternal risks associated with VBAC and ERCS using available national
104 data from the UK Obstetric Surveillance System (UKOSS).

105 METHODS

106 Study Design

107 We conducted a retrospective cohort analysis using data from the UKOSS. Details of the UKOSS
108 methodology are described elsewhere.^{9 10} UKOSS was set up in 2005 to investigate uncommon
109 disorders of pregnancy and 'near-miss' conditions.¹⁰ Case notification cards are sent to all
110 consultant-led obstetric units in the UK every month. An approach of 'nil-reporting' together with
111 rigorous follow-up of non-responders ensures good case ascertainment. For every case reported,
112 details are completed in a data collection form by the clinician responsible for managing the case.

113 Exposure groups were planned vaginal birth after caesarean (VBAC) and elective repeat caesarean
114 section (ERCS). Women who had a history of caesarean section and underwent elective caesarean
115 section during the current pregnancy were included in the ERCS group. Women who had a previous
116 caesarean section, but planned vaginal delivery during current pregnancy were included in the
117 planned VBAC group irrespective of whether they actually had a vaginal delivery.

118 Outcomes of interest were the maternal complications peripartum hysterectomy, severe sepsis,
119 peripartum haemorrhage and failed tracheal intubation, which are suggested to be related to VBAC
120 or ERCS in other studies.^{6 11 12} We had national datasets within UKOSS for the outcomes
121 (peripartum hysterectomy,¹³ severe sepsis,¹⁴ peripartum haemorrhage,^{15 16} and failed tracheal
122 intubation¹⁷) and thus case definitions were based on the standard case definitions used in the
123 UKOSS (provided in Table-1).

124 Table-1: Definitions of outcomes included from the UKOSS national studies

Condition	Definition
Peripartum hysterectomy	Any woman giving birth to an infant and having a hysterectomy during the same clinical episode.
Peripartum haemorrhage	Cases were pregnant women of 20 weeks gestation or more identified as having ≥ 8 units of red blood cell transfusion within a 24 hour period.
Failed tracheal intubation	A case of failed intubation was defined as failure to achieve tracheal intubation during a rapid sequence induction for obstetric anaesthesia, thereby initiating a failed intubation drill.
Severe sepsis	Any pregnant woman (up to six weeks postpartum) diagnosed with severe sepsis (irrespective of the source of infection). A severe sepsis case would be expected to include women in one of the following groups: <ol style="list-style-type: none"> 1. Death related to infection or suspected infection 2. Any women requiring level 2 or level 3 critical care (or obstetric HDU type care) due to severe sepsis or suspected severe sepsis 3. A clinical diagnosis of severe sepsis – based on 2 or more of the following – <ol style="list-style-type: none"> a. Temperature $> 38^{\circ}\text{C}$ or $< 36^{\circ}\text{C}$ measured on 2 occasions at least 4 hours apart b. Heart rate > 100 beats/minute measured on 2 occasions at least 4 hours apart c. Respiratory rate > 20/minute measured on 2 occasions at least 4 hours apart d. White cell count $> 17 \times 10^9/\text{L}$ or $< 4 \times 10^9/\text{L}$ or with $> 10\%$ immature band forms, measured on 2 occasions

125 **Study sample**

126 For each of the four maternal outcomes, for which a national dataset was available, we used the
127 total reported cases. The datasets were from four different UKOSS studies, thus the data included
128 were from different time-periods corresponding to the data collection period for each study (Table-2).
129 Among the cases, those without a previous history of caesarean section were excluded. We also
130 excluded women with placenta praevia/accreta/percreta diagnosed before delivery to exclude known
131 confounding due to these conditions which would be regarded as an absolute indication for ERCS.
132 The final sample of cases that remained were women with any previous caesarean sections and
133 were further divided into planned VBAC and ERCS groups based on planned mode of delivery. If a
134 dataset did not include information on 'planned mode of delivery', we investigated two other
135 variables – 'woman underwent induction of labour with or without prostaglandins and/or oxytocin'
136 and 'woman went into labour'. If either of these were 'true', we categorised the woman as planned
137 VBAC (irrespective of her actual mode of delivery - vaginal or caesarean), otherwise ERCS. If
138 information on any of these criteria was not available, we grouped the cases into a missing category.
139 A schematic diagram of the process of derivation of the study samples for peripartum hysterectomy,
140 severe sepsis, peripartum haemorrhage and failed intubation is provided in figure-1.

141 **Statistical analyses**

142 We calculated the incidence of each of the outcomes of interest with 95% confidence intervals (CI)
143 for the two exposure groups, VBAC and ERCS, using the denominators - total expected VBAC and

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3 144 ERCS maternities in a given year. The method of calculating proxy denominators was similar to that
4 145 used by Fitzpatrick et al. to report the incidence of uterine rupture in VBAC and ERCS groups.⁸ Total
5 146 maternities for the UK in the study period for each of the outcomes were calculated from the
6 147 annually reported birth data for England and Wales,¹⁸ Scotland¹⁹ and Northern Ireland.²⁰ From
7 148 these, we calculated the estimated number of maternities likely to have undergone previous
8 149 caesarean section, which was 13% of the total maternities, derived from a group of population
9 150 based controls comprised of women giving birth in the UK in 2012-13. Based on proportions
10 151 observed in the control group of the UKOSS uterine rupture study,⁸ we further divided the
11 152 maternities with previous caesarean section into women undergoing planned VBAC (44% of the
12 153 total maternities with previous caesarean section) and women undergoing planned ERCS (56% of
13 154 the total maternities with previous caesarean section) which gave the required proxy denominators.

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21 155 In addition, we also tested whether the calculated rates in the exposure groups were significantly
22 156 different from each other using chi square test or Fisher's exact test. We estimated the risk ratios
23 157 and exact 95% confidence intervals (CI) to ascertain the relative risk of severe maternal morbidities
24 158 in the planned VBAC compared to ERCS group. We also used descriptive statistics to compare the
25 159 two exposures groups. In order to account for any differences in known and potential confounding
26 160 factors, we conducted multivariable logistic regression analyses for the outcomes for which we had
27 161 a control group: peripartum hysterectomy, sepsis and failed intubation. The multivariable logistic
28 162 regression analysis results for uterine rupture have been published previously.⁸

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34 163 In the sample for sepsis, 11 cases could not be classified into VBAC or ERCS due to missing
35 164 information, and peripartum haemorrhage and hysterectomy each had one case with missing
36 165 information (Figure-1). We conducted a sensitivity analysis by calculating incidence rates assuming
37 166 extreme scenarios and accordingly including the missing numbers under each of the two exposure
38 167 groups.

39 40 41 42 168 **RESULTS**

43
44 169 A total of 83 confirmed cases of peripartum haemorrhage, 66 cases of hysterectomy, 49 cases of
45 170 severe sepsis and 7 cases of failed tracheal intubation were included in the study (Figure-1). The
46 171 exposure groups, ERCS and planned VBAC, for each of the outcomes were not significantly
47 172 different in terms of maternal age, body mass index (BMI), parity, history of previous pregnancy
48 173 problems and socioeconomic status. The calculated incidence rates of the maternal complications
49 174 were low and were not found to be significantly different between the two groups (Table-2). The
50 175 relative risk of the severe maternal morbidities was not different between the VBAC and ERCS
51 176 groups (Table-2).

177 Table-2: Rate of severe maternal morbidities in VBAC and ERCS groups

Conditions	Study period	Total Maternities for the study period	Maternities with previous Caesarean deliveries*	VBAC			ERCS			P-value of χ^2 test [‡] for outcome difference between VBAC & ERCS	Risk ratios (VBAC to ERCS) (Exact 95% CI)
				Maternities with previous CS with VBAC [†]	Cases	Estimated rate per 100,000 maternities (95% CI)	Maternities with previous CS with ERCS [‡]	Cases	Estimated rate per 100,000 maternities (95% CI)		
Uterine rupture [§]	01/04/2009 to 30/04/2010	852206	127831	56246	116	206.7 (170.5 - 247.3)	71585	20	27.9 (17.1 - 43.2)	<0.001	7.39 (4.58 - 12.55)
Peripartum hysterectomy	01/02/2005 to 29/02/2006	839785	109172	48036	35	72.9 (50.8 - 101.3)	61136	30	49.1 (33.1 - 70.0)	0.110	1.49 (0.89 - 2.50)
Sepsis	01/06/2011 to 31/05/2012	801770	104231	45861	23	50.1 (31.7 - 75.2)	58370	18	30.8 (18.3 - 48.7)	0.119	1.63 (0.84 - 3.19)
Peripartum haemorrhage	01/09/2007 to 31/03/2009 [§]	1176025	152884	67269	31	46.0 (31.3 - 65.4)	85616	51	59.5 (44.3 - 78.3)	0.259	0.77 (0.48 - 1.23)
Failed intubation	01/04/2008 to 31/03/2010	1504593	195597	86062	2	2.3 (0.2 - 8.3)	109535	5	4.5 (1.4 - 10.6)	0.476	0.51 (0.05 - 3.11)

178 *Proportion of maternities likely to have undergone previous caesarean section (based on 13% calculated from the Sepsis controls, 2012-13, drawn from the general
 179 population); [†] Proportion of maternities with previous caesarean section (CS) likely to undergo VBAC (based on 44% calculated from UKOSS-uterine rupture controls as was
 180 done by Fitzpatrick et al (8)); [‡] Proportion of maternities with previous caesarean section (CS) likely to undergo ERCS (based on 56% calculated from UKOSS-uterine rupture
 181 controls as was done by Fitzpatrick et al (8)); VBAC – Vaginal birth after caesarean; ERCS – Elective Repeat Caesarean section; CI – Confidence Interval; [§] For counts <5
 182 Fisher's Exact test was done instead of Pearson's chi squared test, [§] The total maternities for this 18 month study were calculated as: Total maternities in 2008 + half of the
 183 maternities in 2009, as the number of maternities found for 2007 (from the same sources) did not appear to be in complete agreement with the 2005-2012 trend. Owing to
 184 this uncertainty in the 2007 numbers, the 2008 and 2009 maternities have been used here.

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3 185 The unadjusted odds ratios for the adverse outcomes, for which we had a control group, were not
4 186 significantly different between the VBAC and ERCS groups (peripartum hysterectomy: unadjusted
5 187 odds ratio (uOR) = 0.86, 95% CI = 0.46 to 1.62; sepsis: uOR = 0.51, 95% CI = 0.24 to 1.07; failed
6 188 intubation: uOR=0.36, 95% CI = 0.02 to 5.11). The adjusted odds of peripartum hysterectomy
7 189 (adjusted odds ratio=0.92; 95%CI=0.45 to 1.91) and sepsis (adjusted odds ratio =0.51; 95% CI=0.22
8 190 to 1.19) in the ERCS group were not significantly different from that of the VBAC group after
9 191 controlling for current and previous pregnancy problems, number of previous caesarean sections,
10 192 pre-existing medical problems, parity, smoking status, socioeconomic status, ethnic background,
11 193 marital status, BMI and maternal age. The adjusted odds ratio was not meaningful for failed
12 194 intubation which had a total sample size of 15.

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19 195 Sensitivity analysis for cases with missing information showed that although the rates changed
20 196 slightly in the planned VBAC and ERCS groups for peripartum haemorrhage and hysterectomy, it
21 197 did not result in a significant difference in the risk of the adverse outcome between the two exposure
22 198 groups in either scenario. However, for severe sepsis, when all the 11 cases with missing
23 199 information were included in the planned VBAC group, the rate in the VBAC group was found to be
24 200 significantly higher than the rate in the ERCS group (p-value for chi square test=0.002). When these
25 201 cases were included in the ERCS group, the rates of sepsis in the two exposure groups were equal
26 202 (50 per 100,000 maternities).

203 **DISCUSSION**

204 This study using the UKOSS data and a nested retrospective cohort design did not find a significant
205 206 difference in the incidence and relative risk of adverse maternal outcomes between the VBAC and
207 ERCS groups. However, the incidence rates of these outcomes were low.

207 **Strengths and Limitations**

208 Low incidence of severe maternal morbidities in the UK makes it difficult to compare their risks
209 210 between VBAC and ERCS groups. The UKOSS database of research data on rare and potentially
211 212 life threatening conditions in pregnancy provided a unique opportunity to estimate the risk of four
213 214 adverse maternal outcomes between the two groups in a cost-effective manner. The method used to
215 216 generate the exposure groups (planned VBAC and ERCS) could have misclassified some women
217 218 who were planning ERCS, but went into spontaneous labour and were thus included under the
219 VBAC group. However, we do not anticipate a large proportion of such women. Cases which could
220 not be grouped into VBAC or ERCS due to missing information could have biased the study results,
221 222 mainly for the sepsis group. We have thus reported the results of a sensitivity analysis. Further,
223 224 including a proxy denominator calculated from a control population comprising of women giving birth
225 226 in 2012-13 assumes that the rate of caesarean sections and proportions of VBAC and ERCS did not

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3 219 vary over a time-period between 2005-06 and 2012-13. Considering that population level caesarean
4 220 section rates for the UK per year were not available from any source, we employed this alternative
5 221 method used in a previous study by Fitzpatrick et al.⁸ Although we accounted for known
6 222 confounders for each outcome in the multivariable logistic regression analyses, the results cannot
7 223 be interpreted with certainty due to the small sample sizes. While we excluded women diagnosed
8 224 antenatally with placenta praevia/accreta/percreta, we did not have information on other potential
9 225 absolute indications for ERCS, which could bias the study results. A longer term study with a
10 226 greater number of cases would improve the power and possibly show significant differences in the
11 227 outcomes, however, this study intended to take advantage of existing secondary data and the
12 228 results could pave the way for further studies. Furthermore, the adverse outcomes presented in this
13 229 study are immediate risks associated with the current pregnancy in the ERCS and VBAC groups
14 230 and we cannot comment on the risk of morbidity in future pregnancies.

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22 231 While the higher risk of uterine rupture associated with planned VBAC is known,^{4 8 21 22} studies from
23 232 different parts of the world have reported variable relative and absolute risks of other maternal
24 233 complications in ERCS versus VBAC groups. Similar to the findings of this study, a multicentre
25 234 prospective cohort study in the USA,⁴ a Canadian study¹¹ and a meta-analysis of literature published
26 235 between 2000 and 2007²² did not find any difference in the risk of hysterectomy between those that
27 236 underwent a trial of labour and those that had an elective caesarean section. However, a decision
28 237 model analysis conducted by Paré et al. suggested that the decision to undergo VBAC or ERCS
29 238 among women with one prior caesarean section should be guided by the number of planned
30 239 subsequent pregnancies.²³ Based on an analysis of risk of hysterectomy, the authors suggested that
31 240 ERCS should be the strategy of choice for women planning one additional pregnancy, but for
32 241 women who desire two or more subsequent pregnancies VBAC should be attempted to minimise
33 242 morbidity associated with multiple caesarean sections.²³

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41 243 In contrast to our findings, a study in Australia found a 63% lower risk of peripartum haemorrhage in
42 244 the planned ERCS compared to planned VBAC group⁶ and the multicentre study from the USA
43 245 demonstrated a higher odds of transfusion in the VBAC group compared with the ERCS.⁴ However,
44 246 a meta-analysis suggested a lower risk of peripartum haemorrhage in the VBAC group²¹ and other
45 247 studies did not show any difference.^{11 22} A prospective cohort study of obese women using data
46 248 collected through the UKOSS did not find any difference in anaesthetic complications between
47 249 ERCS and planned VBAC groups,²⁴ but this finding cannot be generalised to non-obese women.

52 250 **Conclusion**

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55 251 While the risk of uterine rupture in VBAC and ERCS groups is well understood, this national study
56 252 did not demonstrate any other clear differences in the outcomes we examined. The absolute and
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253 relative risks of maternal complications were small in both groups which is important information to
 254 help pregnant women in their decision making process. Large epidemiological studies with a longer
 255 time-period for data collection are required to assess whether the incidence of these rare outcomes
 256 would significantly differ between VBAC and ERCS groups if a larger number of cases were to be
 257 examined. In the interim, this study contributes additional information to the process of individualised
 258 decision-making about mode of delivery by women who have had a previous delivery by caesarean
 259 section, as recommended in current guidance.

260 REFERENCES

- 261 1. Royal College of Obstetricians and Gynaecologists. Birth After Previous Caesarean Birth (Green-top 45):
 262 RGOG, 2007.
- 263 2. National Institute for Health and Care Excellence. Caesarean section (CG132): NICE, 2011.
- 264 3. Guise J-M, McDonagh MS, Osterweil P, Nygren P, Chan BK, Helfand M. Systematic review of the incidence
 265 and consequences of uterine rupture in women with previous caesarean section. *BMJ: British*
 266 *Medical Journal* 2004;329(7456):19-25.
- 267 4. Landon MB, Hauth JC, Leveno KJ, Spong CY, Leindecker S, Varner MW, et al. Maternal and perinatal
 268 outcomes associated with a trial of labor after prior cesarean delivery. *New England Journal of*
 269 *Medicine* 2004;351(25):2581-89.
- 270 5. Odibo AO, Macones GA. Current concepts regarding vaginal birth after cesarean delivery. *Current opinion*
 271 *in obstetrics & gynecology* 2003;15(6):479-82.
- 272 6. Crowther CA, Dodd JM, Hiller JE, Haslam RR, Robinson JS, on behalf of the Birth After Caesarean Study
 273 Group. Planned Vaginal Birth or Elective Repeat Caesarean: Patient Preference Restricted Cohort
 274 with Nested Randomised Trial. *PLoS Med* 2012;9(3):e1001192.
- 275 7. Law LW, Pang MW, Chung TK-H, Lao TT-H, Lee DT-S, Leung TY, et al. Randomised trial of assigned mode of
 276 delivery after a previous cesarean section-Impact on maternal psychological dynamics. *Journal of*
 277 *Maternal-Fetal and Neonatal Medicine* 2010;23(10):1106-13.
- 278 8. Fitzpatrick KE, Kurinczuk JJ, Alfirevic Z, Spark P, Brocklehurst P, Knight M. Uterine Rupture by Intended
 279 Mode of Delivery in the UK: A National Case-Control Study. *PLoS Med* 2012;9(3):e1001184.
- 280 9. Knight M, Lindquist A. The UK Obstetric Surveillance System: Impact on patient safety. *Best Practice &*
 281 *Research Clinical Obstetrics & Gynaecology* 2013;27(4):621-30.
- 282 10. Knight M, Kurinczuk JJ, Tuffnell D, Brocklehurst P. The UK Obstetric Surveillance System for rare disorders
 283 of pregnancy. *BJOG: An International Journal of Obstetrics & Gynaecology* 2005;112(3):263-65.
- 284 11. McMahon MJ, Luther ER, Bowes WA, Olshan AF. Comparison of a Trial of Labor with an Elective Second
 285 Cesarean Section. *New England Journal of Medicine* 1996;335(10):689-95.
- 286 12. van Ham MAPC, van Dongen PWJ, Mulder J. Maternal consequences of caesarean section. A
 287 retrospective study of intra-operative and postoperative maternal complications of caesarean
 288 section during a 10-year period. *European Journal of Obstetrics & Gynecology and Reproductive*
 289 *Biology* 1997;74(1):1-6.
- 290 13. Knight M, on behalf of UKOSS. Peripartum hysterectomy in the UK: management and outcomes of the
 291 associated haemorrhage. *BJOG: An International Journal of Obstetrics & Gynaecology*
 292 2007;114(11):1380-87.
- 293 14. Acosta CD, Knight M, Lee HC, Kurinczuk JJ, Gould JB, Lyndon A. The Continuum of Maternal Sepsis
 294 Severity: Incidence and Risk Factors in a Population-Based Cohort Study. *PLoS one* 2013;8(7):e67175.
- 295 15. Kayem G, Kurinczuk JJ, Alfirevic Z, Spark P, Brocklehurst P, Knight M. Uterine compression sutures for the
 296 management of severe postpartum hemorrhage. *Obstetrics & Gynecology* 2011;117(1):14-20.
- 297 16. Kayem G, Kurinczuk JJ, Alfirevic Z, Spark P, Brocklehurst P, Knight M. Specific second-line therapies for
 298 postpartum haemorrhage: a national cohort study. *BJOG: An International Journal of Obstetrics &*
 299 *Gynaecology* 2011;118(7):856-64.

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2
3 300 17. Quinn AC, Milne D, Columb M, Gorton H, Knight M. Failed tracheal intubation in obstetric anaesthesia: 2
4 301 yr national case-control study in the UK. *British Journal of Anaesthesia* 2013;110(1):74-80.
5 302 18. Office for National Statistics. Birth summary tables, England and Wales. Newport: Office for National
6 303 Statistics.
7 304 19. General Register Office for Scotland. Vital Events Reference Tables. Edinburgh: General Register Office for
8 305 Scotland.
9 306 20. Northern Ireland Statistics and Research Agency. Registrar General Annual Reports Belfast: NISRA.
10 307 21. Mozurkewich EL, Hutton EK. Elective repeat cesarean delivery versus trial of labor: a meta-analysis of the
11 308 literature from 1989 to 1999. *American Journal of Obstetrics and Gynecology* 2000;183(5):1187-97.
12 309 22. Rossi AC, D'Addario V. Maternal morbidity following a trial of labor after cesarean section vs elective
13 310 repeat cesarean delivery: a systematic review with metaanalysis. *American journal of obstetrics and*
14 311 *gynecology* 2008;199(3):224-31.
15 312 23. Paré E, Quinones JN, Macones GA. Vaginal birth after caesarean section versus elective repeat caesarean
16 313 section: assessment of maternal downstream health outcomes. *BJOG-an International Journal of*
17 314 *Obstetrics and Gynaecology* 2006;113(1):75-85.
18 315 24. Homer CSE, Kurinczuk JJ, Spark P, Brocklehurst P, Knight M. Planned vaginal delivery or planned
19 316 caesarean delivery in women with extreme obesity. *BJOG: An International Journal of Obstetrics &*
20 317 *Gynaecology* 2011;118(4):480-87.
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25 319 **Caption for the figure**

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27 320 Figure 1: Schematic diagram of derivation of study sample
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33 323 **Competing interest:** The authors declare that they have no competing interests.
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35 324 **Ethics statement:** The London Multi-centre Research Ethics Committee approved the UK Obstetric
36 325 Surveillance System (UKOSS) general methodology (04/MRE02/45) and the surveillance of
37 326 individual near-miss maternal morbidities using UKOSS (04/MRE02/73, 10/H0717/20, 08/H0781/1,
38 327 07/MRE02/24).
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42 329 of the article. KS contributed to the writing of the article. NN contributed to the analysis. MK
43 330 designed the study, supervised the data collection and analysis, and contributed to writing the
44 331 article. MG developed the research question, contributed to the design of the study and writing the
45 332 article.
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3 340 **Data sharing statement:** Data sharing is governed by the National Perinatal Epidemiology Unit

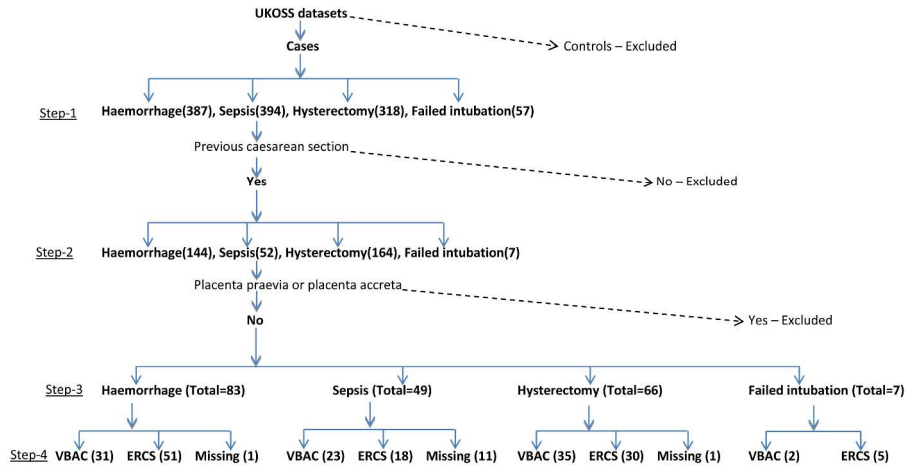
4 341 Data Sharing policy, available on request from Prof. Marian Knight.

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Figure 1: Schematic diagram of derivation of study sample



UKOSS – UK Obstetric Surveillance System; VBAC - Vaginal Birth after Caesarean; ERCS - Elective Repeat Caesarean Section

Figure 1: Schematic diagram of derivation of study sample
275x181mm (300 x 300 DPI)

Review only

STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

	Item No	Recommendation	Page number/s
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1 & 2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4 & 5
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5 (methods of follow-up – not applicable because it is a retrospective cohort analysis)
		(b) For matched studies, give matching criteria and number of exposed and unexposed	Not applicable
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4 & 5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4 & 5
Bias	9	Describe any efforts to address potential sources of bias	5 & 6
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5 & 6
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	5 & 6
		(b) Describe any methods used to examine subgroups and interactions	Not applicable
		(c) Explain how missing data were addressed	6
		(d) If applicable, explain how loss to follow-up was addressed	Not applicable
		(e) Describe any sensitivity analyses	6
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5 & Figure-1
		(b) Give reasons for non-participation at each stage	Not applicable
		(c) Consider use of a flow diagram	Figure-1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential	6

		confounders	
		(b) Indicate number of participants with missing data for each variable of interest	6, 7, 8 & Figure-1
		(c) Summarise follow-up time (eg, average and total amount)	Not applicable
Outcome data	15*	Report numbers of outcome events or summary measures over time	6, 7 & 8
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8
		(b) Report category boundaries when continuous variables were categorized	Not applicable
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	8
Discussion			
Key results	18	Summarise key results with reference to study objectives	8
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	8 & 9
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9
Generalisability	21	Discuss the generalisability (external validity) of the study results	9
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	11

*Give information separately for exposed and unexposed groups.