Does a Caesarean section increase the time to a second live birth? A register-based cohort study

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Submitted on March 20, 2014; resubmitted on July 21, 2014; accepted on July 30, 2014

STUDY QUESTION: Does a primary Caesarean section influence the rate of, and time to, subsequent live birth compared with vaginal delivery?

SUMMARY ANSWER: Caesarean section was associated with a reduction in the rate of subsequent live birth, particularly among elective and maternal-requested Caesareans indicating maternal choice plays a role.

WHAT IS KNOWN ALREADY: Several studies have examined the relationship between Caesarean section and subsequent birth rate with conflicting results primarily due to poor epidemiological methods.

STUDY DESIGN, SIZE, DURATION: This Danish population register-based cohort study covered the period from 1982 to 2010 (N = 832,996).

PARTICIPANTS/MATERIALS, SETTING, METHODS: All women with index live births were followed until their subsequent live birth or censored (maternal death, emigration or study end) using Cox regression models.

MAIN RESULTS AND THE ROLE OF CHANCE: In all 577,830 (69%) women had a subsequent live birth. Women with any type of Caesarean had a reduced rate of subsequent live birth (hazard ratio [HR] 0.86, 95% confidence intervals [CI] 0.85, 0.87) compared with spontaneous vaginal delivery. This effect was consistent when analyses were stratified by type of Caesarean: emergency (HR 0.87, 95% CI 0.86, 0.88), elective (HR 0.83, 95% CI 0.82, 0.84) and maternal-requested (HR 0.61, 95% CI 0.57, 0.66) and in the extensive sub-analyses performed.

LIMITATIONS, REASONS FOR CAUTION: Lack of biological data to measure a woman’s fertility is a major limitation of the current study. Unmeasured confounding and limited availability of data (maternal BMI, smoking, access to fertility services and maternal-requested Caesarean section) as well as changes in maternity care over time may also influence the findings.

WIDER IMPLICATIONS OF THE FINDINGS: This is the largest study to date and shows that Caesarean section is most likely not causally related to a reduction in fertility. Maternal choice to delay or avoid childbirth is the most plausible explanation. Our findings are generalizable to other middle- to high-income countries; however, cross country variations in Caesarean section rates and social or cultural differences are acknowledged.

STUDY FUNDING/COMPETING INTEREST(S): Funding was provided by the National Perinatal Epidemiology Centre, Cork, Ireland and conducted as part of the Health Research Board PhD Scholars programme in Health Services Research (Grant No. PHD/2007/16). L.C.K. is a Science Foundation Ireland Principal Investigator (08/IN.1/B2083) and the Director of the SFI funded Centre, INFANT (12/RC/2272). The authors have no competing interests to declare.

Key words: Caesarean delivery / time to next birth / live birth rate / birth cohort / mode of delivery

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Introduction

Caesarean section rates have increased worldwide over the past three decades (OECD, 2013). Current figures reveal that 25% of all births in the UK are delivered via Caesarean section (Lavender et al., 2012), over 30% in Australia (Dahlen et al., 2012) and the USA (Macdorman et al., 2012) and over 50% in Brazil (Victora et al., 2011) and China (Fu et al., 2010). The rise in Caesarean sections has been attributed to an increase in the section rate among first time mothers, a decrease in the vaginal birth after Caesarean rate, as well as increasing fears of litigation among clinicians and in recent years maternal request for a Caesarean to be performed (Dahlgren et al., 2009; Stavrou et al., 2011; Minkoff, 2012; Roberts et al., 2012).

Several studies have examined the relationship between Caesarean section and the rate and time to subsequent live birth with conflicting results (Hemminki, 1996; Porter et al., 2003; Smith et al., 2006; Tollanes et al., 2007). Time to pregnancy is considered a robust surrogate marker of subfertility (Maheshwari et al., 2008; Rothman et al., 2008) with a recent systematic review and meta-analysis reporting a 10% reduction in subsequent birth rates following Caesarean section (O’Neill et al., 2013). Various mechanisms as to why a previous Caesarean section may lead to a reduction in subsequent birth rates and a longer time to next delivery include placental bed disruption and pelvic adhesion as a result of the procedure (Murphy et al., 2002; Gurol-Urganci et al., 2013). Furthermore, with considerably more women working full time or staying in education longer maternal choice to delay or avoid childbirth is a plausible explanation (Porter et al., 2003; Oral and Elter, 2007; Tollanes et al., 2007).

The research conducted to date has been limited by the availability of key factors considered to be vital in establishing whether a Caesarean section impacts the rate and time to subsequent live birth. Most notably of these are the absence of the indication for mode of delivery, as well as information on a woman’s obstetric history including pre-existing subfertility and access to fertility services in the past. Furthermore, trying to establish whether a pregnancy was planned or unplanned (in order to ascertain voluntary or involuntary delay in the time to next pregnancy or birth) has been difficult, especially in studies using retrospective methods where this information was not recorded. Therefore, careful consideration must be given to any potential obstetric, social, medical and socio-economic factors which are likely to confound the relationship between Caesarean section and the rate and time to subsequent live birth (Murphy et al., 2002).

The aim of this study was to estimate the fecundity (i.e. whether a lower proportion of second live births occurred) in women with a primary Caesarean section compared with spontaneous vaginal delivery (SVD) using a large birth cohort. Mode of delivery in the first live birth and the rate and time to subsequent live birth according to the different mode of delivery groups will be used in this study as a measure of ‘subfertility’. The nationwide Danish Civil Registration System (CRS) data include information on over 830,000 women spanning 28 years of follow-up. Detailed information on the indication for mode of delivery (including operative vaginal delivery, emergency Caesarean, elective Caesarean and the novel ‘maternal-requested’ Caesarean), as well as details on previous recognized pregnancy loss, access to fertility services and underlying medical conditions including diabetes, placenta praevia and pre-eclampsia) and key potential confounders such as smoking and BMI, which are all largely absent from the research conducted to date were available for the current analyses.

Methods

Study design and registers

A cohort study design including data from the Danish CRS was used to estimate the rate and time to next live birth following Caesarean section in the first live birth. The Danish CRS was established in 1968 originally for administrative purposes, but has become an invaluable source of data for epidemiological research in recent years. The system utilizes a civil person register (CPR) number, a unique personal identification number, which enables accurate linkage between and within the many different registers as well as the continuous follow-up of individuals alive and resident in Denmark (Pedersen, 2011).

For the current study the Danish CRS data were linked to the Danish National Hospital Register (NHR) (Andersen and Erb, 2006; Lynge et al., 2011), the Danish Medical Birth Registry (MBR) (Kristensen et al., 1996; Knudsen and Olsen, 1999), the Danish In Vitro Fertilisation (IVF) Register (Andersen et al., 1999; Andersen and Erb, 2006), the Danish Causes of Death Register (Helweg-Larsen, 2011) and Statistics Denmark. The Danish NHR contains countrywide records on all admissions to every Danish hospital since 1977, and information on all emergency and outpatient visits since 1995 (Lynge et al., 2011). The MBR comprises information on all births in Denmark since 1973, including all live births, stillbirths and neonatal deaths (Knudsen and Olsen, 1999). The IVF Register established in 1994 covers all fertility treatments and it is mandatory for all fertility clinics to report treatments administered (Andersen et al., 1999). In addition, all pharmacological treatments administered to women (in fertility clinics, hospitals or by a general practitioner) are recorded in the CRS registers ensuring complete coverage. Statistics Denmark is governed by the Ministry of Economic Affairs and collects, compiles and publishes Danish society statistics including educational attainment, income and other socio-economic variables. The CRS contains detailed information including name, gender, date of birth, place of birth and residence, vital status, CPR number of parents and spouses along with >150 other variables (Pedersen et al., 2006).

Study population and follow-up

The study population was restricted to include all women with an index live birth during the study period. We identified all live births to primiparous women in Denmark between 1 January 1982 and 31 December 2010 using the linked registers. The study population for analyses consisted of 832,996 index live births. These women were followed until the subsequent live birth or until censoring due to maternal death, emigration or study end (31 December 2010). A flow chart of inclusions and exclusions in the study population is shown in Fig. 1.

Mode of delivery

Mode of delivery in the first live birth was classified according to the recorded indication for mode of delivery: (i) SVD, (ii) operative vaginal delivery [assisted forceps or vacuum delivery], (iii) emergency Caesarean section (i.e. unplanned Caesareans due to complications for example, fetal distress), (iv) elective Caesarean section (planned Caesarean section with or without medical indication) and (v) maternally requested Caesarean section (recorded as a tick box option indicating maternal choice to elect a Caesarean). Data for maternally requested Caesarean section were available from 2002 to 2010 only.
Main outcome measure and classification
Diagnostic information is based on the Danish version of the International
Classification of Disease 8th revision (ICD) [from 1977 to 1993], and the
ICD-10th revision (from 1994 to the present time). Rate of subsequent
live birth following the index delivery was the outcome of interest in the
current study. In addition the median time to next live birth was estimated
defined as the time elapsed beginning at the date of birth of the index
child until the date of birth of the subsequent live born child.

Covariate definitions
Maternal covariates of the first live birth included: age in years; country of
origin; BMI [data available for 2003–2010 only]; history of stillbirth, miscar-
criage or ectopic pregnancy before the first live birth; educational attain-
ment; gross income; marital status and co-morbidities (pre-eclampsia,
eclampsia, placenta praevia, placental abruption, diabetes and gestational
diabetes); smoking status [data available for 1997–2010 only] and
history of access to fertility services [data available for 1994–2005 only].
Infant covariates included: gestational age in weeks; birthweight in grams;
length in centimetres (cm) and sex (Supplementary data, Table SI).

Missing data
Variables with missing data in the CRS cohort included: birthweight (n =
6486, 0.8%); BMI (n = 41 663, 18%), educational attainment (n = 41 320,
5%), gestational age (n = 12 741, 1.5%), infant length (n = 17 070, 2%),
father’s income (n = 21 076, 2.5%), mother’s income (n = 10 817, 1.3%)
marital status (n = 14 903, 1.8%) and smoking (n = 26 900, 6.6%) as
shown in Fig. 1. Where a variable had missing data, the data were added as
a separate category using the ‘missing-indicator’ method (Miettinen, 1985)
and included in the various analyses. The main advantage of using the indica-
tor method is that all cases are included in the analyses and as outlined by
Vach et al., adding missing data as a separate category where the proportion
of missing data is small should not impact greatly on the effect estimates (Vach
and Blettner, 1991).

Statistical analysis
The rate of subsequent live birth was compared among the different
modes of delivery using time-to-event analyses including Cox proportion-
al hazards modelling to estimate the hazard ratio (HR) and correspond-
ing 95% confidence intervals (CI). With this method, the gestational age
at birth is taken into account (i.e. gestational age varies according to each
woman’s pregnancy) as well as the fact that some women will have no
further pregnancies. In this study, women were followed up from the
date of birth of the first child until the subsequent live birth. Women
with no subsequent live birth were followed up until the end of the
study period.

Primary analyses
Firstly we performed crude analyses by comparing women with any type of
Caesarean section to the reference group of women with a SVD in the first
live birth. Next we repeated the analyses by indication for mode of delivery.
We performed a priori adjusted analyses as follows including covariates
recorded in the first live birth which are likely to influence a woman’s decision
to have a subsequent birth:

Model 1: maternal age; country of origin; history of stillbirth, miscarriage or
ectopic pregnancy; educational attainment; mother and father’s gross
income; marital status and birth year.

Model 2: adjusted for Model 1 + medical complications in the first live birth:
delivery type (singleton, multiple); diabetes; gestational diabetes; placen-
tal abruption; placenta praevia and hypertensive disorders (eclampsia,
preeclampsia).

Model 3: adjusted for Model 2 + gestational age; birthweight and infant sex
and length.
Variables were categorized in the analyses as presented in Table I and Supplementary data, Table SI.

**Additional adjusted analyses**

Further adjusted analyses were conducted adding variables to each model for which data were only available for specific time points: smoking (data from 1997 to 2010), BMI (data from 2003 to 2010) and previous fertility treatment (data from 1994 to 2005) and history of psychiatric treatment before the first live birth. For example, data on BMI were only available from 2003 to 2010 so the cohort was restricted to this time period and the analyses repeated.

**Additional subgroup analyses**

A time-dependent analysis of infant death within 12 months of the first live birth was also performed as well as subgroup analyses including: smokers only; women of advanced maternal age (35+); term deliveries (>37 weeks); low birthweight (<2500 g); macrosomia (>4.5 kg) and by time period (1982–

<p>| Table I Baseline characteristics of the study population in the first live birth. |</p>
<table>
<thead>
<tr>
<th>Maternal characteristics</th>
<th>Spontaneous vaginal delivery (SVD)</th>
<th>Operative vaginal delivery (OVD)</th>
<th>Emergency Caesarean section</th>
<th>Elective Caesarean section</th>
<th>*Maternal-requested Caesarean section (data 2002–2010 only)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%)</td>
<td>607 252 (72.90)</td>
<td>79 827 (9.58)</td>
<td>104 091 (12.50)</td>
<td>38 950 (4.68)</td>
<td>2876 (1.11)</td>
</tr>
<tr>
<td>Maternal age, years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td>21 883 (3.60)</td>
<td>1555 (1.54)</td>
<td>1994 (1.92)</td>
<td>585 (1.50)</td>
<td>28 (0.97)</td>
</tr>
<tr>
<td>20–25</td>
<td>210 595 (34.68)</td>
<td>17 828 (22.34)</td>
<td>25 840 (24.82)</td>
<td>8356 (21.45)</td>
<td>364 (12.66)</td>
</tr>
<tr>
<td>26–30</td>
<td>245 579 (40.44)</td>
<td>35 687 (44.71)</td>
<td>41 448 (39.81)</td>
<td>15 134 (38.85)</td>
<td>812 (28.23)</td>
</tr>
<tr>
<td>31–35</td>
<td>100 283 (16.52)</td>
<td>18 995 (23.81)</td>
<td>24 760 (23.79)</td>
<td>9888 (25.39)</td>
<td>977 (33.97)</td>
</tr>
<tr>
<td>36–40</td>
<td>25 427 (4.19)</td>
<td>5326 (6.68)</td>
<td>8574 (8.24)</td>
<td>4130 (10.60)</td>
<td>545 (18.95)</td>
</tr>
<tr>
<td>41+</td>
<td>3485 (0.57)</td>
<td>736 (0.92)</td>
<td>1475 (1.42)</td>
<td>857 (2.21)</td>
<td>150 (5.22)</td>
</tr>
<tr>
<td>Maternal origin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Denmark</td>
<td>527 328 (86.82)</td>
<td>79 102 (99.09)</td>
<td>90 540 (86.98)</td>
<td>34 340 (88.16)</td>
<td>2249 (78.20)</td>
</tr>
<tr>
<td>Other</td>
<td>78 003 (12.85)</td>
<td>525 (0.66)</td>
<td>13 243 (12.72)</td>
<td>4470 (11.48)</td>
<td>615 (21.38)</td>
</tr>
<tr>
<td>Unknown</td>
<td>1921 (0.33)</td>
<td>200 (0.25)</td>
<td>308 (0.30)</td>
<td>140 (0.36)</td>
<td>12 (0.42)</td>
</tr>
<tr>
<td>Birth type</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Singleton</td>
<td>601 111 (98.99)</td>
<td>79 455 (99.53)</td>
<td>98 972 (95.08)</td>
<td>35 462 (91.04)</td>
<td>2700 (93.88)</td>
</tr>
<tr>
<td>Multiple (twins or more)</td>
<td>6141 (1.01)</td>
<td>372 (0.47)</td>
<td>5119 (4.92)</td>
<td>3488 (8.96)</td>
<td>176 (6.12)</td>
</tr>
<tr>
<td>*Smoker</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>40 919 (15.13)</td>
<td>6971 (13.55)</td>
<td>8513 (14.31)</td>
<td>2966 (13.99)</td>
<td>362 (12.59)</td>
</tr>
<tr>
<td>Non-smoker</td>
<td>211 833 (78.32)</td>
<td>41 639 (80.91)</td>
<td>46 472 (78.11)</td>
<td>16 580 (78.23)</td>
<td>2343 (81.46)</td>
</tr>
<tr>
<td>Unknown</td>
<td>17 722 (6.55)</td>
<td>2849 (5.54)</td>
<td>4509 (7.58)</td>
<td>1649 (7.78)</td>
<td>171 (5.95)</td>
</tr>
<tr>
<td>BMI data</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>&lt; 18.5</td>
<td>9673 (6.54)</td>
<td>1874 (6.32)</td>
<td>1609 (4.41)</td>
<td>758 (5.88)</td>
<td>209 (7.42)</td>
</tr>
<tr>
<td>18.5–25</td>
<td>84 390 (56.94)</td>
<td>17 379 (58.67)</td>
<td>19 072 (52.22)</td>
<td>7092 (55.01)</td>
<td>1667 (59.16)</td>
</tr>
<tr>
<td>26–30</td>
<td>17 482 (11.80)</td>
<td>3757 (12.68)</td>
<td>5812 (15.91)</td>
<td>1707 (13.24)</td>
<td>414 (14.69)</td>
</tr>
<tr>
<td>31–35</td>
<td>601 I (4.02)</td>
<td>1199 (4.05)</td>
<td>2409 (6.60)</td>
<td>662 (5.13)</td>
<td>157 (5.57)</td>
</tr>
<tr>
<td>36–40</td>
<td>1877 (1.27)</td>
<td>360 (1.22)</td>
<td>930 (2.55)</td>
<td>250 (1.94)</td>
<td>49 (1.74)</td>
</tr>
<tr>
<td>41+</td>
<td>827 (0.57)</td>
<td>153 (0.52)</td>
<td>472 (1.29)</td>
<td>128 (0.99)</td>
<td>24 (0.85)</td>
</tr>
<tr>
<td>Unknown</td>
<td>27 950 (18.86)</td>
<td>4900 (16.54)</td>
<td>6218 (17.02)</td>
<td>2297 (17.81)</td>
<td>298 (10.57)</td>
</tr>
<tr>
<td>Educational attainment</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Primary education</td>
<td>164 565 (27.11)</td>
<td>14 899 (18.66)</td>
<td>24 502 (23.54)</td>
<td>8679 (22.28)</td>
<td>501 (17.42)</td>
</tr>
<tr>
<td>High school</td>
<td>278 573 (45.87)</td>
<td>39 660 (49.68)</td>
<td>49 058 (47.13)</td>
<td>18 423 (47.30)</td>
<td>1178 (40.96)</td>
</tr>
<tr>
<td>Third level degree</td>
<td>100 762 (16.59)</td>
<td>16 054 (20.11)</td>
<td>19 544 (18.78)</td>
<td>7551 (19.39)</td>
<td>585 (20.34)</td>
</tr>
<tr>
<td>Masters/PhD</td>
<td>31 386 (5.17)</td>
<td>6184 (7.75)</td>
<td>6469 (6.21)</td>
<td>2726 (7.00)</td>
<td>377 (13.11)</td>
</tr>
<tr>
<td>Unknown</td>
<td>31 966 (5.26)</td>
<td>3030 (3.80)</td>
<td>4518 (4.34)</td>
<td>1571 (4.03)</td>
<td>235 (8.17)</td>
</tr>
<tr>
<td>Prior fertility treatment</td>
<td>13 383 (2.20)</td>
<td>2604 (3.26)</td>
<td>4729 (4.52)</td>
<td>2584 (6.27)</td>
<td>172 (5.98)</td>
</tr>
</tbody>
</table>

*Data are n (%) unless otherwise specified.*

*Maternal-requested Caesarean section: data available from 2002 to 2010 only (cohort n = 258 445).*

*Smoking data: available 1997–2010 only (n = 405 498).*

*BMI data: available 2003–2010 only (n = 230 066).*

*Prior fertility treatment: data from 1994 to 2005 (n = 353 650).*
Median time to next birth in days
In women with a subsequent live birth only, the median time to next live birth with corresponding 95% confidence intervals was calculated according to mode of delivery using the proc univariate command in SAS and crude estimates. For maternal-requested Caesarean, data were restricted to 2002–2010 as outlined previously.

All analyses were performed using SAS© version 9.2 software (SAS Institute, Inc., Cary, NC, USA).

Ethical approval
Approval to use the data was secured from the National Board of Health and Statistics Denmark for the current study (DNBH, 2013).

Results
Population characteristics
A summary of the demographic, maternal and infant characteristics according to mode of delivery in the first live birth for all women in the study cohort are presented in Table I (with more detailed information presented in Supplementary data, Table SI). There were 832,996 first live births in the cohort. Of these, 607,252 (73%) were by SVD; 79,827 (9.6%) were by operative vaginal delivery; 104,091 (12.5%) were by emergency Caesarean section and 38,950 (4.7%) were by elective Caesarean section. From 2002 to 2010 there were 2876 (1.1%) maternal-requested Caesarean sections. The Caesarean section rate for the entire study population over the 28-year follow-up was 17.6%. Overall, there was a trend of increasing Caesarean section rates, with a rate of 12.8% in 1982 rising to 22.8% in 2010. For maternally requested Caesarean section, a similar increasing trend was found, with a rate of 2% in 2002 and over 14% in 2010.

Rate of subsequent live birth
Of the 832,996 women in the study cohort, 577,830 (69%) had a subsequent live birth during the study period. Women with any type of Caesarean section (emergency, elective, maternal-requested) in the first live birth were significantly less likely to have a subsequent live birth in both the crude and adjusted analyses (HR 0.86, 95% CI 0.85, 0.87) compared with a SVD or operative vaginal delivery. Analysis by type of Caesarean showed that women with an emergency Caesarean were 13% less likely (HR 0.87, 95% CI 0.86–0.88), women with an elective Caesarean were 17% less likely (HR 0.83, 95% CI 0.82–0.84) and women with a maternally requested Caesarean were 39% less likely (HR 0.61, 95% CI 0.57–0.66) (Table II).

Table II: Caesarean section and rate of subsequent live birth.

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Crude model</td>
<td>Adjusted HR (95% CI)</td>
</tr>
<tr>
<td>Live birth (n = 577,830)</td>
<td></td>
<td>Model 1</td>
</tr>
<tr>
<td>Spontaneous vaginal (n = 437,608)</td>
<td>Ref (1.01, 1.03)</td>
<td>1.00 (0.99, 1.01)</td>
</tr>
<tr>
<td>Operative vaginal (n = 54,047)</td>
<td>0.76 (0.75, 0.77)</td>
<td>0.81 (0.80, 0.82)</td>
</tr>
<tr>
<td>All Caesarean sections (n = 86,175)</td>
<td>0.80 (0.79, 0.81)</td>
<td>0.83 (0.82, 0.84)</td>
</tr>
<tr>
<td>Emergency Caesarean (n = 63,341)</td>
<td>0.69 (0.68, 0.70)</td>
<td>0.75 (0.74, 0.76)</td>
</tr>
<tr>
<td>Elective Caesarean (n = 22,085)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Live birth (n = 127,222)</td>
<td></td>
<td>Model 1</td>
</tr>
<tr>
<td>Spontaneous vaginal (n = 84,866)</td>
<td>Ref (1.01, 1.03)</td>
<td>1.01 (0.99, 1.03)</td>
</tr>
<tr>
<td>Operative vaginal (n = 17,392)</td>
<td>0.76 (0.75, 0.77)</td>
<td>0.79 (0.78, 0.80)</td>
</tr>
<tr>
<td>All Caesarean sections (n = 24,964)</td>
<td>0.79 (0.78, 0.80)</td>
<td>0.82 (0.81, 0.84)</td>
</tr>
<tr>
<td>Emergency Caesarean (n = 18,044)</td>
<td>0.70 (0.69, 0.72)</td>
<td>0.75 (0.73, 0.77)</td>
</tr>
<tr>
<td>Elective Caesarean (n = 6171)</td>
<td>0.49 (0.45, 0.52)</td>
<td>0.58 (0.54, 0.62)</td>
</tr>
</tbody>
</table>

Data refer to: Cr: HR: crude hazard ratio (95% confidence interval); Adj. HR: adjusted hazard ratio (95% CI).
*Mode of delivery: number of events (live births) for each mode of delivery in parentheses.
1Model 1: adjusted for maternal age, maternal origin, previous stillbirth, miscarriage or ectopic pregnancy and measures of socio-economic status including educational attainment, mother and father’s gross income, marital status and birth year.
2Model 2: adjusted for Model 1 + medical complications in the first live birth including delivery type (singleton, twins or more), diabetes or gestational diabetes, placental abruption, placenta praevia and hypertensive disorders (including eclampsia and pre-eclampsia).
3Model 3: adjusted for Model 2 + gestational age, birthweight, infant sex and length.
Additional adjusted analyses
When smoking, BMI, prior fertility treatment and history of psychiatric illness were adjusted for in the models, the overall results were unchanged (Supplementary data, Table SII).

Additional subgroup analyses
When a time-dependent covariate analysis based on infant death within 1 year was performed, the hazard rate of a subsequent live birth among women with a maternal-requested Caesarean section increased from 62 to 84% (HR 0.84, 95% CI 0.79, 0.89). Restricting the analyses to smokers only, women of advanced maternal age, term deliveries, low birthweight deliveries, macrosomia deliveries, by the various time periods and by censoring follow-up in women at age 50 years did not change the overall conclusions (Supplementary data, Table SIII).

Median time to next birth in days
The median birth interval with 95% confidence intervals for women with a second live birth according to mode of delivery is presented in Table III. Women with an emergency Caesarean (median 1101 days, 95% CI 1097, 1106) or elective Caesarean (median 1097 days, 95% CI 1088, 1105) section had a slightly longer median time to next birth compared with women with an operative vaginal delivery (median 1043 days, 95% CI 1038, 1047) or SVD (median 1083 days, 95% CI 1081, 1085). When the cohort was restricted to 2002–2010, women with maternal-requested Caesarean had a median time to second birth of 914 days (95% CI 883, 949) compared with a median of 907 (95% CI 904, 910) among women with a SVD during this time period. The rate and time to next birth by mode of delivery are shown in Fig. 2 (1982–2010) and Fig. 3 (2002–2010, for maternal-requested Caesarean section). The underlying proportional hazards assumption was tested using the SAS proportionality test command, with no violations found in the entire cohort from 1982 to 2010 (P = 0.7729) and in the years for which maternal-requested Caesarean section data (2002–2010) were available (P = 0.5752).

Discussion

Main findings
Women with any type of Caesarean section in their first live birth had a 14% reduced rate of subsequent live birth compared with women with a SVD. Analyses by type of Caesarean section revealed a significantly reduced rate of subsequent live birth particularly among women with a primary maternally requested Caesarean section indicating that it is a voluntary decision by women to delay or avoid subsequent childbirth (i.e. maternal choice). A 13% reduction in subsequent birth rates was found in women with an emergency Caesarean and a 17% reduction in women with an elective Caesarean; however, the underlying indication for these procedures may explain the reduced birth rates. These results did not differ in the various additional adjusted and subgroup
analyses undertaken apart from the time-dependent analysis based on infant death within 12 months of birth. Here we found that where a child died within the first 12 months of birth, the rate of subsequent live birth among women with maternal-requested Caesarean section increased significantly (from 61 to 84%). A small reduction in the rate of live birth remained, however, among women with emergency and elective Caesarean, which might be as a result of residual confounding or as a consequence of the Caesarean section. This finding is in line with that of a large Norwegian register-based study (Tollanes et al., 2007).

Moreover, in line with a reduced rate of subsequent live birth among women with a Caesarean in their first live birth, there was also a slightly longer median waiting time in women with a subsequent live birth. However, when the cohort was restricted to 2002–2010 (as data for maternal-requested Caesarean were only available for this period) the median time to second birth among women with maternal requested Caesarean was similar to that of women with a SVD. This might suggest that it is maternal choice that leads to a lower rate of subsequent live birth, and in women who actually have second births; it is again maternal choice to have this second baby quicker.

Voluntary delay in time to next birth?
Maternal choice to intentionally delay conception or avoid a subsequent birth is a plausible explanation for any proposed association between Caesarean section and the rate and time to subsequent live birth. Bahl et al. reported that 25–33% of research studies have shown that women who experienced traumatic childbirths including neonatal trauma, maternal pelvic floor morbidity, tears or ruptures or long labour duration have a real fear of childbirth following an operative vaginal delivery (Bahl et al., 2004). Furthermore, the stress of an emergency Caesarean section as well as the potential for infection and rupture, are all plausible explanations for women to voluntarily delay childbirth. Many social or financial factors including desired family size, lifestyle, age and lack of a partner have also been proposed (Murphy and Liebling, 2003; Bahl et al., 2004).

Strengths and weaknesses
The strengths of the CRS cohort include firstly that it is a nationwide register-based cohort capturing the complete population of Denmark, whilst also combining accurate linkage between and within registers through the unique CPR number. This linkage enhances the data presented in the current study including detailed obstetric data on the indication for mode of delivery, particularly Caesarean section and novel ‘maternally requested’ Caesarean section. Furthermore, the extensive subgroup analyses performed and the various potential confounders which were adjusted for increase the plausibility of the current results. Particularly important are the details on whether a woman had accessed fertility treatment, which was available for 11 years of the cohort (1994–2005), allowing us to perform a subgroup analysis including already subfertile women only. Furthermore, details on infant death allowed us to perform a time-dependent analysis based on infant death within 12 months, to test whether maternal choice to replace the loss of their first born child affected the overall findings. To our knowledge this is also the largest study to date investigating the time to next birth following Caesarean section to answer this long debated issue, with a lengthy period of follow-up spanning almost three decades.

There are, however, some limitations to the study which include firstly lack of data on personal and social choices. For example, we do not know whether the women in this cohort planned to have any further pregnancies and therefore whether they were actively trying to get pregnant again or not. Furthermore, we do not know whether the first live born child was born with any physical or mental disability, malformation or serious illness which may impact on a couple’s decision to have a subsequent child. In addition, we do not have any data on whether a change in marital status occurred (i.e. lack of a long-term partner may influence the likelihood of having another baby). Limited availability of data for maternal BMI, smoking, access to fertility services and missing data are acknowledged limitations; however, as the percentage of missing data were considered small, and did not warrant doing multiple imputation, we included missing as a separate category. Furthermore, fertility treatment in Denmark is only available to childless couples with a limit of three cycles offered to married, unmarried or single people. The purpose of adjusting for history of access to fertility treatment before the first live birth in this study however is to control for the potential confounding effects of women with pre-existing fertility issues prior to having a Caesarean in their first live birth. Another possible weakness of the CRS cohort includes that the data span across three decades (from 1982 to 2010). Many changes in maternity care, as well as obstetric training and techniques, changes in the Caesarean section rates and societal behaviour may influence the association between Caesarean section and time to next birth. However, sub-analyses investigating the cohort effect (where the data were split up into three equal time periods) did not alter the overall findings. Another limitation is the possibility of miscoding and data entry errors and under-reporting or under- utilization on new variables such as maternal-requested Caesarean for example. These are, however, considered minimal in the Danish registers where data are continuously updated and citizens have the option to update and correct information personally. Residual confounding cannot be ruled out in the present study as is the case with many epidemiological observational studies and there are no randomized control trials (RCTs) on this topic to date. There were, however, two RCTs assigning women to receive a Caesarean published in 2013 (Barrett et al., 2013; Glavind et al., 2013).

Conclusions
The findings of the current study, which is the largest and most comprehensive to date, indicate that a prior Caesarean section is associated with a reduction in subsequent births in the population-based CRS cohort. The findings may be due to women intentionally delaying or avoiding a subsequent birth, consistent with previous studies (Albrechtsen et al., 1998; Smith et al., 2006; Tollanes et al., 2007; Kjerulf et al., 2013), and this may be for a multitude of reasons (financial, social, cultural), beyond the scope of this paper, requiring a qualitative approach to answer why. Further large-scale research is necessary to confirm the findings of the current study. Moreover, each woman and each pregnancy is different and the appropriate mode of delivery and care provided should be discussed at an individual level with a midwife or obstetrician.

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

We would like to acknowledge the staff of the National Perinatal Epidemiology Centre (NPEC) and the Irish Centre for Fetal and Neonatal Translational Research (INFANT) in Ireland, the staff of the National Centre for Register-based Research (NCRR) in Aarhus, Denmark, and in particular data managers Malene Thaysen and Michael Pedersen, as well as the Danish National Board of Health and Statistics Denmark for data approval.

Authors’ roles

S.M.O.N., A.S.K., T.B.H., L.C.K., P.M.K., P.B.M., R.A.G. and E.A. conceived and designed the study. E.A. acquired the data and S.M.O.N. analysed the data. S.M.O.N., A.S.K., T.B.H., L.C.K., P.M.K., P.B.M., R.A.G. and E.A. interpreted the findings from the data. S.M.O.N. drafted the manuscript. S.M.O.N., A.S.K., T.B.H., L.C.K., P.M.K., P.B.M., R.A.G. and E.A. critically revised the manuscript for important intellectual content. All authors agreed on the final manuscript and approved its submission for publication. S.M.O.N. will act as guarantor for the paper.

Funding

This work was funded by the National Perinatal Epidemiology Centre, Cork, Ireland and conducted as part of the Health Research Board PhD Scholars programme in Health Services Research, Grant No. PHD/2007/16. L.C.K. is a Science Foundation Ireland Principal Investigator (08/IN.1/B2083) and the Director of the SFI funded Centre, INFANT (12/RC/2272).

Conflict of interest

None declared.

References


Andersen AN, Erb K. Record data on assisted reproductive technology (ART) in Europe including a detailed description of ART in Denmark. Int J Androl 2006;29:12–16.


Funding

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