Alma Mater Studiorum – Università di Bologna

DOTTORATO DI RICERCA

Sanità Pubblica e Medicina del Lavoro
Ciclo XXIV
Settore scientifico disciplinare di afferenza: MED/42

Determinants of cesarean delivery, a population-based study in the Emilia Romagna Region

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Esame finale anno 2013

To Pippo and Giacomino

Acknowledgments

First and foremost I would like to thank Prof. Maria Pia Fantini who made this thesis possible. I am deeply grateful for her support, guidance and confidence in my work throughout my PhD.

I would like to thank Jacopo Lenzi for his great support in the statistical analyses, he has known the answer to every question I've ever asked regarding multilevel analyses.

I am indebted to Paola Rucci for her help with some statistical parts. I also thank her for her invaluable suggestions and comments on writing style during these years.

I am very grateful to Elena Berti, a collegue and friend for reading my thesis and giving me very precious comments.

I also thank all current and past students and researchers of "the III floor" who have contributed immensely to my professional and personal time at the University of Bologna.

Abstract

Cesarean Delivery (CD) rates are rising in many parts of the world. In order to define strategies to reduce them, it is important to explore the role of clinical and organizational factors. This thesis has the objective to describe the contemporary CD practice and study clinical and organizational variables as determinants of CD in all women who gave birth between 2005 and June 2010 in the Emilia Romagna region (Italy).

All hospital discharge abstracts of women who delivered between 2005 and mid 2010 in the region were selected and linked with birth certificates. In addition to descriptive statistics, in order to study the role of clinical and organizational variables (teaching or non-teaching hospital, birth volumes, time and day of delivery) multilevel Poisson regression models and a classification tree were used.

A substantial inter-hospital variability in CD rate was found, and this was only partially explained by the considered variables. The most important risk factors of CD were: previous CD (RR 4,95; 95%CI: 4,85-5,05), cord prolapse (RR 3,51; 95% CI:2,96-4,16), and malposition/malpresentation (RR 2,72; 95%CI: 2,66-2,77). Delivery between 7 pm and 7 am and during non working days protect against CD in all subgroups including those with a small number of elective CDs while delivery at a teaching hospital and birth volumes were not statistically significant risk factors. The classification tree shows that previous CD and malposition/malpresentation are the most important variables discriminating between high and low risk of CD.

These results indicate that other not considered factors might explain CD variability and do not provide clear evidence that small hospitals have a poor performance in terms of CD rate. Some strategies to reduce CD could be found by focusing on the differences in delivery practice between day and night and between working and no-working day deliveries.

Il ricorso al taglio cesareo (TC) è in crescita in molte parti del mondo. Per poter ridurre il ricorso al TC, è importante esplorare il ruolo di fattori clinici ed organizzativi. Questa tesi ha l'obiettivo di descrivere la pratica ostetrica attuale e

studiare i determinanti clinici ed organizzativi del TC in Emilia Romagna tra il 2005 ed la metà del 2010.

Le schede di dimissioni ospedaliere delle partorienti tra il 2005 e la metà del 2010 sono state selezionate e linkate con i certificati di assistenza al parto. Oltre a statistiche descrittive, per studiare le variabili cliniche ed organizzative (ospedale universitario o non, volumi di nascite, ora e giorno del parto) sono stati utilizzati dei modelli di Poisson multilivello e alberi di classificazione.

Gli ospedali della regione presentano una grande variabilità nelle proporzioni di TC, solo in parte spiegata dalle variabili considerate. I più importanti fattori di rischio sono: aver avuto un precedente TC (RR 4,95; 95%CI: 4,85-5,05), il prolasso del cordone (RR 3,51; 95%CI: 2,96-4,16) e la malposizione fetale (RR 2,72; 95%CI: 2,66-2,77). I parti tra le ore 19 e le 7 e nei giorni festivi hanno un minor rischio di TC in tutti i sottogruppi, compresi quelli con un minor numero di TC elettivi mentre i parti in ospedale universitario ed i volumi non rappresentano fattori di rischio statisticamente significativi. L'albero di classificazione mostra che il precedente TC e la malposizione sono le più importanti variabili discriminanti l'alto dal basso rischio di TC.

I risultati indicano che altri fattori, non considerati, spiegano la variabilità del fenomeno e non forniscono prove evidenti che gli ospedali più piccoli ricorrano maggiormente al TC. Alcune strategie per ridurre il TC potrebbero essere individuate analizzando le differenze nell'approccio al parto esistenti tra il giorno e la notte e tra giorni lavorativi e quelli festivi.

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Abbreviations

aRR: adjusted relative risk
CD: cesarean delivery
CedAP: certificati di assistenza al parto (birth certificates)
CI: confidence interval
CRT: classification and regression trees
DRG: disease related group
NTCS: nulliparous, at term, cephalic presentation, singleton
PAR: population attributable risk
PCV: proportional change in variance
RER: Regione Emilia Romagna
RR: relative risk
SDO: schede di dimissione ospedaliera (hospital discharge abstracts)
TGCS: ten group classification system
VBAC: vaginal birth after cesarean
WHO: World Health Organization

Foreword

The Department of Public Health of the University of Bologna that has recently become part of the Department of Biomedical and Neuromotor Sciences, has a particular interest in outcomes research and for various years has been studying the methodological aspects related to the evaluation of heath services with the main goal to improve health. In relation to Obstetrics and Gynaecology it has been studying the best methods to evaluate inter-hospital variability in terms of cesarean delivery (CD) rate and maternal and neonatal outcomes according to mode of delivery.

This thesis arises from the ongoing activities with the objective to better understand the contemporary CD practice and the determinants of CD in the Emilia Romagna region (RER), and assess whether organizational activities such as birth volumes, affiliation and time and working days are determinants of CD.

In the introduction, epidemiological aspects of CD in Italy and in the world and the main indications for cesarean birth are presented. Some questionable risk factors are discussed, and an overview of risks and benefits of CD is provided.

After presenting the study rationale and the objectives, the methodology of the study is described. In the result session the general characteristics of deliveries in the RER between 2005 and June 2010 are described, and the results of univariate and multivariate analyses relative to the study population and the following subgroups of women are presented:

- all deliveries meeting the inclusion/exclusion criteria
- women without a previous caesarean section
- only nulliparous women with singleton, cephalic at term deliveries
- women with spontaneous labour
- women with induced labour
- women belonging to the V TGCS group
- women belonging to the I, IIa, III, Iva TGCS group

Characteristics of women who delivered without labour, undergoing elective and urgent CD are also tabulated.

In each subgroup the crude and adjusted risk of CD is estimated for a series of predefined risk factors. Furthermore, additional models have been fitted to study time of delivery, days of the week (working vs non-working), affiliation and birth volumes.

Classification trees are also used to study determinants.

The conclusion summarizes the main findings in relation to previous literature and the most relevant limits of the study, and provides the consequential research and policy implications.

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Introduction

Cesarean delivery rates, as a percentage of all live births, have increased worldwide during the last decades especially in middle and high income countries (Villar, 2006; Betran, 2007). CD has become the most common major surgical procedure in many parts of the world. Approximately 18.5 million CD rates are performed yearly according to a recent WHO publication (Gibbons, 2010).

An ecological analysis (Betran, 2007) estimated the global rate of CD as 15% with a great variability across countries: higher in developed countries and in Latin America and the Caribbean, and lower in other developing countries.

In the above mentioned WHO publication, it is reported that CD rates range from 0.4 % in Chad (in 2004) and Burkina Faso (in 2003) to 45.9% in Brazil (in 2006) and that about 40% of the countries have CD rates < 10%, 10% have rates between 10 and 15% and about 50% have CD rates >15% (Gibbons, 2010).

In Europe (27 countries), CD rates are highest in Italy (38.7%) and Portugal (36%) and lowest in the Netherlands (14% of all live births), and are relatively low also in other Nordic countries (Finland, Slovenia, Sweden) (HFA-DB, 2012).

Italy presents a great interregional variability in CD rates. In 2010, rates ranged from 24% in Friuli Venezia Giulia to 62.0% in Campania as table 1 shows. Rates are generally higher in the regions of the South than in the North.

The temporal comparison of regional CD rates shows that, in all the Italian regions, except Emilia Romagna and Basilicata, there is a trend of increasing CD rates in the last ten years, and that the trend is mostly statistically significant. However, the comparison of the CD rates relative to the last two-three years, shows that some regions have slightly reversed the trend of rising cesarean rates since 2001.

Table 1. Cesarean delivery rates in Italian regions, beta and p (2001-2010).

Region	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	Beta	P
Piemonte	28.73	28.9	30.17	31.9	31.42	32.51	32.67	32.57	32.11	30.22	0.311	0.054
V. d'Aosta	22.98	27.46	27.21	27.42	30.41	33.58	34	33.39	34.53	34.55	1.26	<0.001
Lombardia	25.33	26.5	26.61	27.34	28.24	28.46	28.33	28.48	28.65	29.16	0.376	<0.001
Bolzano	14.12	19.92	19.58	23.01	*23.37*	*25.01*	*24.2*	26.9	23.61	25.36	1.02	0.003
Trento	24.86	27.24	27.09	28.15	*27.17*	*27.59*	*27.99*	25.36	27.4	27.62	0.105	0.412
Veneto	26.36	27.36	27.9	28.61	28.89	29.03	28.88	28.41	28.73	28.37	0.189	0.029
Friuli V.G.	20.33	21.08	22.42	23.11	23.93	23.93	24.51	23.64	24.55	23.99	0.409	0.001
Liguria	30.49	31.25	32.43	32.39	34.82	32.22	34.06	37.41	37.61	38.12	0.852	<0.001
RER	29.32	30.85	30.39	30.96	30.39	29.56	29.97	28.83	29.19	29.92	-0.108	0.184
Toscana	22.88	24.5	25.43	26.1	26.09	26.17	27.26	26.48	27.49	26.79	0.394	0.001
Umbria	26.86	28.22	30.58	31.67	30.7	32.31	31.92	31.73	32.16	32.23	0.509	0.003
Marche	34.09	34.67	35.43	35.36	34.84	35.37	35.44	35.42	35.25	34.41	0.046	0.425
Lazio	36.52	37.58	37.55	39.37	41.08	44.42	44.24	45.32	44.64	44.41	1.074	<0.001
Abruzzo	35.52	38.67	39.75	40.59	43.11	46.88	45.42	44.84	43.59	44.64	0.971	0.003
Molise	39.25	40.35	42.28	49.2	48.91	49.77	49.75	47.76	50.3	46.27	0.986	0.021
Campania	54.28	56.41	58.16	59.02	59.95	61.86	61.93	61.96	61.96	61.72	0.821	<0.001
Puglia	40.47	42.96	43.47	45.94	47.72	50	50.41	50.18	47.85	47.10	0.868	0.008
Basilicata	46.49	51	51.41	50.45	50.37	48.39	49.95	48.8	49.74	46.64	-0.145	0.474
Calabria	36.92	40.06	41.09	43.27	43.14	46.83	46.86	48.15	43.72	42.75	0.775	0.028
Sicilia	42.01	45.32	48.14	50.49	52.35	53.14	52.88	53.27	53.33	52.18	1.1	0.002
Sardegna	32.6	33.42	36.78	39.33	38.88	38.31	39.14	38.32	40.36	41.16	0.801	0.001
ITALY	**31.92**	**33.99**	**34.95**	**36.37**	**38.32**	**39.3**	**39.29**	**39.19**	**39.01**	**38.71**	**0.771**	**0.001**

(Source of data: Ministry of Health. SDO. Years 2001-2010)

In Italy, as in other countries (Niino, 2011) there is a great variability among hospitals with different funding systems. CD rates are substantially superior in private, accredited (60.5%) or non accredited (75%) clinics than in public birth units (34.8%). Rates vary by volume of activities as well, with higher rates in hospitals with the lowest number of deliveries (Ministero della Salute, 2011) (Table 2).

CD was introduced in clinical practice as a life-saving procedure both for the mother and the baby (Gibbons, 2010). Several studies have shown an inverse association between CD rates and maternal and infant mortality at population levels in low income countries where large sectors of the population lack access to basic obstetric care (Althanbe, 2006; Ronsmans, 2006; Betran, 2007). On the other hand, CD rates above a certain limit have not shown additional benefit for

the mother or the baby, and some studies have even shown that high CD rates could be linked to negative consequences in maternal and child health (Hall 1999; Barros, 2005; Althabe, 2006; Villar, 2006; Belizan, 2007; Betran, 2007; Zizza, 2011).

Table 2. CD rates by volume of activity.

Mean annual number of deliveries	CD rate
< 500	49.7
500-799	43.5
800-999	40.3
1000-2499	35.0
>2499	33.5
Total	**37.8**

(Source: Ministry of health. CedAP, 2008)

In a recent publication, 'Monitoring Emergency Obstetric Care: a handbook' (WHO, 2009), the WHO states that, “Both very low and very high rates of cesarean section can be dangerous, but the optimum rate is unknown” and that “although WHO has recommended since 1985 that the rate not exceed 10-15%, there is no empirical evidence for an optimum percentage or range of percentages, despite a growing body of research that shows a negative effect of high rates”.

Recently Betran et al. (2007) again found that 15% was a marker below which there is a correlation with increased maternal mortality and perinatal mortality, but above which “risks to reproductive health outcomes may begin to outweigh benefits”.

Some services have been able to considerably reduce cesarean rates without adversely affecting perinatal outcomes. Furthermore, in various countries, services skilled in and committed to low-technology approach have maintained excellent outcomes and CD rates below 2% (Sakala, 1993; Sakala, 1993b). In fact, in Vienna, the clinic Ignaz Semmelweiss Frauenklink had a CD rate for the 20-year period from 1966 through 1985 of 1.3%, compared to 8% in the rest of Vienna, even declining from the first to the second decade against the trend in the rest of the developed world (Sakala, 1993b).

In Italy, where CD rates are by far above the 15% WHO marker, there is no evidence of an association between higher CD rates and a reduced fetal-maternal risk nor improvement in perinatal outcomes. On the contrary, data report higher perinatal mortality in the Southern Region of Italy where the CD rates are highest (SNLG, 2012).

The great geographical variability among countries and regions that have CD rates higher than 15% suggests an inappropriate use of CD, due to multiple non clinical factors like structural and organizational aspects, incompetencies of the staff, a social and cultural attitude of women and society toward birth management and financial aspects (SNLG, 2012). It is not known whether these variables are woman-related (e.g. intolerance of difficult birth) or clinician-related (e.g. fear of litigation). It is clear that, variation in the incidence of clinical problems during pregnancy or difficult labour among countries or regions cannot explain the different CD rates as many other unknown variables may cause this variation in practice.

Indications for cesarean delivery

Weaver et al. (2004) observed that according to many studies, three of the same major reported justifications for CD apply today as they did in the 1980s, when the rate first began to rise: dystocia, fetal distress and breech presentation. The fourth major factor however has changed: a proportionally high number of cesarean sections used to be performed to protect small or pre-term infants, but nowadays the more frequent justification for the operation is as a repeat procedure. In the developed world, dystocia or poor progress in labour contributes at least a third to the overall CD rate, and repeat CD following primary cesarean section contributes at least another third (Penn, 2001). Breech presentation and fetal distress are the other two major indications of CD. The National sentinel Cesarean Section audit report found that in England and Wales in 2000, the most frequently reported primary indications for cesarean section were presumed fetal compromise (22.0% of the total number of CD), failure to progress in labour (20.4%), previous cesarean section (13.8%) and breech presentation (10.8%) (Thomas, 2001). Sakala opinioned, "The vast majority of cesareans performed in the US are attributed to official 'diagnoses'

that are ambiguous and/or for which a cesarean offers no or highly questionable benefit (Sakala, 2008)." In particular, the four major indications of CD, previous cesarean, obstructed labor, fetal distress and breech presentation are gray areas (Sakala, 1993). Therefore, at least on the face of it, the main reasons for performing CD are still clinical, although criticism has been raised that, not all these 'clinically' indicated operations were probably necessary (Wagner, 2001).

The determinants for a CD are very complex and do not include only clinical indications, but also economic aspects, the physicians and their attitudes toward birth management and the social and cultural attitudes of women and the societies in which they live. CD has become an established procedure for some particular indications, even if the benefits on both the infant and mother are small or often not quantified at all. The medical indications for CD are very subjective and culture-bound such that there is a significant variability among countries with respect to CD rates for particular medical indications. Also, the country differences are salient regarding the rate at which particular common indications for cesarean birth apply to childbearing women (Arrieta, 2010).

According to the 2011 Clinical Guideline by the National Institute for Clinical Excellence (NICE, 2011), a planned CD should be offered to women with:

- a term singleton breech if external cephalic version is contraindicated or has failed
- a twin pregnancy with first twin breech
- HIV and not receiving any retroviral therapy/ HIV and a viral load equal to or greater than 400 copies/ml regardless of any antiretroviral therapy
- both HIV and hepatitis C
- primary genital herpes in the third trimester
- grade 3 and 4 placenta previa

and should not be offered routinely to women with:

- an uncomplicated twin pregnancy at term where the first twin is cephalic
- preterm birth
- a small for gestational age baby
- HIV receiving HAART therapy with a viral load less than 400 copies/ml
- HIV receiving any retroviral therapy with a viral load less than 50 copies/ml
- Hepatitis B and C virus

- Recurrent genital herpes at term
- A body mass index of over 50 and no other risk factors.

We will discuss hereby some frequent medical conditions that are often risk factors for CD, though evidence for the benefits of CD are not always established.

Obstructed labour or dystocia

CD is often performed in case of dystocia or obstructed labour (6,16). In 1987, in the USA, dystocia accounted for 40% of primary cesareans (Sakala, 1993). In 1980, 1.1% of births in the USA were labelled as involving obstructed labour; by 1989, the figure had risen to 4.3% (Sakala, 1993).

Dystocia is not an absolute indication for CD. After diagnosing poor progress in labour, physicians should first try to optimize uterine activity. Proponents of active management of labour consider that a package of strict criteria for the diagnosis of the onset of labour, early amniotomy, early use of oxytocin and continuous professional support will enhance optimal progress in labour and hence normal delivery. If uterine activity has been optimized, as above, and labour is still difficult, then mechanical factors may be implicated: there may be absolute or relative cephalopelvic disproportion due to malposition of the head (Penn, 2001). Absolute cephalopelvic disproportion requires CD; whereas (SNLG, 2012) some relative disproportions may be managed by assisted vaginal delivery, if full dilation has been achieved. However, also for relative cephalopelvic disproportion in some cases, cesarean section may be preferable to a difficult instrumental delivery. It is clear that, with widely differing CD rates for difficult labour, there are many unknown variables that may cause this variation in practice, and the diagnosis of cephalopelvic disproportion is a key factor. The Italian clinical guidelines underscores that foot measure, pelvimetry, maternal height and fetal estimates are not predictors of failure to progress during labour and should not be used as the unique criteria to decide mode of delivery (SNLG, 2012).

Fetal distress

Fetal distress is also a common indication of CD. The increasing rate of cesarean births is associated with an increased diagnosis of fetal distress (Niino, 2011).

While 1.7% of all births were designated as involving fetal distress in 1980; in 1989, 8.8% were so designated (Sakala, 1993). The introduction of continuous electronic fetal monitoring (EFM) has been suggested as a cause of the rising CD rate for fetal distress. A meta-analysis has shown an increase in the CD rate associated with EFM. The same meta-analysis shows that continuous EFM reduces the risk of neonatal seizure but has no effect on the rate of neonatal death or development of cerebral palsy in comparison with intermittent auscultation (Alfirevic, 2006). It has been estimated that the false positive rate for cerebral palsy from EFM can be very high (99%) (Nelson, 1996).

Access to fetal blood sampling may reduce the rate of unnecessary cesarean sections for abnormal fetal heart rate patterns. Newer methods, such as fetal ECG waveform analysis and computerized CTG, may contribute to a further reduction in the future (Wijngarden, 1998).

Previous cesarean section

Another frequent indication for CD is a previous CD. When the most common cesarean section was the “classical cesarean section”, clinicians feared scar rupture in labour, and repeat CD was considered mandatory for all subsequent births. However, it became clear that lower segment cesarean section was not associated with disastrous ruptures and the concept of “trial of scar” in subsequent deliveries became current (Penn, 2001). Overall, the chances of successful planned vaginal birth after CD (VBAC) are 72-76%. However the percentage of women delivering vaginally after a previous CD in practice remains low (Penn, 2001). Both trial of labour and elective repeat CD for a pregnant woman with one prior transverse uterine incision have important risks and benefits, and these risks and benefits differ for the woman and her fetus. This poses a profound ethical dilemma for the woman as well as her caregivers, because benefit for the woman may come at the price of increased risk for the fetus and vice versa (NIH, 2010).

Various studies have examined the association between mode of delivery after a previous cesarean and maternal and neonatal mortality and morbidity. Repeated CD increases the risk of maternal mortality, deep venous thrombosis, longer hospitalizations, anomalies in the placenta during subsequent pregnancies with a

higher risk of hysterectomy and uterine hemorrhage (NIH, 2010; Stivanello, 2010). Repeated CD is also associated with a delayed contact with the infant and respiratory problems of the child. However the risk of uterine rupture is higher after trial of labour, and there are some suggestions that VABG is associated with perinatal mortality and ischaemic encephalopathy when compared with a repeated CD.

There are different practice recommendations regarding delivery after a previous cesarean, however CD is not considered an absolute indication. The National Institute of Health (2010) concludes that given the available evidence, trial of labour is a reasonable option for many pregnant women with one prior low transverse uterine incision. The Agency for Healthcare Research and Quality favours vaginal delivery after CD for most women especially because of the problems caused by multiple CDs (2010). The Royal College of Obstetrics and Gynaecologists discussed the risks and benefits of VBAC in the Green-top guideline n°45 (2007), which states that "women with a prior history of one uncomplicated lower-segment transverse cesarean section, in an otherwise uncomplicated pregnancy at term, with no contraindication to vaginal birth, should be able to discuss the option of planned VBAC and the alternative of a repeat cesarean section". However after three or more cesarean section, women should be offered a repeated CD.

The Italian CD guideline (SNLG, 2012) states that trial of labour should be offered to all women with a previous CD in the absence of specific contra-indications. As far as the increased risk of uterine rupture, a previous uterine rupture, a previous longitudinal uterine section, three or more previous cesarean sections contraindicate a vaginal delivery. Adequate monitoring, surveillance in an appropriate delivery structure should be offered to such women.

Breech presentation

A Cochrane review indicates that in case of breech presentation the group with CD presents a reduced perinatal or neonatal mortality in comparison to the group with vaginal delivery, with a slight increase in short term maternal morbidity. Women long term effects and economic aspects were not among the outcomes of these studies.

Nice guidance and the Italian guideline (NICE, 2011; SNLG, 2012) recommend that women who have an uncomplicated singleton breech pregnancy at 36 weeks' gestation should be offered external cephalic version. Exceptions include women in labour and women with a uterine scar or abnormality, fetal compromise, ruptured membranes, vaginal bleeding or medical conditions. Pregnant women with a singleton breech presentation at term, for whom external cephalic version is contraindicated or has been unsuccessful, should be offered CD because it reduces perinatal mortality and neonatal morbidity. Evidence relative to benefits and risks of version in case of a previous CD remain debatable.

Audit and monitoring activities have reported that some hospitals had extremely high cases of breech presentation or other rare malpresentations, especially if not easily identifiable. Given the frequency of breech presentation and other malpresentations in the choice of mode of delivery, some authors found that some hospitals intentionally overused this diagnosis (Di Martino, 2012).

Antepartum hemorrhage (placenta abruptio, previa, vasa previa)

In case of major placenta abruption, the outcome for the fetus is generally always very poor. In non-randomized trials, higher perinatal mortality rates have been observed for vaginal delivery when compared to CD. Other retrospective studies have demonstrated only a small advantage or no advantage at all for the fetus delivered by CD (Colais, 2009).

The Italian Guideline (SNLG, 2012) does not identify experimental studies on the benefit of CD over vaginal delivery in case of placenta previa. Retrospective studies suggest that the safety of vaginal deliveries increases with the distance between placenta and the internal uterine os. A narrative review underscores that in case of total or partial placenta previa (at less than 2 cm from the uterine os), planned CD is indicated (Oyelese, 2006). The Royal College of Obstetricians and Gynaecologists (2011) and the Italian guidelines (SNLG, 2012) also consider that a diagnosis of central placenta previa or a previa with a margin at less than 2 cm from the uterine is usually an indication for CD.

Vasa previa is a rare condition that carries a high fetal mortality due to fetal exsanguination resulting from tearing of the vessels when they lie within the

membranes (Bashaat, 1998; Oyelese, 1999). When vasa previa is diagnosed antenatally, an elective CD should be offered prior to the onset of labour (Gagnon, 2009).

Twins

The optimum mode of delivery of twins remains controversial. Much will depend on the chorionicity of the pregnancy, the presence of additional fetal or maternal complications, gestation at delivery and the presentation of both twins (Penn, 2001). The Nice guidance (2011) considers that in otherwise uncomplicated twin pregnancies at term, where the presentation of the first twin is cephalic, perinatal morbidity and mortality is increased for the second twin. However, the effect of planned CD in improving outcome for the second twin remains uncertain and therefore CD should not routinely be offered outside a research context. In twin pregnancies where the first twin is not cephalic the effect of CD in improving outcome is uncertain, but current practice is to offer a planned CD. The Italian guideline (SNLG, 2012) recommends that vaginal delivery should be done in bicorial/biamniotic deliveries with a cephalic presentation of both twins in the absence of additional risk factors, because the efficacy of CD in reducing neonatal mortality and morbidity is not clear. It adds that literature does not provide clear evidence to support routine CD in case of bicorial/biamniotic deliveries with breech presentation of one of the twins.

The Royal College of Obstetricians and Gynaecologists (2008) recommends an elective vaginal delivery at 36-37 weeks in monocorial non complicated pregnancies and elective CD in case of specific indications such as breech presentation of the first twin or a previous CD and in monocorial and monoamniotic pregnancies CD.

Cord prolapse

Cord prolapse has been defined as the descent of the umbilical cord through the cervix alongside or past the presenting part in the presence of ruptured membranes (Lin, 2006). The overall incidence of cord prolapse ranges from 0.1% to 0.6%. A cesarean section is the recommended mode of delivery in cases of

cord prolapse when vaginal delivery is not imminent, to prevent hypoxia–acidosis (RCOG, 2008).

Maternal infections

Neonatal herpes simplex virus is a severe infection caused by the maternal transmission of the virus to the fetus. The risk of infection is especially high if the primary infection occurs during the last weeks of pregnancy, it is lower (less than 1%) if the infection occurs during the first half of the pregnancy or if it is a recurrent event. There is a consensus to recommend CD if the primary infection occurred in the last six weeks of the pregnancy. CD should not be recommended on a routine basis in case of a recurrent infection because it's efficacy to reduce the risk of infection is uncertain (SNLG, 2012).

Newborns that acquire the HCV infection in uteru or at delivery are at risk of developing a chronic hepatopathy at an older age. There are no evidences that CD reduces the risk of HCV mother to child transmission but in case of HIV and HCV co-infection there are evidences that CD does reduce the HCV vertical transmission (Schackman, 2004). The Italian Guideline (SNLG, 2012) recommends elective CD in case of HIV and HCV co-infection if viral charge is superior to 50 copies/ml, and/or the women is not under HAART.

As for the mother to child transmission of HBV there are no conclusive evidences to recommend elective CD in favour of vaginal delivery. CD is not necessary in case of vaccination and immunoglobulines (SNLG, 2012).

80% of mother to child HIV vertical transmissions occur during delivery after the rupture of the membranes or during the passage through the birth canal.

Elective CD was the mode of the delivery of choice when antiretroviral treatment was not available. Nowadays, with antiretroviral treatment the risk of vertical transmission in women with low viral charge (less than 50 copies/ml) is very low and the appropriateness of CD is less clear. The Italian Guideline recommends an elective CD at the 38th week or afterwards in case of a HAART with viral charge greater than 50 copies/ml, monotherapies with ZDV, HIV and HCV co-infection without HAART or with viral charge greater than 50 copies/ml.

A labour can be offered to women under HAART and with viral charge with less than 50 copies/ml, limiting all procedures that favour blood contamination.

Other maternal diseases

CD has been advocated for various maternal diseases. It used to be recommended in case of congenital or acquired cardiac diseases, but current evidence favours vaginal delivery, especially in the presence of maternal pulmonary vascular disease where a surgery significantly worsens the prognosis (Penn, 2001).

Maternal diabetes in pregnancy has been associated with an increased rate of CD to reduce unexpected intrauterine deaths and fetal trauma associated with fetal macrosomia. The role of elective CD remains controversial. Gestational or pre-gestational diabetes is neither an indication for a CD nor a contra-indication for a VBAC (SNLG, 2012). The Royal College of Obstetricians and Gynaecology (2008) and the American College of Obstetrician and Gynaecologists (2001, 2005) recommend an elective CD in diabetic women with a suspicion of macrosomia (weight over 4500 gr) in order to prevent difficulties or trauma during the delivery. The Italian guideline (SNLG, 2012) recommends a CD in case of fetus with a weight superior to 4500 gr after the 38th week.

Other maternal diseases, such as idiopathic thrombocytopenic purpura and obstetric cholestasis, are associated with increased CD rates to avoid fetal morbidity and mortality, but the evidence to support this practice is scanty (Penn, 2001).

Similarly, in pre-eclampsia there is a higher risk of cesarean section, with some authors describing CD rates higher than 80% in gestations below 30 weeks. Even at pre-term gestation, however, vaginal delivery is possible (Penn, 2001).

Fetal conditions

CD does not affect neonatal outcomes significantly in pre-terms labour if there are no maternal or fetal risk factors (SNLG, 2012). In case of premature breech presentation, the choice of mode of delivery is often dictated by other clinical circumstances, such as placental abruption or severe pre-eclampsia, rather than the presentation. The last Italian guideline recommends that delivery should be carried out in birth units with proper capacities to manage neonatal, fetal and maternal emergencies and that the choice of mode of delivery should take account of local experiences and cases.

Fetal macrosomia (from any cause) carries an increased fetal and maternal morbidity. Numerous studies have shown that fetal weight estimation and actual birth weight are of limited value in predicting neonatal brachial plexus injury (Penn, 2001). The rates of long-term morbidity do not justify elective CD in infants weighing less than 5000gr and without other complications. As already mentioned, the Italian guideline (2012) recommends a CD if the fetal weight is superior to 4500gr.

A variety of congenital conditions are associated with high CD rates. In many cases the decision about mode of delivery and the high rates of cesarean section for fetal diseases are dictated by the necessity for highly skilled paediatric assistance at the time of birth and the timing of reconstructive surgery in the newborn period. It is these logistic considerations that often mandate cesarean section rather than convincing evidence that the fetus fares better after CD (Penn, 2001).

Both small for gestational age and intrauterine growth restriction fetuses have a higher risk of intrauterine death (still born) and morbidities. The choices of the most appropriate procedures of monitoring and the mode of delivery are controversial. However, planned CD is not recommended if fetal and umbilical Doppler ultrasound are normal. In case of abnormalities in the fetal and umbilical Doppler ultrasound, CD has to be evaluated according to the severity of the case (SNLG, 2012)

Maternal and neonatal outcomes associated with CD compared to vaginal delivery

There is evidence from various authors (Murphy, 2001, Allen, 2003; Ecker, 2004) that medically unnecessary cesarean sections could increase morbidity risks to mother and newborn. According to Childbirth Connection (2009), CD is riskier than vaginal delivery in 33 areas, and vaginal birth is riskier than cesarean delivery in four areas.

Overall, the Childbirth Connection review strongly favors vaginal birth. Harms that differed and favored vaginal birth included:

- shorter-term harms of CD in mothers, such as infection, surgical injury, and more severe and longer-lasting pain
- social and emotional harms of CD on mothers, such as less early contact with babies and poorer overall functioning
- ongoing physical harms of cesarean to mothers, chronic pelvic pain and bowel obstruction
- harms of CD to babies, including accidental surgical cuts, respiratory problems, failure to establish breastfeeding, and asthma in childhood and adulthood
- harms of CD in future pregnancies, including reproductive capacity, infertility, ectopic pregnancy, placenta accreta and placental abruption, stillbirth and malformations.

The review found that planned cesareans have advantages relative to unplanned cesareans with respect to short-term surgical injury and emotional toll. Planned and unplanned cesareans are likely to involve similar harm for conditions associated with scarring and adhesions, such as chronic pelvic pain, bowel obstruction, and all of the harm of CD for women's future reproductive capacity and babies in future pregnancies.

A much shorter list of harm favored cesarean sections: brachial plexus injury in babies, perineal/vaginal pain, urinary and bowel incontinence in mothers.

In an ecological study, Zizza et al. (2011) found that above 15% CD rates there is a positive and significant relation between CD and neonatal mortality rate. Niino (2011) reports that maternal mortality is two to seven times higher, and morbidity five to ten times higher, in CD compared to vaginal delivery.

The quality of the evidence in favor of vaginal or cesarean delivery is however very variable.

According to the State-of-the-Science Conference Statement on Cesarean Delivery on Maternal Request by NIH (2006), with the exception of three outcome variables with moderate-quality evidence (maternal hemorrhage, maternal length of stay, and neonatal respiratory morbidity), all remaining outcome assessments considered by the panel were based on weak evidence. Further maternal outcomes have a weak-quality evidence which favour planned vaginal delivery,

always according to the 2006 NIH State-of-the-Science Conference Statement on Cesarean Delivery on Maternal Request: infection, anesthetic complications, subsequent placenta previa and breastfeeding.

Maternal outcomes with weak-quality evidence that favour CD on maternal request are: urinary incontinence and surgical and traumatic complications (NIH, 2006).

The National Institute for Clinical Excellence provides a summary of the effects of CD compared with vaginal birth for women and their babies (NICE, 2011).

Complications reduced after a planned CD are: perineal and abdominal pain during birth, perineal and abdominal pain three days after postpartum, injury to vagina, early post-partum hemorrhage, obstetric shock.

Complication reduced after a planned vaginal birth: hysterectomy due to postpartum hemorrhage, cardiac arrest, length of hospital stay, neonatal intensive care unit admission.

Conditions which show no differences after a CD are: perineal and abdominal pain 4 months after postpartum, wound infection, genital tract injury, injury to bladder, cervix, ureter, iatrogenic surgical injury, pulmonary embolism, intraoperative trauma, uterine rupture, assisted ventilation or intubation, acute renal failure. Hypoxic-ischemic encephalopathy (CNS depression, seizures, pH < 7), intracranial hemorrhage, neonatal respiratory morbidity (intermittent positive pressure ventilation, transient tachypnea, endotracheal tube insertion, pneumonia).

Complication where studies show conflicting findings are: maternal death, deep vein thrombosis, blood transfusion, infection-wound and postpartum hysterectomy, anaesthetic complications, neonatal mortality, 5 min Apgar score <7 (NICE, 2011).

Needless to say, medically unnecessary cesarean surgeries are a huge waste of medical resources; WHO reported in 2010 that the global cost of excess cesarean sections was estimated at approximately US$2.32 billion. Money spent on medically unnecessary CD are taken away from other necessary or desirable medical care (Gibbons, 2010).

Study rationale

In Emilia Romagna, the CD rate is about 30%, a level that is far above the WHO recommended 15%. In developing countries where caesarean CD rate is very low, the increase in CD rate is associated with an improvement of maternal and newborn outcomes. On the contrary, in developed countries, the increase in CD rate is not associated by an improvement of these outcomes and a high CD rate is an indicator of low quality of care or inappropriateness.

The rise in CD is a major public health concern due to potential maternal and neonatal risks and costs issues. It questions also the meaning of pregnancy in our society as a non-medical moment of life.

This rise in CD has been attributed to a range of factors, including maternal requests (Jackson, 1998; Minkiff, 2003; Hannah, 2004), medico-legal concerns (Savage, 1994), the increasing age of women giving birth and the subsequent increase of complicated pregnancies (Bell, 2001).

International publications report on studies about determinants of CD in China (Qin, 2011; Zhou, 2012), Senegal (Briand, 2011), Australia (Howell, 2009). In the early nineties, Parazzini (1992) described determinants of CD in Italy. More recently Kambale (2011) studied social determinants of CD in Italy, while other authors focused on the Campania region, where the CD rate is highest (Giani, 2011).

Knowing the determinants of CD is a first step in the effort to reduce unnecessary cesarean sections, and studying the role of organizational determinants such as volumes of activity, academic affiliation and time and day of delivery may further contribute to this goal. Volumes of activity are considered an important issue in improving the quality of care and increasing efficiency. In the recent years, small hospitals have been closed due to the need to improve the quality of care and reduce costs. The relation between surgical volume and health outcomes was first described in the late seventies, and many publications have reconfirmed a positive volume-outcome relationship, especially for high risk surgical procedures (Luft, 1979; Birkmeyer, 2002; Chowdhury, 2007). In striving for the best possible care, there is an ongoing debate about centralizing surgical care to high volume

centres (van Gijin, 2010). A systematic review found that there is no conclusive evidence to establish an association between volumes of CD performed per year and outcomes, though a positive association between number of newborns in intensive newborn therapy and neonatal outcomes has been observed (Davoli, 2012). The recent Italian guideline (SNLG, 2012) reports that at high level of activities (high level of deliveries per year), the proportion of CD is lower that at low level of activities.

The impact of academic affiliation on health care resource utilization and clinical outcomes has been examined for a variety of medical diagnoses and procedures (Kuhn, 1994; Jollis, 1994; Rosenthal, 1997; Rutledge, 1997). These studies have generally found that academic affiliation is also related to better health, including having a reduced CD rate (Garcia, 2001; Bianchi, 2012). However important differences exist in structure, functioning and organization of academic hospitals and how they relate to and differentiate from community hospitals across countries.

As far as days of the week (working or non-working days) and time of delivery, results are mixed in respect to outcome. Gould et al. (2005) found that neonatal outcomes at night are worse than in the day, Bailit et al. (2006) found that maternal and neonatal complications of CD do not increase during the night shift. Various studies found that neonatal outcomes are not very different on weekends than on week days (Stewart, 1998; Gould 2003; Stephannson, 2003; Gijsen, 2012). Studies (Mossialos, 2005; Signorelli, 1991) provide different results in risk of CD. Differences in elective CD are obviously expected, as they are planned during the day of working days, however, differences in urgent CD should not exist. Differences in urgent CD could reflect inappropriateness in performing these CDs and should therefore be highlighted.

The thesis has the following objectives:

- to describe the contemporary cesarean delivery practice in the Emilia Romagna regional population and identify the determinants of CD in: 1) women delivering between 2005 and June 2010; 2) women without a previous caesarean section; 3) low risk women (i.e: nulliparous, term singleton vertex); 4) women with spontaneous labour; 5) women with induced

labour; 6) women with a previous caesarean section, with no other important CD risk factors; 7) nulliparous or multiparous women with term singleton vertex and either induced or spontaneous labour.

- to study the role of determinants of time, working days, birth volumes and academic affiliation as determinants of CD in the Emilia Romagna region in: 1) women delivering between 2005 and June 2010; 2) women without a previous caesarean section; 3) low risk women (i.e: nulliparous, term singleton vertex); 4) women with spontaneous labour; 5) women with induced labour; 6) women with a previous caesarean section, with no other important CD risk factors; 7) nulliparous or multiparous women with term singleton vertex and either induced or spontaneous labour.

Methods

Source of data and population

Since 1995, in the RER, a 4,4 million inhabitants region of Northern Italy, all hospital discharge abstracts (SDO) have been electronically recorded, using a Hospital Information System. The data stored in the system includes demographics [gender, date and place of birth, place of residence], discharge ID, admission and discharge dates, discharge diagnoses and procedures (International Classification of Diseases, 9th Revision, Clinical Modification ICD-IX-CM), ward(s) of hospitalization, date(s) of in-hospital transfer, and the regional code of the admitting facility.

Since 2002, the RER has adopted a Birth certificate (Certificate of birth attendance, CedAP, hereafter). This register reports information on socio-demographic characteristics of both parents (age, education, occupational status, etc.), obstetric history and pregnancy (previous pregnancies and/or abortions, duration, characteristics, etc.) and prenatal care (clinical examinations, ultrasounds, amniocentesis, etc.), delivery (place, type, etc.), and information on the newborn (gender, birth order, birth weight, gestational age, Apgar score at 5 minutes, etc.).

All hospital discharge abstracts of women who delivered in the 36 maternity units in the region from 1 January 2005 to 30 June 2010, were selected and identified by the Disease Related Groups (DRG) codes 370-375 or ICD-9 CM code in principal or secondary diagnosis V27xx or 640.xy-676.xy, where y=1 or 2, or intervention codes 72.x, 73.2, 73.5, 73.6, 73.8, 73.9, 74.0, 74.1, 74.2, 74.4, 74.99. SDO were linked with CedAP relative to the same time period using the mother's discharge ID and the year of hospitalization.

This study takes as its sample live births for which the SDO of the mother and CedAP were linked. In case of multiple pregnancy, only one CedAP was retained. I excluded: 1) mothers discharged from hospital without an operating room; 2) mothers with one of the following discharge diagnosis: 656.4-intrauterine death,

V27.1-single stillborn, V27.4-twins, both stillborn, V27.7-multiple births, all stillborn.

A CD was identified by DRG codes 370 and 371 or ICD9 CM diagnosis code 669.7 or intervention code 74.0, 74.1, 74.2, 74.4, 74.99. CD rates were calculated by using the formula:

$$\frac{\text{Number cesarean deliveries} \times 100}{\text{Total number of deliveries}}$$

Potential determinants of CD

Information relative to the potential determinants of cesarean section were retrieved from SDO of women and/or CedAP. A previous study (Stivanello, 2013) suggested that information added to hospital discharge abstracts relative to hospitalizations within two years from discharge did not improve the performance of predictive models, and therefore they were not collected.

The following socio-demographic variables were collected: maternal age (<18, 18-24, 25-29, 30-34, 35-39, >39), education level (university, high, middle and primary or less) of the mother and the father, citizenship, (Italian, developing countries, non developing countries other than Italy), marital status (married, divorced-separated, single, widow, non declared).

The following maternal and fetal clinical factors were retrieved: HIV, diabetes, hypertension, thyroid diseases, lung diseases, other severe comorbidities, genital herpes, substance abuse, eclamsia or pre-eclampsia, abruptio or placenta previa or hemorrhage, cefalolopelvic disproportion, RH isoimmunization, polihydramnios, oligohydramnios, premature rupture of membranes of the amnios, cord prolapse, other problems of the amnios, malposition and malpresentation, intrauterine growth retardation, dystocia and fetal distress fetal anomalities, gestational age (pregnancy at term, preterm and post-term), infant birth weight (less than 1501 gr, between 1501 and 2499gr, between 2500 and 3900gr, more than 4000gr. previous still births/abortion, previous cesarean delivery, pluriparity. These factors were defined using the primary and all secondary discharge diagnoses of the SDO and/or using CedAP variables (see Table 3).

Table 3. Source and definition of study determinants.

Description	Source	ICD 9-CM code	CEDAP field
Age	SDO		
Citizenship	CEDAP		cittad_m
Marital status	CEDAP		statociv_m
Maternal education	CEDAP		Titolom
Paternal education	CEDAP		Titolop
HIV	SDO	042, V08	
Diabetes	SDO	250.0-250.9, 6480, 6488	
Hypertension	SDO	401-405, 64200, 64201, 64203, 6421-6422, 64230, 64231, 64233, 64290, 64291, 64293	
Lung diseases	SDO	010-018, 480-519, 647.30,	
Thyroid diseases	SDO	647.31, 64733, 66800, 66801 66803, 240-246. 648.1	
Genital herpes	SDO	54.1	
Substance abuse	SDO	303-305; 648.30 648.31 648.33	
Other severe diseases	SDO	140.0-208.9, 282.4, 282.6, 286, 287, 342, 344, 340, 341.9, 390.0-398, 410-429, 430-438, 441, 442, 4464, 580-589, 646.21, 646.23, 648.5, 648.6, 659.3, 669.11, 669.13, 745-747	
Previous still births/abortion	CEDAP		aborti or natimor
Previous CD	SDO	654.2	
abortion threads / assisted fecundation / supervision of high risk pregnancy	SDO	63, 640, 644.0, 6463, V26, V230, V232, V234, V235, V237, V238	
eclampsia/ preeclampsia	SDO	642.4-642.7	
rh-isoimmunization	SDO	656.1	
abruptio or placenta previa or ante-partum hemorrhage	SDO	641	
Polyhydramnios	SDO	657	
Oligohydramnios	SDO	658.0.	
Premature rupture of membranes	SDO	658.1	
Other problems of the amnios	SDO	658.4, 658.8, 658.9	
Cord prolapsed	SDO	663.0.	
Dystocia	SDO	660.4, 661.4	
Fetopelvic disproportion	SDO	653, 65660, 65661, 65663	
Multiple pregnancy	SDO or CEDAP	651 V272-V279; V31-V37	Genere
Malposition and malpresentation of fetus	SDO or CEDAP	652	Presentazione
intrauterine growth retardation	SDO or CEDAP	6565	dif_accr
Fetal stress	SDO	656.3	
Fetal anomalities	SDO or CEDAP	655	Malformazioni
Pregnancy length	CEDAP		Durgrav
Infant birth weight (grams)	CEDAP		Peso
Type of hospital	SDO		
Volumes	SDO		
Delivery on non working days	CEDAP		dt_parto
Delivery between 7 pm and 7 am	CEDAP		hh_par
Pluriparity	CEDAP		parti_precenti

In addition I retrieved information relative to organizational aspects: time of delivery (between 7 am and 7 pm or between 7 pm and 7 am) and day of delivery (working and non working days such as Saturday, Sunday, national holidays). As for hospital characteristics, I retrieved information on the affiliation (teaching or non-teaching) and volumes of deliveries (mean annual number of deliveries). The latter were categorized as: <500, 501-799, 800-999, 1000-2499, >2500 deliveries

per year following the classification used by the Italian Ministry of Health (SNLG, 2012).

I therefore collected both patient- and hospital-related variables, the latter included just affiliation and volumes of deliveries. All the other variables were patient-level variables.

By using CedAP variables, the deliveries were classified according to a modified version of the Robson Ten Group Classification System (TGCS) (Brennan, 2009) (Table 4).

Table 4. Ten Group Classification System (TGCS)

Groups	Parameters
I	Nulliparous, singleton, cephalic, ≥ 37 weeks, spontaneous labor
II	Nulliparous, singleton, cephalic, ≥ 37 weeks, induced (IIa) or prelabour CD (IIb)
III	Multiparous, singleton, cephalic, ≥ 37 weeks, spontaneous labor
IV	Multiparous, singleton, cephalic, ≥ 37 weeks, induced (IVa) or prelabour CD (IVb)
V	Previous CD, singleton, cephalic, ≥ 37 weeks
VI	All nulliparous breeches
VII	All multiparous breeches (including previous CD)
VIII	All multiple pregnancies (including previous CD)
IX	All abnormal lies (including previous CD)
X	All singleton, cephalic, ≤ 36 weeks, (including previous CD)

Statistical analysis

Determinants of cesarean deliveries were studied in the following cohorts:

- all deliveries meeting the inclusion/exclusion criteria (study population)
- all deliveries meeting the inclusion/exclusion criteria and excluding women with a previous cesarean delivery (ICD IX CM 654.2x) (subgroup without previous CD)
- all deliveries meeting the inclusion/exclusion criteria and including only women in the I and II TGCS group (nulliparous, singleton, cephalic at term deliveries: subgroup NTCS)
- all deliveries meeting the inclusion/exclusion criteria occurring after a previous CD after excluding deliveries with the CD risk factors considered in the VI-X TGCS groups (subgroup V TGCS)

- all deliveries meeting the inclusion/exclusion criteria in nulliparous or multiparous term singleton vertex with either induced or spontaneous labour (subgroup I, IIa, III, IVa TGCS)
- all deliveries meeting the inclusion/exclusion criteria with a spontaneous labour (subgroup spontaneous labour)
- all deliveries meeting the inclusion/exclusion criteria with an induced labour (subgroup induced labour)

Descriptive analyses

CD rate was calculated for the study population, the above-mentioned subgroups and by using the TGCS. CD rate was calculated by type of labour and by hospital. Inter-hospital variance statistics were calculated as well.

Frequency of all potential determinants, CD rate for each potential determinant, relative risks (RR) and the population attributable risk (PAR) were calculated for the study population and the subgroups. The PAR was calculated by using the adjusted RRs from the multivariable analysis (Steenland, 2006).

Because the CD rate has a frequency higher than 10%, crude and adjusted RRs, instead of odds ratios, were calculated (Mc Nutt, 2005).

Frequency of the above-mentioned determinants was calculated by the following subgroups who underwent CD:

- all deliveries meeting the inclusion/exclusion criteria without labour (subgroup without labour)
- all deliveries meeting the inclusion/exclusion criteria with an elective cesarean section (subgroup with elective cesarean section)
- all deliveries meeting the inclusion/exclusion criteria with an urgent cesarean section (subgroup with an urgent cesarean section)

Multivariate analyses

To estimate the effect of variables collected at patient and hospital level on the risk of CD for the seven elected cohorts, a multilevel (also known as hierarchical) statistical approach (Rice, 1997) was adopted. This approach is suitable for data that are clustered into higher level units (e.g. deliveries clustered into hospitals)

and properly accounts for variability at each level of analysis. It also permits the examination of predictors of that variability at each level on analysis.

For this purpose, several two-level hierarchical Poisson regression models with levels corresponding to (1) patient and (2) hospital were constructed. The first model did not include any explanatory variables and estimated only the overall outcomes rate as well as their differences among hospital (two-level variance) (Model A). The second model included patient-related variables (sociodemographic, clinical, time and day of delivery) (Model B), and the third model included hospital-level variables (affiliation and volumes) as well (Model C).

Since multilevel modelling is computationally intensive, significant patient-related predictors of CD to be included in models B and C were identified using a preliminary non-hierarchical backward Poisson regression with a significance level of removal set at 0.05. This procedure includes initially all factors identified as potential predictors of CD and then removes those unrelated with CD.

I did not consider dystocia and fetal distress as potential risk factors, because they might often be reported as reasons for an ex-post justification of the performed CD rather than objectively assessed conditions (Capon, 2005; Lieberman, 1998). Comparisons between nested models were made using the likelihood ratio (LR) test, and after calculating the proportional change in variance (PCV) versus the null and previous model, pseudo R^2 were also calculated.

The procedure was replicated for each of the seven cohorts and the results of the two-level models are provided.

For inter-hospital comparisons, the reference category included hospitals with the lowest adjusted risk estimated by fitting the Poisson model with age and the above-mentioned clinical variables (Model D).

In order to study the role of volume, academic affiliation, time of delivery and delivery on working days as exposure, separate multilevel Poisson regression models (Model E) were fitted, using one variable at a time as an independent variable. This was done because the high correlation of these variables may lead to collinearity problems. In addition, in this model socio-demographic (except for age) variables were not included. Adjustment for socio-demographic variables is controversial in inter-hospital comparison and in studies on organizational

variables because such factors may be associated with differences in health care delivery (Keeler, 1997; Bailit, 1999; Bailit, 2008; Spertus, 2010; Stivanello, 2013)
I carried out a sensitivity analysis, omitting intrauterine growth retardation and cephalopelvic disproportion as potential risk factors (Model F). Both these risk factors could be used in an opportunistic way as post-hoc justification after a CD as fetal distress and dystocia (see above).

In summary, for every subgroup of women the following models were carried out:

- Model A: multilevel Poisson model without explanatory variables
- Model B: multilevel Poisson model with patient level variables (sociodemographic+ clinical+ time and day of delivery)
- Model C: multilevel Poisson model with patient and hospital level variables (volume and affiliation as well)
- Model D: Poisson model with age, clinical variables and hospital
- Model E: multilevel Poisson model with age, clinical variables and volumes (or affiliation or time and day of delivery)
- Model F: multilevel Poisson model with age, clinical variables excluding cephalopelvic disproportion and uterine growth retardation and volumes (or affiliation or time and day of delivery)

In addition, interactions between some variables were also tested: between citizenship and affiliation or volumes in the study population and between time or day of delivery and affiliation in the I, IIa, III, IVa subgroup.
CD rates and volumes were plotted using scatter plots with lowess smoothing and funnel plots. Funnel plots were used to examine the variation among hospitals in risk-adjusted rates of CD. These plots allow to determine whether the rate of CD differs significantly from the average of the RER, assuming the hospital's rate is only influenced by sampling variation (that is, random error). The plot contains two control limits. Assuming differences arise from random error alone, the chance of the hospital being within the limits is 95% for the inside funnel and 99.8% for the outer funnel (Bragg, 2010).

Classification tree

Classification tree analysis was used to determine the ability of socio-demographic, clinical characteristics and time and day of delivery to discriminate subgroups of patients with a differential risk in CD.

The Classification regression trees (CRT) growing method was used. CRT splits the data into subgroups that are as homogeneous as possible with respect to the dependent variable. A terminal node in which all cases have the same value for the dependent variable is a homogeneous, "pure," node. The homogeneity of each node is measured with the Gini index. I avoided overfitting the model by pruning the tree: the tree is grown until stopping criteria are met, and then it is trimmed automatically to the smallest subtree based on the specified maximum difference in risk applied.

The Classification tree analysis based on the CRT is represented graphically as an inverted tree. Beginning with a root node that includes all cases, the tree branches and grows iteratively until the procedure is completed. The final nodes (or the ‘leaves’ of the tree) comprise subgroups with different proportion of CD.

The statistical analysis was performed using Stata Version 10 and SPSS 17. The latter was used only for the classification trees.

Results

Between 1st January 2005 and 30th June 2010, 213539 women delivered in the Emilia Romagna Region: 148917 (69.74%) by vaginal deliveries and 64622 (30,26%) by CD.

The number of deliveries in the subgroup without previous CD was 189843 and of these, 22,42% were CD (Table 5). The NTCS CD rate was 24.48%

Table 5. Number of deliveries and CD in the study population, in women without previous CD and in NTCS.

Cohort	N. deliveries	CD	% CD
Study population	213539	64622	30.26
Without previous CD	189843	42563	22.42
NTCS	102250	25034	24.48

Most deliveries (60,66%) presented spontaneous labour, the others had either an induced labour (19,56%) or occurred as CD without labour (19,77%). The risk of CD was more than double after an induced labour than after a spontaneous labour (p<0.001) (Table 6).

Table 6. Frequency of deliveries and CD by type of labour and RR of induced labour.

Labour	N. deliveries	CD	% CD	RR	95% CI		P
Spontaneous	129539	13320	10.28	1.00			
Induced	41778	9328	22.33	2.17	2.12	2.22	<0.001
No labour	42222	42222	100				

Since 2007, CedAP contains a variable that distinguishes elective and urgent CD: 57,94% of the CD were elective and mostly (91,44%) occurred before labour, only a small percentage were programmed but occurred during labour (spontaneous or induced). 42,06% of the CD were urgent. Among the urgent CD, 37,08% occurred during a spontaneous labour, 32,5% without labour and 30.42% during an induced labour (Table 7).

Table 7. Type of CD by type of labour (2007-mid 2010)

Type of labour	Spontaneous		Induced		No labour		Total	
	N.	%	N.	%	N,	%	N.	%CD
Elective CD	1615	6.66	459	1.89	22158	91.44	24232	57.94
Urgent CD	6523	37.08	5350	30.42	5717	32.50	17590	42.06
Total	8138	19.46	5809	13.89	27875	67.00	41822	100.00

By analysing deliveries by TGCS groups the highest CD rate pertains to the last five groups as table 8 shows, though the most numerous classes of CD pertain to the first two groups, followed by the V group.

Table 8a. Deliveries and CD by TGCS and relative contributions.

TGCS	N. deliveries	N. CD	CD rate	Prop. of all deliveries	CD % of all deliveries	CD % of all CD
I	65346	7,463	11.42	30.60	3.49	11.55
II	36904	17,571	47.61	17.28	8.23	27.19
I-II	102250	25,034	24.48	47.88	11.72	38.74
III	52406	1,488	2.84	24.54	0.70	2.30
IV	16957	5,674	33.46	7.94	2.66	8.78
I-IIa-III-Iva	156719	17511	11.17	73.39	8.20	27.10
V	17350	15,065	86.83	8.12	7.05	23.31
VI	5347	5,097	95.32	2.50	2.39	7.89
VII	2804	2,590	92.37	1.31	1.21	4.01
VIII	3128	2,762	88.30	1.46	1.29	4.27
IX	1287	827	64.26	0.60	0.39	1.28
X	12010	6,085	50.67	5.62	2.85	9.42
Total	213539	64,622	30.26	100	30.26	100

Table 8b. Deliveries and CD by TGCS and relative contributions.

TGCS	CD % of all CD	spontaneous labour %	induced deliveries %	Elective CD of all CD %	Urgent CD of all CD %
I	11.55	100	0	8.64	91.64
II	27.19	0	72.62	41.11	58.99
I-II	38.74	63.91	26.21	31.52	68.63
III	2.30	100	0	18.97	83.00
IV	8.78	0	71.75	67.23	32.88
I-IIa-III-IVa	27.10	75.14	25.86	8.86	91.55
V	23.31	20.59	2.13	87.76	12.25
VI	7.89	16.08	1.44	79.61	20.39
VII	4.01	20.36	1.78	77.33	22.72
VIII	4.27	23.95	5.05	72.31	27.69
IX	1.28	54.08	18.49	36.69	63.31
X	9.42	44.45	15.98	50.13	49.92
Total	100	60.66	19.56	58.00	42.11

The highest proportion of spontaneous and induced labour patients pertains to the first 4 classes. As expected the highest proportion of urgent CDs is in group 1 and the highest proportion of elective CDs is in groups V-VIII, with a corresponding fewer number of urgent CD in these categories.

CD rates decreased from 30.49% in 2005 to 29,61% in 2010 (Table 9).

Table 9. Deliveries and CD by year.

Year	N. deliveries	CD	CD rate
2005	35779	10910	30.49
2006	38189	11537	30.21
2007	39057	11868	30.39
2008	40618	12338	30.38
2009	40916	12349	30.18
2010	18980	5620	29.61

The CD rate varied from 20,86 to 56,76% among the hospitals (Table 10), with 10 hospitals presenting a risk 50% greater than the hospitals of the reference group category represented by three hospitals (E, N, T).

Inter-hospital variability in crude CD rates is observed for all subgroups as table 11 shows. The greatest differences in crude CD rates are observed among deliveries with spontaneous labour, the smallest in the V TGCS group.

Differences among hospitals are observed also in terms of adjusted CD, though variability is reduced in all subgroups but in the induced labour subgroup (Table 12).

Table 10. CD rate and crude RRs by hospital.

Hospital	n. deliveries	n. CD	% CD	RR	95%IC		P
A	5,686	1,683	29.60	1.40	1.32	1.47	<0.001
B	1,144	375	32.78	1.55	1.41	1.69	<0.001
C	9,016	2,041	22.64	1.07	1.01	1.12	0.013
D	1,304	493	37.81	1.78	1.65	1.93	<0.001
E	3,921	822	20.96	Ref			
F	12,110	2,895	23.91	1.13	1.08	1.18	<0.001
G	2,220	1,260	56.76	2.68	2.55	2.81	<0.001
H	4,634	1,117	24.10	1.14	1.07	1.21	<0.001
I	3,477	929	26.72	1.26	1.18	1.34	<0.001
J	4,141	1,373	33.16	1.56	1.48	1.65	<0.001
K	8,029	2,348	29.24	1.38	1.31	1.45	<0.001
L	4,608	1,315	28.54	1.35	1.27	1.42	<0.001
M	6,182	1,955	31.62	1.49	1.42	1.57	<0.001
N	5,413	1,167	21.56	Ref			
O	16,191	4,632	28.61	1.35	1.29	1.41	<0.001
P	3,290	891	27.08	1.28	1.20	1.36	<0.001
Q	4,784	1,471	30.75	1.45	1.37	1.53	<0.001
R	3,008	904	30.05	1.42	1.33	1.51	<0.001
S	13,713	5,026	36.65	1.73	1.66	1.80	<0.001
T	2,618	546	20.86	Ref			
U	7,606	2,680	35.24	1.66	1.59	1.74	<0.001
V	17,889	5,441	30.42	1.43	1.38	1.49	<0.001
W	7,196	2,259	31.39	1.48	1.41	1.55	<0.001
Y	15,379	4,602	29.92	1.41	1.35	1.47	<0.001
Z	13,153	3,821	29.05	1.37	1.31	1.43	<0.001
AA	19,143	6,720	35.10	1.66	1.59	1.72	<0.001
AB	5,794	1,866	32.21	1.52	1.44	1.60	<0.001
AC	4,035	1,309	32.44	1.53	1.45	1.62	<0.001
AD	7,855	2,681	34.13	1.61	1.54	1.69	<0.001

Table 11. Hospital crude CD rates, main statistics and measures of variation in the study population and in other subgroups of women.

	Study population	Primary	NTCS	I-IIa-III-IVa	V	Spontaneous labour	Induced labour
Hospital			**CD rate**				
A	29.60	23.49	26.57	13.37	88.04	10.59	31.46
B	32.78	25.12	28.06	12.12	92.50	11.62	34.62
C	22.64	15.57	15.72	5.32	73.86	4.88	12.12
D	37.81	25.94	30.28	14.48	97.67	15.60	29.06
E	20.96	15.18	17.48	8.17	71.38	7.91	15.70
F	23.91	16.45	16.74	7.52	86.16	5.71	17.78
G	56.76	44.24	47.85	18.19	98.03	23.63	22.81
H	24.10	17.36	23.91	10.86	73.09	9.84	22.22
I	26.72	18.87	20.60	10.31	97.31	9.10	23.70
J	33.16	23.59	28.24	12.39	92.21	10.81	27.68
K	29.24	21.11	23.50	11.66	95.92	7.06	29.27
L	28.54	18.79	21.52	9.65	95.80	8.39	19.02
M	31.62	22.25	24.54	13.55	94.59	12.64	24.74
N	21.56	16.50	18.93	8.71	70.78	7.55	23.20
O	28.61	21.36	21.96	10.41	85.30	7.70	22.55
P	27.08	17.59	22.35	8.35	89.71	8.82	18.45
Q	30.75	22.34	25.45	12.41	82.91	9.38	22.34
R	30.05	23.58	26.37	12.17	75.16	13.06	16.57
S	36.65	29.04	29.88	16.03	87.70	16.13	30.13
T	20.86	15.72	15.82	6.03	82.89	5.14	15.43
U	35.24	26.46	30.90	14.80	91.72	15.09	30.63
V	30.42	23.53	25.82	11.56	73.85	11.35	21.84
W	31.39	24.42	25.01	11.54	89.92	11.91	21.11
Y	29.92	21.23	21.88	8.19	87.72	7.49	7.49
Z	29.05	19.98	18.27	8.12	86.32	7.89	18.72
AA	35.10	28.11	33.35	15.24	92.83	13.27	24.88
AB	32.21	23.17	28.63	12.85	91.38	10.74	23.07
AC	32.44	23.34	26.79	12.22	98.14	10.63	23.39
AD	34.13	26.09	22.95	12.76	94.85	16.53	23.83
MIN	20.86	15.18	15.72	5.32	70.78	4.88	12.12
MAX	56.76	44.24	47.85	18.19	98.14	23.63	34.62
MEAN	30.46	22.42	24.48	11.34	87.51	10.28	22.33
DS	6.83	5.71	6.44	3.01	8.68	4.03	5.46
CV	22.43	25.45	25.96	26.55	9.92	37.64	23.90
VARIANCE	3.95	4.93	5.43	7.59	0.68	12.26	5.07

Table 12. Hospital adjusted CD rates, main statistics and measures of variation in the study population and in other subgroups of women.

Hospital	Study population	Primary	NTCS	I-IIa-III-IVa Adjusted CD rate	V	Spontaneous labour	Induced labour
A	30.51	24.37	26.83	13.29	86.96	12.47	31.88
B	33.01	26.72	29.32	11.82	92.59	12.40	35.96
C	22.81	16.38	16.72	5.36	75.22	5.56	12.84
D	33.86	26.46	30.69	14.66	97.67	15.78	30.78
E	20.96	15.18	17.48	8.17	71.38	7.91	15.70
F	22.96	15.64	17.03	7.72	85.39	6.68	18.84
G	36.05	29.73	41.24	16.08	97.08	15.16	22.16
H	22.94	16.69	22.47	10.27	72.67	10.53	21.25
I	27.21	19.50	21.12	9.75	96.35	11.00	22.31
J	31.18	23.79	28.24	12.40	91.95	11.78	28.15
K	29.66	21.36	24.43	11.36	95.56	8.45	29.95
L	28.89	19.98	22.75	9.90	96.21	10.16	21.13
M	28.50	20.22	24.00	12.75	94.13	13.12	24.80
N	21.56	16.50	18.93	8.71	70.78	7.55	23.20
O	24.41	17.51	19.44	8.98	84.95	8.40	21.04
P	23.42	17.68	22.63	7.79	90.08	8.28	18.33
Q	29.24	22.27	26.04	11.65	83.36	10.27	23.08
R	28.27	21.77	23.85	11.53	73.65	12.25	17.43
S	29.25	22.00	28.10	13.97	87.26	11.92	27.94
T	20.86	15.71	15.82	6.03	82.89	5.14	15.43
U	33.10	25.26	30.38	14.99	90.92	16.34	30.43
V	25.46	20.99	25.59	11.17	73.97	10.57	22.53
W	27.29	19.95	23.56	10.61	89.07	11.09	20.09
Y	27.07	20.53	23.19	8.21	87.74	8.37	16.61
Z	25.12	17.39	18.47	8.33	85.67	8.62	19.09
AA	28.18	22.80	30.50	13.21	92.14	12.23	23.75
AB	28.08	22.33	29.37	12.85	91.75	11.54	25.66
AC	32.70	24.90	28.09	12.56	97.66	13.15	24.95
AD	26.96	18.68	20.94	10.31	94.41	12.20	20.92
MIN	20.86	15.18	15.82	5.36	70.78	5.14	12.84
MAX	36.05	29.73	41.24	16.08	97.67	16.34	35.96
MEAN	27.40	20.69	24.38	10.80	86.57	10.50	22.98
DS	4.13	3.81	5.59	2.72	8.60	2.86	5.57
CV	15.09	18.39	22.94	25.15	9.94	27.25	24.23
VARiANCE	1.62	2.51	3.74	6.51	0.02	7.44	5.24

Important differences among hospitals are observed also in the relative frequency of elective CD (Table 13).

Table 13. Proportion of elective and urgent CD of all deliveries.

	Proportion of all deliveries %	
	Elective CD	Urgent CD
A	13.07	16.28
B	21.6	12.93
C	13.61	7.14
D	20.77	17.72
E	12.63	7.61
F	13.49	10.3
G	40.68	13.02
H	12.75	10.11
I	17.01	9.43
J	20.35	13.63
K	13.71	15.16
L	17.94	9.1
M	19.67	12.34
N	11.08	12.07
O	17.32	11.58
P	16.95	9.03
Q	17.08	12.63
R	19.63	5.43
S	23.32	14.1
T	9.94	10.89
U	19.93	15.08
V	14.96	15.96
W	20.41	12.21
Y	14.67	13.88
Z	17.83	10.53
AA	20.45	14.58
AB	18.57	13.35
AC	20.73	12.03
AD	18.43	14.27
MIN	9.94	5.43
MAX	40.68	17.72
Mean	17.88	12.15
DS	5.58	2.88
CV	31.22	23.69

The study population

Table 14 presents the CD rate by clinical and organizational characteristics, the crude and adjusted RR (with their relative 95% CI) and the population attributable risk in the study population. The highest crude RR of CD were observed in case of a previous CD (RR 4,15; 95% CI: 4,11-4,19), malposition/malpresentation (RR 3,48; 95% CI: 3,45-3,51), cord prolapse (RR 3,24; 95% CI: 3,16-3,32), abruption or placenta previa or ante-partum hemorrhage (RR 3,23; 95% CI: 3,20-3,27), genital herpes (RR 3,21; 95% CI: 3,28-3,32).

Of the 32 significant variables included in the model (model C) the greatest RR were found for a previous CD (RR 4,95; 95% CI: 4,85-5,05), cord prolapse (RR 3,51; 95% CI: 2,96-4,16), feto-pelvic disproportion (RR 2,64; 95% CI: 2,51-2,71) and malposition/malpresentation (RR 2,72; 95% CI: 2,66-2,77). As far as the organizational variables are concerned, performing less than 500 deliveries per year and being a teaching hospital is significantly associated with a higher risk of CD in univariate analyses but not in the multivariate analyses, where low birth volumes hospitals show just a trend to have higher risk of CD.

Deliveries occurring in non-working days and between 7 pm and 7 am are significantly ($p<0.001$) associated with a reduced risk of CD.

A previous CD, malpresentation/malposition, delivering between 7 pm and 7 am and deliveries on non-working days show the highest population attributable fractions.

The variables of model B explain about 59% of the inter-hospital variability, while those of model C explain 65% of this variability as table 15 shows. Hospital-level variables explain 15% of the inter-hospital variability.

Table 14. Frequency, crude, adjusted RR (aRR) and population attributable risk (PAR) for sociodemographic, clinical and organizational characteristics in the study population.

		N. deliveries	N. CD	prop of the population %	% CD	Crude RR	IC		P	aRR*	IC		P	PAR
							Low	High			Low	high		
Age	<18	707	113	0.33	15.98	0.53	0.45	0.63	<0.001	0.60	0.49	0.72	<0.001	-0.12
	18-24	23677	4827	11.09	20.39	0.68	0.66	0.70	<0.001	0.77	0.74	0.79	<0.001	-2.27
	24-29	48436	12402	22.68	25.60	0.86	0.84	0.87	<0.001	0.91	0.89	0.93	<0.001	-1.81
	30-34	76593	22921	35.87	29.93	1.00				1.00				0.00
	35-39	52265	19012	24.48	36.38	1.22	1.20	1.23	<0.001	1.10	1.08	1.13	<0.001	2.79
	>39	11861	5347	5.55	45.08	1.51	1.47	1.54	<0.001	1.23	1.19	1.26	<0.001	1.53
Citizenship	Italian	159979	50334	74.92	31.46	1.00			<0.001	1.00				0.00
	high income	1997	547	0.94	27.39	0.87	0.81	0.94	<0.001	0.90	0.82	0.98	0.012	-0.10
	Low income	51563	13741	24.15	26.65	0.85	0.83	0.86	<0.001	0.99	0.97	1.01	0.303	-0.24
Marital status	Single	52995	15989	24.82	30.17	1.00	0.99	1.02	0.798	1.03	1.01	1.05	0.001	0.77
	Married	144153	43578	67.51	30.23	1.00								
	Divorced/separated	5133	1904	2.40	37.09	1.23	1.18	1.28	<0.001	1.06	1.00	1.13	0.06	0.16
	Widow	346	141	0.16	40.75	1.35	1.19	1.53	<0.001	1.12	0.95	1.32	0.186	0.02
	not declared	10912	3010	5.11	27.58	0.91	0.88	0.94	<0.001	1.05	1.00	1.11	0.054	0.22
Maternal education	Primary	9749	2749	4.57	28.20	0.95	0.92	0.99	0.006	1.01	0.97	1.06	0.554	0.05
	Secondary	58661	18106	27.47	30.87	1.03	1.01	1.05	0.005	1.04	1.02	1.06	<0.001	1.03
	High-school	96551	29118	45.21	30.16	1.00				1.00				0.00
	University	48578	14604	22.75	30.06	1.00	0.99	1.02	0.709	0.96	0.94	0.98	<0.001	-0.92
Paternal education	Primary	6507	1898	3.05	29.17	0.97	0.93	1.01	0.131					
	Secondary	68922	20726	32.28	30.07	1.00	0.98	1.02	0.632					
	High-school	81059	24468	37.96	30.19	1.00	0.99	1.03	0.287					
	University	33837	10285	15.85	30.40	1.00								
HIV		182	175	0.09	96.15	3.18	3.09	3.28		2.40	2.07	2.79	<0.001	0.16
Diabetes		3105	1635	1.45	52.66	1.76	1.70	1.82	<0.001	1.23	1.17	1.29	<0.001	0.47
Hypertension		4198	2204	1.97	52.50	1.76	1.71	1.81	<0.001	1.40	1.34	1.46	<0.001	0.97
Lung diseases		190	145	0.09	76.32	2.53	2.33	2.73	<0.001	1.48	1.26	1.74	<0.001	0.07
Thyroid diseases		342	143	0.16	41.81	1.28	1.22	1.57	<0.001					
Genital herpes		17	17	0.01	100.00	3.21	3.28	3.32	<0.001					
Substance abuse		51	26	0.02	50.98	1.68	1.29	2.21	<0.001	1.75	1.19	2.57	0.005	0.02
Other severe diseases		1196	751	0.56	62.79	2.09	2.00	2.18	<0.001	1.50	1.40	1.62	<0.001	0.39
Previous still births/abortion		36673	12665	17.17	34.53	1.17	1.16	1.19	<0.001	1.21	1.10	1.33	<0.001	3.45
Previous CD		23696	22059	11.10	93.09	4.15	4.11	4.19	<0.001	4.95	4.85	5.05	<0.001	27.23
Abortion threads/assisted fecundation/supervision of high risk pregnancy		668	459	0.31	68.71	2.28	2.17	2.40	<0.001	1.21	1.11	1.34	<0.001	0.13
Eclampsia/ preeclampsia		3175	2319	1.49	73.04	2.47	2.41	2.52	<0.001	1.89	1.81	1.97	<0.001	1.69

Rh-isoimmunization		1871	496	0.88	26.51	0.88	0.81	0.94	<0.001	1.07	0.97	1.17	0.167	0.05
Abruptio or placenta previa or ante-partum hemorrhage		2675	2546	1.25	95.18	3.23	3.20	3.27	<0.001	2.59	2.49	2.70	<0.001	2.42
Polyhydramnios		491	315	0.23	64.15	2.13	1.99	2.27	<0.001	1.40	1.25	1.57	<0.001	0.14
Oligohydramnios		7550	2560	3.54	33.91	1.13	1.09	1.16	<0.001	1.31	1.26	1.36	<0.001	0.93
Premature rupture of membranes		28971	5690	13.57	19.64	0.62	0.60	0.63	<0.001	0.81	0.79	0.84	<0.001	-2.04
Other problems of the amnios		176	120	0.08	68.18	2.26	2.04	2.50	<0.001	2.09	1.74	2.50	<0.001	0.10
Cord prolapsed		138	135	0.06	97.83	3.24	3.16	3.32	<0.001	3.51	2.96	4.16	<0.001	0.15
Dystocia		7054	3583	3.30	50.79	1.72	1.68	1.76						
Fetopelvic disproportion		2514	1843	1.18	73.31	2.46	2.40	2.53	<0.001	2.64	2.51	2.77	<0.001	1.77
Multiple pregnancy		3222	2826	1.51	87.71	2.99	2.94	3.03	<0.001	1.51	1.45	1.58	<0.001	1.48
Malposition and malpresentation of fetus		12965	11870	6.07	91.55	3.48	3.45	3.51	<0.001	2.72	2.66	2.77	<0.001	11.60
intrauterine growth retardation		6602	3695	3.09	55.97	1.90	1.86	1.94	<0.001	1.23	1.19	1.28	<0.001	1.07
Fetal stress		5721	5086	2.68	88.90	3.10	3.07	3.14						
Fetal anomalies		2309	1076	1.08	46.60	1.55	1.48	1.62	<0.001	1.24	1.16	1.31	<0.001	0.32
Pregnancy lengh	At term	193893	54205	90.80	27.96	1.00								
	Pre-term	15664	9430	7.34	60.20	2.15	2.11	2.20	<0.001	1.12	1.09	1.16	<0.001	1.59
	Post-term	3733	910	1.75	24.38	0.87	0.82	0.93	<0.001	1.14	1.07	1.22	<0.001	0.17
Infant birth weight (grams)	2500-3999	185432	52306	86.84	28.21	1.00								
	1500-2500	1783	1506	0.83	84.46	2.99	2.93	3.06		1.23	1.16	1.31	<0.001	1.23
	<1500	10633	6534	4.98	61.45	2.18	2.14	2.22	<0.001	1.23	1.19	1.27	<0.001	1.23
	>4000	15471	4178	7.25	27.01	0.96	0.93	0.98	<0.001	1.02	0.99	1.06	0.182	1.02
Pluriparity		96444	28922	45.16	29.99	0.98	0.97	1.00	0.002	0.53	0.52	0.54	<0.001	0.53
Type of hospital	Teaching	58600	19868	27.44	33.90	1.17	1.16	1.19	<0.001	1.03	0.89	1.18	0.718	1.03
	Non teaching	154939	44754	72.56	28.88	1.00								
Volumes	100-500	7286	2674	3.41	36.70	1.18	1.13	1.23	<0.001	1.18	0.98	1.41	0.074	1.18
	501-799	21872	6228	10.24	28.47	0.91	0.89	0.94	<0.001	1.04	0.89	1.23	0.616	1.04
	800-999	19439	5070	9.10	26.08	0.84	0.81	0.86	<0.001	0.95	0.80	1.14	0.587	0.95
	1000-2499	96340	29255	45.12	30.37	0.97	0.96	0.99	0.003	1.06	0.92	1.21	0.438	1.06
	>2500	68602	21395	32.13	31.19	1								
Delivery on non working days		55274	11340	25.88	20.52	0.61	0.60	0.62	<0.001	0.69	0.67	0.70	<0.001	-8.06
Ddelivery between 7 pm and 7 am		70610	13289	33.07	18.82	0.52	0.52	0.53	<0.001	0.65	0.64	0.67	<0.001	-10.95
Total		213539	64622	100.00	30.26									

The LT test indicates that model B is significantly different from the null model and that model C (with patient and hospital level variables) is not different in terms of goodness of fit of the model from model B containing only patient level variables.

Table 15. Variance, proportional change in variance (PCV) and LR test in models on all deliveries (n = 213071),

	Null Model A	patient level Model B	patient and hospital level Model C
Hospital variance	0.040	0.016	0.014
Hospital PCV vs. null model	-	-58.95	-65.29
Hospital PCV vs. previous			-15.46
Pseudo R^2	-	0.136	0.129
LR test vs. previous model		p>0.0001	0.2881

Similarly, when I analyzed birth volumes and type of hospital (teaching vs non teaching) separately, adjusting by clinical variables only (Model E), these variables are not significant though a trend to have a higher risk of CD is noted in women who deliver in hospitals with less than 500 deliveries a year. When the analyses is repeated with a model without fetal disproportion and fetal growth retardation (Model F), hospitals with 100-500 deliveries per year are significantly associated with a greater risk of CD as table 16 shows.

Table 16. aRR of CD for type of hospital and volumes after adjustment with model E and F.

Variable		Model E				Model F			
		aRR	IC		P	aRR	IC		P
Type of hospital	Teaching	1.15	0.86	1.00	0.965	1.00	0.86	1.16	0.966
	Non teaching								
Volumes	100-500	1.19	0.99	1.42	0.058	1.23	1.03	1.47	0.023
	501-799	1.05	0.90	1.23	0.539	1.06	0.90	1.24	0.469
	800-999	0.96	0.80	1.14	0.615	0.97	0.81	1.15	0.732
	1000-2499	1.05	0.91	1.21	0.5	1.05	0.91	1.22	0.466
	>2500	1				1			
Delivery on non working days		0.69	0.52	0.54	0.001	0.68	0.66	0.69	<0.001
Delivery between 7 pm and 7 am		0.65	0.67	0.70	0.001	0.65	0.63	0.66	<0.001

Delivery between 7 am and 7 pm and delivery on working days are significant risk factors in both additional analyses.

The graphs below (Figure 1 and 2), show the relation between birth volumes (number of deliveries per year) and adjusted CD rates. It shows that hospitals with less deliveries have a greater variation in adjusted CD rate with more outliers in the upper part of the graph. The lowess curve rapidly falls vertically and then maintains an almost horizontal line.

Figure 1. Funnel plot with adjusted CD rates in the study population.

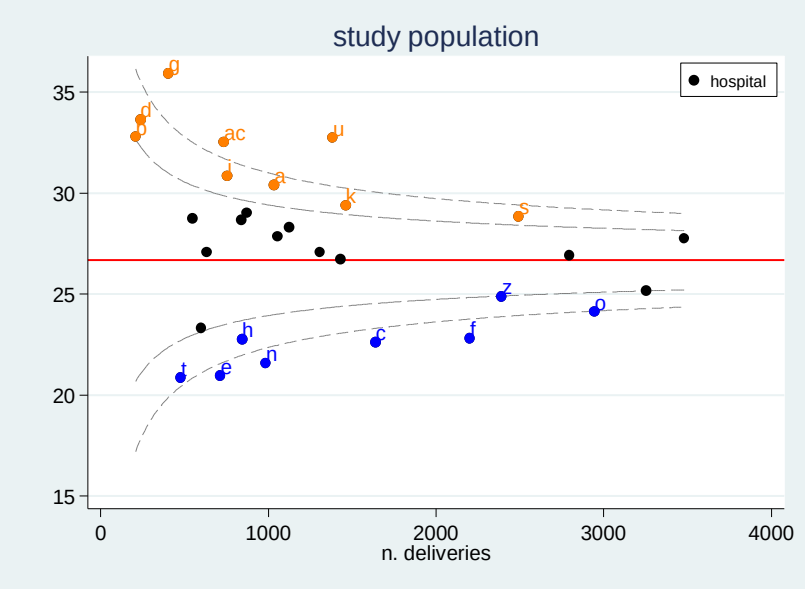
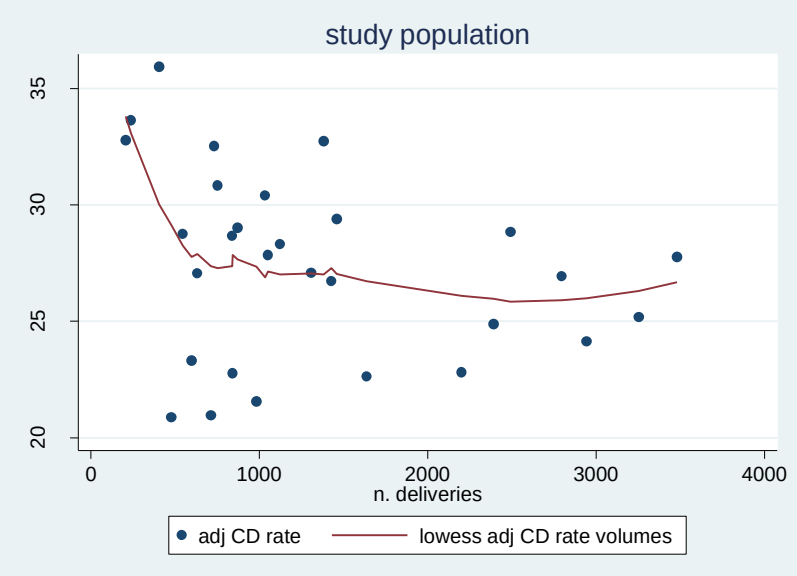


Figure 2. Scatter plot of adjusted CD rates and birth volumes with lowess curve (study population).



The interaction of affiliation and birth volumes with citizenship was tested. There was no interaction between affiliation and citizenship, but there was an interaction between women coming from low income countries and delivering in hospitals with a number of annual deliveries between 500 and 800 (p=0.007). Below, the table 17 presents the results of the stratified analyses.

Table 17. Association between volumes and CD in italian and in women from low income countries.

	Italian				Low income countries			
Volumes	**aRR**	**IC**		**P**	**aRR**	**IC**		**P**
100-500	1.19	0.99	1.43	0.068	1.18	0.97	1.43	0.095
501-799	1.07	0.91	1.26	0.413	0.98	0.84	1.14	0.806
800-999	0.96	0.80	1.15	0.669	0.94	0.80	1.11	0.495
1000-2499	1.06	0.92	1.22	0.464	1.02	0.89	1.16	0.802

Subgroup without previous CD

Table 18 presents the primary CD rate by clinical and organizational characteristics, the crude and adjusted RR (with their relative 95% CI) and the population attributable risk.

Of the 30 significant variables included in the model (model C) the highest RR were found for cord prolapse (RR 3,72; 95% CI: 3,13-4,42), HIV (RR 3,73; 95% CI: 3,15-4,41) and malposition/malpresentation (RR 3,54; 95% CI: 3,45-3,62), abruption or placenta previa or ante-partum hemorrhage (RR 3,24; 95% CI: 3,10-3,39).

As far as the organizational variables are concerned, the significant association between birth volumes or teaching hospitals observed in univariate analyses disappeared after controlling for all other variables. Deliveries occurring on non-working days and between 7 pm and 7 am are significantly (p<0.001) associated with a reduced risk of CD also in multivariate analyses

Malposition/malpresentation, delivering during non working days and between 7 pm and 7 am show the highest population attributable fractions.

Model B explains almost 50% of inter-hospital variability, while model C explains almost 60%. The LR test indicates that model A and B are significantly different, but not model B and C (see Table 19).

Table 18. Frequency, crude, adjusted RR and population attributable risk (PAR) for sociodemographic, clinical and organizational characteristics in the subgroup of women without previous CD.

		N. deliveries	N. CD	Prop of the population %	% CD	Crude RR	IC		P	aRR	IC		P	PAR
							Low	High			Low	High		
Age	<18	701	106	0.37	15.12	0.69	0.57	0.82	<0.001	0.57	0.47	0.69	<0.001	-0.19
	18-24	22697	3944	11.96	17.38	0.79	0.77	0.81	<0.001	0.72	0.69	0.75	<0.001	-3.58
	24-29	44687	8969	23.54	20.07	0.91	0.89	0.93	<0.001	0.88	0.86	0.90	<0.001	-2.91
	30-34	68088	15065	35.87	22.13	1			<0.001	1.00				0.00
	35-39	43927	11149	23.14	25.38	1.15	1.12	1.17	<0.001	1.18	1.15	1.21	<0.001	3.95
	>39	9743	3329	5.13	34.17	1.54	1.5	1.59	<0.001	1.41	1.36	1.47	<0.001	2.29
Citizenship	Italian	142024	33450	74.81	23.55	1								
	High income	1816	385	0.96	21.20	0.9	0.82	0.84	0.021	0.94	0.85	1.04	0.212	-0.06
	Low income	46003	8728	24.23	18.97	0.81	0.79	0.82	<0.001	1.02	0.99	1.05	0.197	0.36
Marital status	Single	49355	12580	26.00	25.49	1.2	1.18	1.23	<0.001	1.02	1.00	1.05	0.047	0.65
	Married	125952	26672	66.35	21.18	1				1.00				0.00
	Divorced/separated	4284	1095	2.26	25.56	1.21	1.15	1.27	<0.001	1.14	1.07	1.21	0	0.32
	Widow	288	88	0.15	30.56	1.44	1.21	1.72	<0.001	1.22	0.99	1.51	0.059	0.04
	Not declared	9964	2128	5.25	21.36	1.01	0.97	1.05	0.671	0.95	0.89	1.01	0.112	-0.27
Maternal education	Primary	8544	1699	4.50	19.89	1.08	1.05	1.1	<0.001	1.05	1.00	1.11	0.069	0.20
	Secondary	51172	11127	26.95	21.74	1.08	1.02	1.06	0.001	1.07	1.04	1.10	<0.001	1.70
	High-school	86252	19447	45.43	22.55	1				1.00			1	0.00
	University	43875	10290	23.11	23.45	0.91	0.87	0.96	<0.001	0.95	0.93	0.98	<0.001	-1.17
Ppaternal education	Primary	5587	1038	2.94	18.58	0.86	0.81	0.91	<0.001					
	Secondary	60667	13091	31.96	21.58	1.06	1.4	1.8	<0.001					
	High-school	72561	16598	38.22	22.87	1								
	University	30245	6973	15.93	23.06	1.07	1.04	1.1	<0.001					
HIV		145	138	0.08	95.17	4.26	0.69	0.76	<0.001	3.73	3.20	4.41	<0.001	0.24
Diabetes		2531	1081	1.33	42.71	1.93	1.84	2.02	<0.001	1.40	1.32	1.49	<0.001	0.73
Hypertension		3735	1753	1.97	46.93	2.14	2.07	2.66	<0.001	1.54	1.46	1.61	<0.001	1.44
Lung diseases		165	121	0.09	73.33	3.28	2.99	3.59	<0.001	1.65	1.38	1.98	<0.001	0.11
Thyroid diseases		291	96	0.15	32.99	1.47	1.25	1.73	<0.001					
Genital herpes		15	15	0.01	100.00	4.46	4.24	4.5	<0.001					
Substance abuse		48	23	0.03	47.92	2.14	1.59	2.87	<0.001	2.19	1.46	3.30	<0.001	0.03
Other severe diseases		1034	595	0.54	57.54	2.59	2.46	2.73	<0.001	1.77	1.63	1.923	<0.001	0.61
Previous still births/abortion		31127	7443	16.40	23.91	1.08	1.06	1.1	<0.001					
Previous CD		189843		100.00	0.00									
Abortion threads / assisted fecundation / supervision of high risk pregnancy		599	392	0.32	65.44	2.94	2.77	3.11	<0.001	1.16	1.04	1.28	0.005	0.13
Eclampsia/ Preeclampsia		2874	2025	1.51	70.46	3.25	3.17	3.33		2.10	2.00	2.20	<0.001	2.49
Rh-isoimmunization		1697	340	0.89	20.04	0.89	0.812	0.98	0.018					

Abruptio or placenta previa or ante-partum hemorrhage		2406	2280	1.27	94.76	4.41	4.35	4.47	<0.001	3.24	3.10	3.39	<0.001	3.70
Polyhydramnios		429	253	0.23	58.97	2.64	2.44	2.86	<0.001	1.48	1.31	1.68	<0.001	0.19
Oligohydramnios		7268	2301	3.83	31.66	1.44	1.39	1.49	<0.001	1.38	1.32	1.44	<0.001	1.49
Premature rupture of membranes		27773	4728	14.63	17.02	0.73	0.71	0.75	<0.001	0.80	0.78	0.83	<0.001	-2.73
Other problems of the amnios		164	110	0.09	67.07	3	2.69	3.34	<0.001	2.35	1.94	2.83	<0.001	0.15
Cord prolapsed		133	130	0.07	97.74	4.37	4.25	4.49	<0.001	3.72	3.13	4.42	<0.001	0.22
Dystocia		6801	3402	3.58	50.02	2.34	2.28	2.4	<0.001					
Fetopelvic disproportion		2314	1648	1.22	71.22	3.26	3.18	3.35	<0.001	3.09	2.93	3.26	<0.001	2.62
Multiple pregnancy		2929	2536	1.54	86.58	4.04	3.98	4.11	<0.001	1.52	1.46	1.59	<0.001	2.05
Malposition and malpresentation of fetus		11598	10504	6.11	90.57	5.04	4.98	5.1	<0.001	3.54	3.45	3.62	<0.001	17.70
Intrauterine growth retardation		6011	3129	3.17	52.05	2.43	2.36	2.49	<0.001	1.27	1.22	1.33	<0.001	1.57
Fetal stress		5524	4893	2.91	88.58	4.33	4.28	4.39	<0.001					
Fetal anomalies		2020	805	1.06	39.85	1.79	1.7	1.89	<0.001	1.37	1.27	1.47	<0.001	0.51
Pregnancy lengh	At term	172520	34341	90.88	19.91	1								
	Pre-term	13490	7361	7.11	54.57	2.74	2.69	2.79	<0.001	1.19	1.14	1.23	<0.001	2.73
	Post-term	3608	803	1.90	22.26	1.12	1.05	1.19	<0.001	1.24	1.15	1.32	<0.001	0.36
Infant birth weight (grams)	2500-3999	164398	32736	86.60	19.91	1								
	1500-2500	1631	1360	0.86	83.38	4.19	4.09	4.29	<0.001	1.17	1.10	1.26	<0.001	0.47
	<1500	9382	5347	4.94	56.99	2.86	2.81	2.92	<0.001	1.27	1.22	1.32	<0.001	2.69
	>4000	14233	3043	7.50	21.38	1.07	1.04	1.11	<0.001	1.10	1.06	1.15	0.719	0.66
Pluriparity		18559	2378	9.78	12.81	0.55	0.53	0.57	<0.001	0.43	0.42	0.44	<0.001	0.00
Type of hospital	Teaching	51918	13842	27.35	26.66	1.28	1.26	1.3	<0.001	1.07	0.90	1.26	0.47	2.00
	Non teaching	137925	28721	72.65	20.82	1								
Volumes	100-500	6246	1679	3.29	26.88	1.18	1.13	1.23	<0.001	1.20	0.96	1.50	0.101	0.66
	501-799	19496	3967	10.27	20.35	0.91	0.89	0.94	<0.002	1.03	0.85	1.26	0.749	0.30
	800-999	17405	3243	9.17	18.63	0.84	0.81	0.86	<0.001	0.92	0.74	1.14	0.437	-0.68
	1000-2499	85628	19147	45.10	22.36	0.97	0.96	0.99	<0.001	1.01	0.85	1.20	0.915	0.42
	>2500	61068	14527	32.17	23.79	1								
Delivery on non-working days		52465	9005	27.64	15.77	0.7	0.69	0.72	<0.001	0.69	0.68	0.67	<0.001	-9.75
Delivery between 7 pm and 7 am		95856	15120	50.49	12.81	0.62	0.61	0.63	<0.001	0.65	0.65	0.63	<0.001	-19.18
Total		189843	42563	100%	22.42									

Table 19. Variance, proportional change in variance (PCV) and LR test in models on deliveries without a previous CD (n = 189420).

	Null (2 levels) Model A	Patient level Model B	Patient and hospital level Model C
Hospital variance	0.049	0.025	0.020
Hospital PCV vs. null model	-	-49.10	-59.84
Hospital PCV vs. previous model			-21.11
Pseudo R^2	-	0.124	0.126
LR test vs. previous model		P<0.0001	0.2537

As table 20 shows, in multivariate analyses the subgroup of women without a previous CD has significantly higher risk of CD in hospitals with less than 500 deliveries per year, if adjustment is performed excluding fetal disproportion and intrauterine growth retardation (Model F).

Table 20. aRR of CD for type of hospital and volumes after adjustment with model E and F.

		Model E				Model F			
			IC				IC		
		aRR	Low	High	P	aRR	Low	High	P
Type of hospital	Teaching	1.04	0.86	1.24	0.706	1.04	0.86	1.25	0.697
	Non teaching	1							
Volumes	100-500	1.18	0.95	1.47	0.134	1.26	1.01	1.56	0.043
	501-799	1.01	0.83	1.23	0.949	1.02	0.84	1.25	0.813
	800-999	0.90	0.73	1.12	0.348	0.92	0.74	1.15	0.464
	1000-2499	0.99	0.83	1.18	0.882	0.99	0.83	1.19	0.933
	>2500	1							
Deliveries on non-working days		0.70	0.68	0.71	0.001	0.69	0.67	0.70	0.001
Deliveries between 7 pm and 7 am		0.66	0.65	0.68	0.001	0.65	0.64	0.69	0.001

The graphs (Figure 3 and 4) have the same pattern as in the study population.

Figure 3. Funnel plot with adjusted CD rates in women without a previous CD.

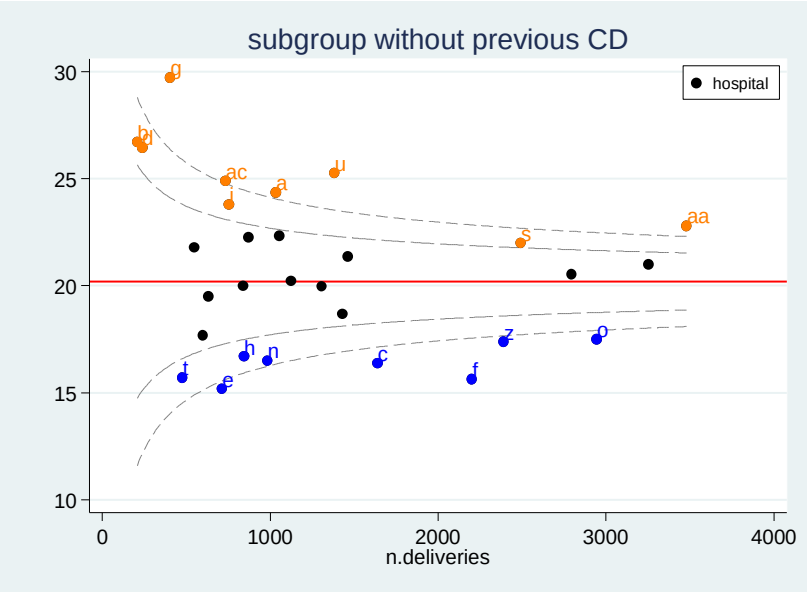
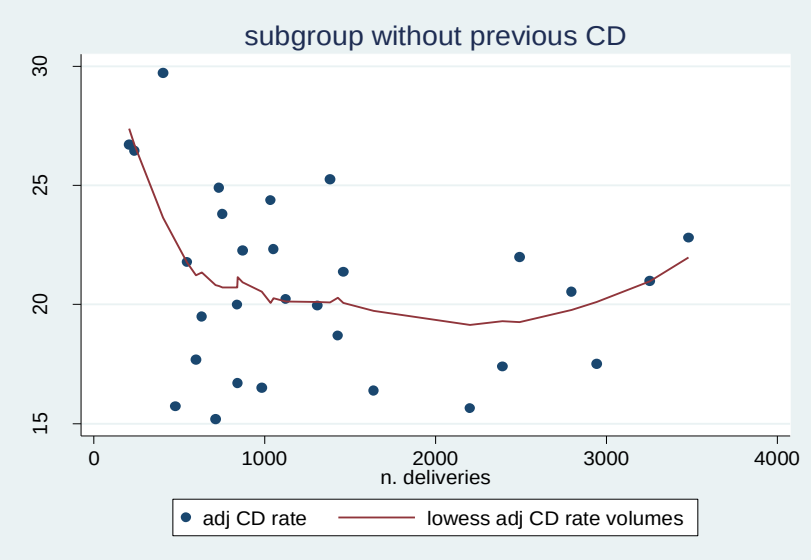


Figure 4. Scatter plot of adjusted CD rates and birth volumes with lowess curve (women without a previous CD).



Nulliparous, term, cephalic, singleton deliveries

Table 21 presents the NTCS deliveries by clinical and organizational characteristics, the crude and adjusted RR (with their relative 95% CI) and the population attributable risk.

Of the 27 significant variables included in the model (model C) the highest RR were found for abruption or placenta previa or ante-partum hemorrhage (RR 3,22; 95% CI: 3,00-3,47), HIV (RR 3,04; 95% CI: 2,41-3,84) and other problems of the amnios (RR 2,86; 95% CI: 2,18-3,75).

As far as the organizational variable is concerned, they were all significantly associated with CD in univariate analyses, hospitals with less than 500 deliveries per year and deliveries in teaching hospitals have a greater risk of CD. Hospitals with more than 500 but less than 2500 and deliveries occurring on non-working days and between 7 pm and 7 am have a protective effect. However, when performing multivariate analyses only variables related to the time of delivery were significantly ($p<0.001$) associated with a reduced risk of CD.

Delivering between 7 pm and 7 am and on non-working days show the highest population attributable fractions.

Model B explains the 31% of the hospital variance while model C explains 44% of hospital variance. As in the previous subgroups, the LR test indicates the models A and B are significantly different but model B and C are not (Table 22).

Similarly, by using model E and F, multivariate analyses does not yield significant RR for volumes and type of hospital in women classified in the NTCS group. Time of delivery and delivery on working days are instead significant (Table 23).

Table 21. Frequency, crude, adjusted RR and population attributable risk (PAR) for sociodemographic, clinical and organizational characteristics in NTCS.

		N. deliveries	N. CD	% CD	Prop of the population %	Crude RR	IC		P	aRR	IC		P	PAR
							Low	High			Low	High		
Age	<18	587	69	0.57	11.75	0.47	0.38	0.59	<0.001	0.47	0.37	0.60	<0.001	-1.13
	18-24	16304	2561	15.95	15.71	0.63	0.61	0.66	<0.001	0.63	0.60	0.66	<0.001	-6.11
	24-29	27202	5551	26.60	20.41	0.82	0.80	0.85	<0.001	0.83	0.80	0.86	<0.001	-4.53
	30-34	35943	8897	35.15	24.75	1.00				1.00				0.00
	35-39	18565	6167	18.16	33.22	1.34	1.31	1.38	<0.001	1.28	1.24	1.32	<0.001	5.39
	>39	3649	1789	3.57	49.03	1.98	1.91	2.06	<0.001	1.72	1.64	1.81	<0.001	3.00
Citizenship	Italiana	78818	20161	77.08	25.58	1.00								
	High income	979	219	0.96	22.37	0.87	0.78	0.98	0.025					
	Low income	22453	4654	21.96	20.73	0.81	0.79	0.83	<0.001					
Marital status	Single	33384	8064	32.65	24.16	0.98	0.96	1.00	0.065	0.97	0.94	1.00	0.036	-0.95
	Married	61411	15166	60.06	24.70	1.00				1.00				0.00
	Divorced/separated	1565	497	1.53	31.76	1.29	1.19	1.38	<0.001	1.01	0.92	1.102	0.845	0.02
	Widow	91	32	0.09	35.16	1.42	1.08	1.88	0.013	1.01	0.89	1.15	0.43	0.00
	Not declared	5799	1275	5.67	21.99	0.89	0.85	0.94	<0.001	1.08	0.76	1.53	0.669	-0.55
Maternal education	Primary	3952	822	3.87	24.96	1.03	1.01	1.06	0.02	1.03	0.95	1.12	0.479	0.10
	Secondary	24605	6189	24.06	20.80	1.04	1.01	1.07	0.004	1.12	1.09	1.16	<0.001	2.74
	High-school	47863	11576	46.81	25.15	1.00								
	University	25830	6447	25.26	24.96	0.86	0.81	0.92	<0.001	0.93	0.90	0.96	<0.001	-1.83
Paternal education	Primary	2123	490	2.08	23.08	1.03	1.00	1.06	0.056					
	Secondary	30579	7384	29.91	24.15	0.98	0.95	1.00	0.072					
	High-school	40394	9991	39.51	24.73	1.00								
	University	17063	4349	16.69	25.49	0.93	0.86	1.01	0.088					
HIV		75	72	0.07	96.00	3.93	3.75	4.12	<0.001	3.04	2.41	3.84	<0.001	0.19
Diabetes		1177	580	1.15	49.28	2.04	1.92	2.16	<0.001	1.45	1.33	1.57	<0.001	0.72
Hypertension		2007	917	1.96	45.69	1.90	1.81	1.99	<0.001	1.57	1.47	1.67	<0.001	1.32
Lung diseases		71	49	0.07	69.01	2.82	2.41	3.30	<0.001	1.93	1.45	2.55	<0.001	0.09
Thyroid diseases		166	55	0.16	33.13	1.35	1.09	1.68	0.0095					
Genital herpes		9	9	0.01	100.00	4.09	4.04	4.13	<0.001					
Substance abuse		29	14	0.03	48.28	1.97	1.35	2.88	0.0029	1.95	1.15	3.29	0.013	0.03
Other severe diseases		544	317	0.53	58.27	2.40	2.31	2.58	<0.001	1.88	1.68	2.10	<0.001	0.59
Previous still births/abortion		12,423	3637	12.15	29.28	1.23	1.19	1.27	<0.001	1.06	1.02	1.10	0.002	0.79
Previous CD														
Abortion threads/assisted fecundation/supervision of high risk pregnancy		153	102	0.15	66.67	2.73	2.44	3.06	<0.001	1.64	1.35	2.00	<0.001	0.16

Eclampsia/ preeclampsia		1312	819	1.28	62.42	2.60	2.49	2.72	<0.001	2.27	2.11	2.44	<0.001	1.83
Rh-isoimmunization		889	174	0.87	19.57	0.80	0.70	0.91	0.0006	0.96	0.83	1.12	0.618	-0.03
Abruptio or placenta previa or ante-partum hemorrhage		832	776	0.81	93.27	3.90	3.82	3.98	<0.001	3.22	3.00	3.47	<0.001	2.14
Polyhydramnios		184	120	0.18	65.22	2.67	2.40	2.97	<0.001	1.67	1.39	2.00	<0.001	0.19
Oligohydramnios		4623	1509	4.52	32.64	1.35	1.30	1.41	<0.001	1.36	1.29	1.44	<0.001	1.61
Premature rupture of membranes		16417	2871	16.06	17.49	0.68	0.65	0.70	<0.001	0.75	0.72	0.78	<0.001	-3.87
Other problems of the amnios		79	53	0.08	67.09	2.74	2.25	3.20	<0.001	2.86	2.18	3.75	<0.001	0.14
Cord prolapsed		45	45	0.04	100.00	4.09	4.05	4.13	<0.001					
Dystocia		5251	2,932	5.14	55.84	2.45	2.39	2.52	<0.001					
Fetopelvic disproportion		1556	1,298	1.52	83.42	3.54	3.45	3.63	<0.001	2.72	2.56	2.89	<0.001	3.28
Multiple pregnancy														
Malposition and malpresentation of fetus														
Intrauterine growth retardation		2574	945	2.52	36.71	1.52	1.44	1.60	<0.001	1.17	1.09	1.26	<0.001	0.55
Fetal stress		4029	3545	3.94	87.99	4.02	3.96	4.09	<0.001					
Fetal anomalies		1018	377	1.00	37.03	1.52	1.40	1.65	<0.001	1.32	1.19	1.47	<0.001	0.37
Pregnancy lengh	At term	99708	24,301	97.51	24.37									
	Pre-term													
	Post-term	2411	692	2.36	28.70	1.80	1.10	1.26	<0.001					
Infant birth weight (grams)	2500-3999	93377	21666	91.32	23.20	1.00								
	1500-2500	2375	1011	2.32	42.57	2.96	2.13	4.12	<0.001	1.56	0.86	2.82	0.143	1.45
	<1500	16	11	0.02	68.75	1.83	1.75	1.93	<0.001	1.41	1.32	1.52	<0.001	0.01
	>4000	6431	2,338	6.29	36.36	1.57	1.51	1.62	<0.001	1.33	1.27	1.39	<0.001	2.33
Pluriparity														
Type of hospital	Teaching	28234	8,191	27.61	29.01	1.27	1.25	1.30	<0.001	1.16	0.93	1.43	0.179	4.46
	Non teaching	74016	16843	72.39	22.76	1.00								
Volumes	100-500	3309	996	3.24	30.10	1.15	1.07	1.22	<0.001	1.22	0.93	1.61	0.152	0.73
	501-799	10403	2473	10.17	23.77	0.91	0.87	0.95	<0.001	1.03	0.80	1.32	0.832	0.26
	800-999	9340	2082	9.13	22.29	0.85	0.81	0.89	<0.001	0.96	0.73	1.26	0.761	-0.36
	1000-2499	45330	10600	44.33	23.38	0.89	0.87	0.92	<0.001	1.00	0.80	1.23	0.965	-0.20
	>2500	33868	8883	33.12	26.23	1.00				1.00				
Delivery on non-working days		28642	5683	28.01	19.84	0.75	0.74	0.77	<0.001	0.67	0.65	0.70	<0.001	11.00
Delivery between 7 pm and 7 am		51826	9949	50.69	19.20	0.72	0.70	0.74	<0.001	0.66	0.64	0.68	<0.001	20.75
Total		102250	25034	100%	24.48									

Table 22. Variance, proportional change in variance (PCV) and LR test in models in NTCS (n = 102199).

A	Null (2 levels) Model A	Patient level Model B	Patient and hospital level Model C
Hospital variance	0.054	0.037	0.031
Hospital PCV vs. null model	-	-31.12	-43.54
Hospital PCV vs. previous model			-18.04
R^2	-	0.057	0.059
LR test vs. previous l model		P<0.0001	0.3832

Table 23. aRR of CD for type of hospital and volumes after adjustment with model E and F.

		Model E				Model F			
A		aRR	IC		p	aRR	IC		p
Type of hospital	Teaching	1.11	0.89	1.38	0.354	1.11	0.88	1.40	0.373
	Non teaching								
Volumes	100-500	1.17	0.88	1.54	0.274	1.24	0.93	1.66	0.138
	501-799	0.96	0.75	1.23	0.745	0.98	0.76	1.27	0.890
	800-999	0.91	0.69	1.19	0.482	0.94	0.71	1.25	0.657
	1000-2499	0.95	0.76	1.19	0.656	0.96	0.76	1.21	0.711
	>2500								
Delivery between 7 pm and 7 am		0.66	0.64	0.68	<0.001	0.64	0.63	0.66	<0.001
Delivery on non-working days		0.67	0.65	0.69	<0.001	0.66	0.64	0.68	<0.001

The graphs (Figure 5 and 6) show that there is a greater variability in adjusted CD rate among low volumes hospitals and that between about 1500 and 3000 deliveries per year there are more outliers in the lower part.

Figure 5. Funnel plot with adjusted CD rates in NTCS.

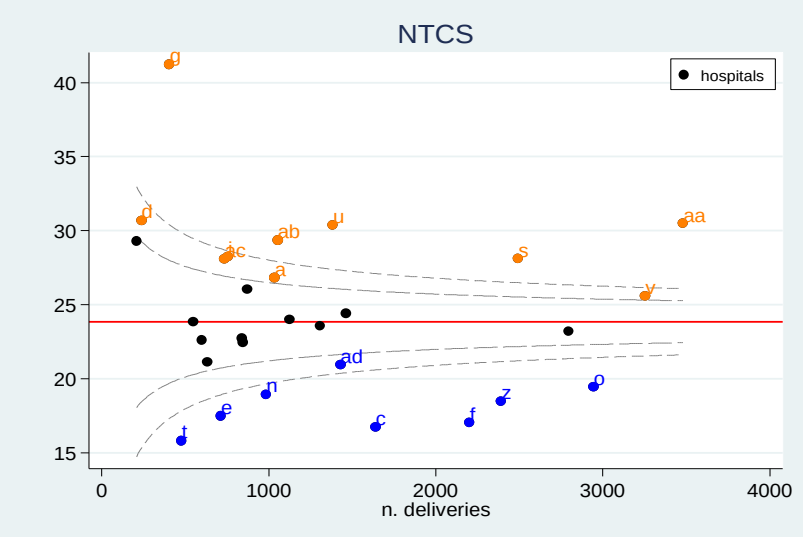
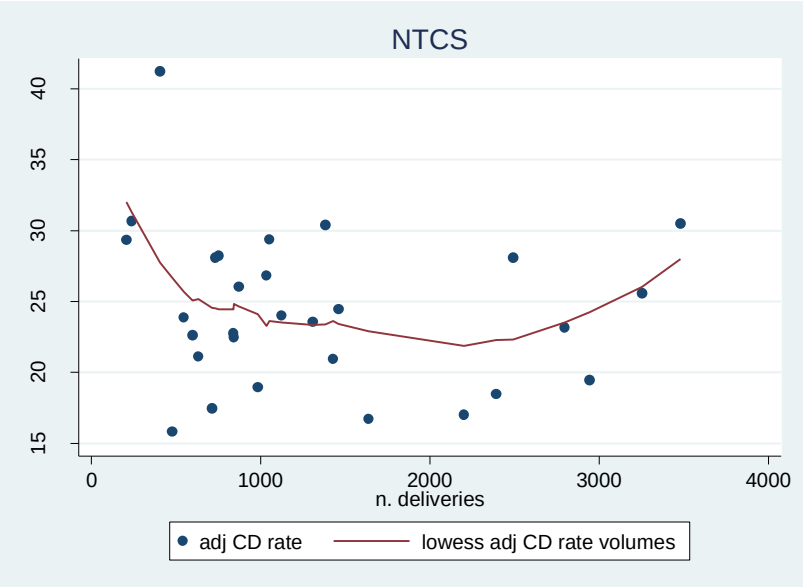


Figure 6. Scatter plot of adjusted CD rates and birth volumes with lowess curve in NTCS.



I-IIa-III-IVa group

Table 24 presents the deliveries of the women of the I, IIa, III and IVa TGCS group by clinical and organizational characteristics, the crude and adjusted RR (with their relative 95% CI) and the population attributable risk.

Of the 27 significant variables included in the model (model C) the greatest RR were found for cord prolapse (RR 5,82; 95% CI: 4,66-7,25), HIV (RR 5,55; 95% CI: 3,22-9,57) and placenta previa or abruption or antepartum hemorrhage (RR 5,36; 95% CI: 4,80-5,99).

As far as the organizational variables are concerned, they were all significantly associated with CD in univariate analyses: women delivering in teaching hospitals and in hospitals where between 500 and 1000 deliveries are performed per year have a smaller risk of CD. Deliveries occurring on non-working days and between 7 pm and 7 am are significantly ($p<0.001$) associated with a reduced risk of CD. However, when performing multivariate analyses only variables related to the time of delivery were significantly ($p<0.001$) associated with a reduced risk of CD.

Table 24. Frequency, crude, adjusted RR and population attributable risk (PAR) for sociodemographic, clinical and organizational characteristics in I, IIa, III, Iva subgroup.

		N. deliveries	N. CD	Proportion of the population	% CD	Crude RR	IC Low	IC High	P	aRR	IC Low	IC High	P	PAR
Age	<18	593	47	0.38	7.93	0.70	0.53	0.92	0.011	0.46	0.34	0.61	<0.001	-1.18
	18-24	19665	1876	12.55	9.54	0.84	0.80	0.88	<0.001	0.64	0.60	0.67	<0.001	-6.14
	24-29	38056	4102	24.28	10.78	0.95	0.92	0.99	0.009	0.84	0.81	0.88	<0.001	-4.31
	30-34	56548	6405	36.08	11.33	1.00				1.00				
	35-39	34944	4141	22.30	11.85	1.05	1.01	1.09	0.016	1.16	1.12	1.21	<0.001	3.33
	>39	6913	940	4.41	13.60	1.20	1.13	1.28	<0.001	1.45	1.35	1.55	<0.001	1.66
Citizenship	Italian	116234	13378	74.17	11.51	1.00								
	High income	1474	148	0.94	10.04	0.87	0.75	1.02	0.082	0.93	0.79	1.09	0.364	-0.07
	Low income	39011	3985	24.89	10.22	0.89	0.86	0.92	<0.001	1.10	1.06	1.15	<0.001	2.11
Marital status	Single	40068	5364	25.57	13.39	1.29	1.24	1.33	<0.001	1.04	1.01	1.08	0.02	1.21
	Married	104706	10839	66.81	10.35	1.00				1.00				
	Divorced/separated	3400	404	2.17	11.88	1.15	1.05	1.26	0.004	1.16	1.05	1.28	0.004	0.31
	Widow	215	26	0.14	12.09	1.17	0.81	1.68	0.398	1.29	0.87	1.89	0.201	0.03
	Not declared	8330	878	5.32	10.54	1.02	0.95	1.09	0.587	0.96	0.86	1.07	0.445	-0.21
Maternal education	Primary	7075	666	4.51	11.69	0.84	0.78	0.90	<0.001	1.20	1.10	1.31	<0.001	0.63
	Secondary	42286	4627	26.98	9.41	0.97	0.94	1.01	0.142	1.12	1.08	1.16	<0.001	2.84
	High-school	71178	7990	45.42	10.94	1.00								
	University	36180	4228	23.09	11.69	1.04	1.01	1.08	<0.001	0.94	0.90	0.97	0.001	-1.60
Paternal education	Primary	4722	448	3.01	9.49	0.82	0.75	0.90	0.056					
	Secondary	50417	6954	32.17	13.79	0.95	0.92	0.99	0.006					
	High-school	59981	6954	38.27	11.59	1.00								
	University	24937	2845	15.91	11.41	0.98	0.94	1.03	0.443					
HIV		18	13	0.01	72.22	6.47	4.85	8.62	<0.001	5.55	3.22	9.57	<0.001	0.06
Diabetes		1637	346	1.04	21.14	1.91	1.74	2.10	<0.001	1.55	1.39	1.72	<0.001	0.70
Hypertension		2412	598	1.54	24.79	2.26	2.10	2.43	<0.001	1.79	1.64	1.94	<0.001	1.50
Lung diseases		62	22	0.04	35.48	3.18	2.27	4.45	<0.001	2.27	1.49	3.45	<0.001	0.07
Thyroid diseases		216	30	0.14	13.89	1.24	0.89	1.73	0.2049					
Genital herpes		3	3	0.01	100.00	8.95	8.83	9.08	<0.001					
Substance abuse		27	4	0.02	14.81	1.33	0.54	3.28	0.5481					
Other severe diseases		522	120	0.33	22.99	2.06	1.76	2.42	<0.001	1.59	1.33	1.91	<0.001	0.26
Previous still births/abortion		24885	2709	15.88	10.89	0.97	0.93	1.01	0.1166	1.09	1.04	1.14	0.1166	1.26
Previous CD Abortion threads / assisted fecundation / supervision		127	30	0.08	23.62	2.12	1.55	2.89	<0.001	1.12	0.78	1.62	0.545	0.02

of high risk pregnancy													
Eclampsia/ preeclampsia		1208	460	0.77	38.08	3.47	3.23	3.74	<0.001	2.68	2.44	2.95	<0.001	1.65
Rh-isoimmunization		1400	103	0.89	7.36	0.66	0.54	0.79	0.622	0.87	0.71	1.06	0.162	-0.09
Abruptio or placenta previa or ante-partum hemorrhage		429	327	0.27	76.22	6.93	6.56	7.32	<0.001	5.36	4.80	5.99	<0.001	1.52
Polyhydramnios		240	79	0.15	32.92	2.95	2.47	3.54	<0.001	2.21	1.76	2.78	<0.001	0.25
Oligohydramnios		6029	1219	3.85	20.22	1.87	1.78	1.97	<0.001	1.77	1.66	1.88	<0.001	3.02
Premature rupture of membranes		23,256	2542	14.84	10.93	0.97	0.93	1.01	0.1275	0.97	0.93	1.01	0.181	-0.44
Other problems of the amnios		83	41	0.05	49.40	4.43	3.56	5.51	<0.001	3.24	2.38	4.41	<0.001	0.16
Cord prolapsed		84	82	0.05	97.62	8.77	8.46	9.10	<0.001	5.82	4.66	7.25	<0.001	0.39
Dystocia		6074	2882	3.88	47.45	4.89	4.74	5.04	<0.001					
Fetopelvic disproportion		1473	821	0.94	55.74	5.18	4.94	5.44	<0.001	3.43	3.17	3.70	<0.001	3.32
Multiple pregnancy														
Malposition and malpresentation of fetus														
Intrauterine growth retardation		3,025	509	1.93	16.83	1.52	1.40	1.65	<0.001	1.22	1.11	1.35	<0.001	0.53
Fetal stress		4021	3418	2.57	85.00	1.40	1.24	1.59	<0.001					
Fetal anomalies		1306	204	0.83	15.62	1.32	1.19	1.47	<0.001	1.20	1.05	1.38	0.01	0.20
Pregnancy lengh	At term	153125	16859	97.71	11.01	1.00								
	Pre-term													
	Post-term	3400	625	2.17	18.38	1.66	1.55	1.79	<0.001					
Infant birth weight (grams)	2500-3999	141071	14949	90.02	10.60									
	1500-2500	12	3	0.01	25.00	2.36	0.88	6.29	0.086	1.22	0.39	3.79	0.734	0.00
	<1500	2503	504	1.60	20.14	1.90	1.76	2.06	<0.001	1.32	1.20	1.45	<0.001	0.69
	>4000	13048	2049	8.33	15.70	1.48	1.42	1.55	<0.001	1.47	1.40	1.55	<0.001	3.76
Pluriparity		64573	2454	41.20	3.80	0.23	0.22	0.24	<0.001	0.21	0.20	0.22	<0.001	0.00
Type of hospital	Teaching	41283	5756	26.34	13.94	1.37	1.33	1.41	<0.001	1.17	0.87	1.58	0.299	4.81
	Non teaching	115436	11755	73.66	10.18									
Volumes	100-500	4927	560	3.14	11.37	0.99	0.91	1.07	0.738	1.15	0.78	1.68	0.485	0.41
	501-799	16663	1763	10.63	10.58	0.92	0.87	0.97	0.001	1.09	0.76	1.54	0.648	0.79
	800-999	15014	1549	9.58	10.32	0.9	0.85	0.94	<0.001	1.01	0.69	1.47	0.957	0.09
	1000-2499	70582	7930	45.04	11.24	0.97	0.94	1.01	0.118	1.09	0.81	1.46	0.591	3.56
	>2500	49533	5709	31.61	11.53	1.00				1.00				
Delivery on non-working days		46144	4968	29.44	10.77	0.95	0.92	0.98	<0.001	0.92	0.89	0.96	<0.001	-3.06
Delivery between 7 pm and 7 am		60181	6492	38.40	10.79	0.95	0.92	0.97	0.0001	0.92	0.89	0.95	<0.001	-1.19
Total		156,719	17,511	100	11.17									

Age, teaching hospitals and fetopelvic disproportion show the highest population attributable fractions.

Model B explains the 14% of the inter-hospital variability and model C explains the 24% of the inter-hospital variability. The LR test indicates that model A and B are significantly different while the latter is similar to model C (Table 26).

Table 25. Variance, proportional change in variance (PCV) and LR test in models in I, IIa, III, Iva (n = 156440).

	Null (2 levels) Model A	patient level Model B	patient and hospital level Model C
Hospital variance	0.0758605	0.065147	0.0575056
Hospital PCV vs. null model	-	-14.12	-24.20
Hospital PCV vs. previous model			-11.73
Pseudo R^2	-	0.1592467	0.1621902
LR test vs. previous model		P<0.0001	0.6532

In this population the interaction between affiliation and time of delivery tested significantly (p=0.035). I provide stratified results for this population. Risk of CD is significantly reduced during the night or during non-working days only in non-teaching hospitals (Table 26).

Table 26. Association between delivery on working days and between 7 pm and 7 am by type of hospital.

	Teaching hospitals				Non teaching hospitals			
	aRR	IC		P	aRR	IC		P
delivery on non working days	0.94	0.88	1.00	0.063	0.91	0.87	0.95	<0.001
delivery between 7 pm and 7 am	0.98	0.92	1.04	0.451	0.89	0.85	0.93	<0.001

By using model E and F, only time of delivery and deliveries on working days are significant (Table 27).

Table 27. aRR of CD for type of hospital and volumes after adjustment with model E and F

		Model E				Model F			
		aRR	IC		P	aRR	IC		P
Type of hospital									
	Teaching	1.18	0.91	1.52	0.223	1.19	0.91	1.54	0.200
	Non teaching								
Volumes	100-500	1.12	0.79	1.60	0.516	1.20	0.85	1.71	0.305
	501-799	1.01	0.74	1.39	0.927	1.04	0.76	1.42	0.803
	800-999	0.96	0.68	1.36	0.838	1.01	0.71	1.43	0.974
	1000-2499	1.04	0.78	1.38	0.782	1.05	0.79	1.40	0.716
	>2500	1				1			
Delivery on non-working days		0.92	0.89	0.95	<0.001	0.92	0.89	0.96	<0.001
Delivery between 7 pm and 7 am		0.92	0.89	0.96	<0.001	0.92	0.89	0.96	<0.001

The graphs (Figure 7 and 8) are similar to those of the above subgroups.

Figure 7. Funnel plot showing adjusted CD rates in the I, IIa, III, IVa subgroup.

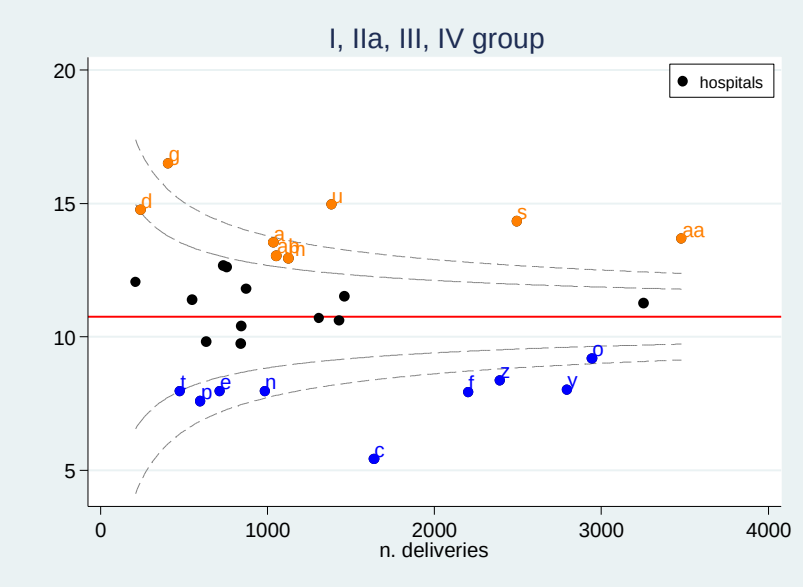
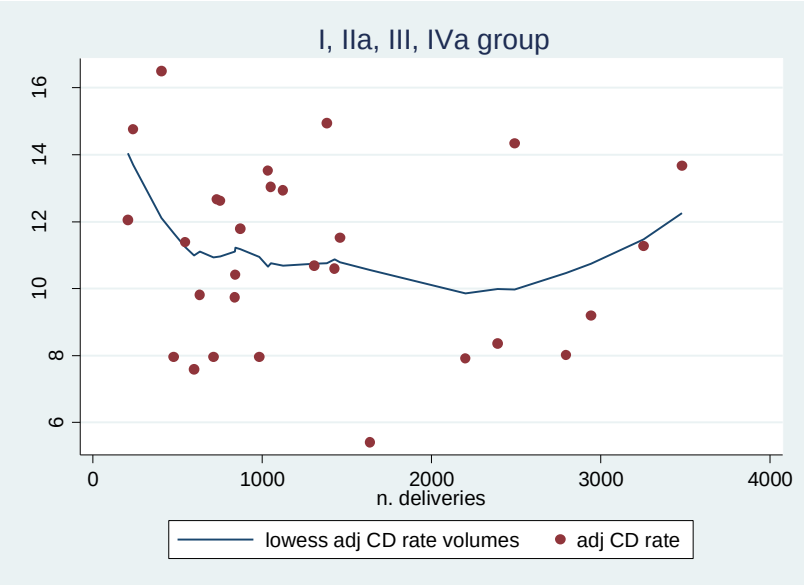


Figure 8. Scatter plot of adjusted CD rates and birth volumes with lowess curve (I, IIa, III, IVa subgroup).



V group

Table 28 presents the deliveries of the women of the V TGCS group by clinical and organizational characteristics, the crude and adjusted RR (with their relative 95%CI) and the population attributable risk. Of the 15 variables included in model C the highest, but not significant, RR were found for placenta previa or abruption or ante-partum hemorrhage (RR 1,17; 95%CI: 0,98-1,40) and fetopelvic disproportion (RR 1,14; 95%CI: 0,98-1,13). The premature rupture of membranes is a significant protective factor against CD.As far as the organizational variables are concerned, they were all significantly associated with CD in univariate analyses: in teaching hospitals there is a lower risk of CD, and where the deliveries are less than 2500 per year (except when the number of deliveries lies between 800 and 999 deliveries), there is a greater risk of CD. Deliveries occurring on non-working days and between 7 pm and 7 am are significantly ($p<0.001$) associated with a reduced risk of CD. However, when performing multivariate analyses only variables related to the time of delivery were significantly ($p<0.001$) associated with a reduced risk of CD.

Table 28. Frequency, crude, adjusted RR and population attributable risk (PAR) for sociodemographic, clinical and organizational characteristics in the V subgroup.

		N. deliveries	N. CD	Proportion of the population	% CD	Crude RR	IC		P	aRR	IC		P	PAR
							Low	High			Low	High		
Age	<18	5	4	0.03	80.00	0.93	0.60	1.45	0.76	0.90	0.34	2.39	0.828	0.00
	18-24	741	618	4.27	83.40	0.97	0.94	1.01	0.119	0.98	0.90	1.06	0.575	-0.10
	24-29	2851	2420	16.43	84.88	0.99	0.97	1.01	0.332	1.00	0.95	1.05	0.946	-0.03
	30-34	6257	5360	36.06	85.66									
	35-39	6013	5331	34.66	88.66	1.03	1.02	1.05	<0.001	1.03	0.99	1.07	0.163	0.95
	>39	1483	1483	8.55	100.00	1.05	1.03	1.07	<0.001	1.03	0.97	1.09	0.402	0.25
Citizenship	Italian	12908	11378	74.40	88.15									
	High income	106	79	0.61	74.53	0.85	0.76	0.95	0.003	0.91	0.73	1.14	0.421	-0.05
	Low income	4336	3608	24.99	83.21	0.94	0.93	0.96	<0.001	0.98	0.94	1.02	0.297	-0.54
Marital status	Single	2608	2309	15.03	88.54	1.02	1.01	1.04	0.004	1.02	0.97	1.06	0.511	0.23
	Married	13519	11706	77.92	86.59									
	Divorced/separated	580	534	3.34	92.07	1.06	1.04	1.09	<0.001	1.03	0.94	1.12	0.58	0.09
	Widow	40	33	0.23	82.50	0.95	0.83	1.10	0.507	0.93	0.66	1.32	0.697	-0.02
	not declared	603	483	3.48	80.10	0.93	0.89	0.96	<0.001	0.95	0.85	1.06	0.399	-0.16
Maternal education	Primary	835	636	3.67	76.17	0.94	0.91	0.97	<0.001	0.97	0.90	1.06	0.521	-0.15
	Secondary	6513	5638	32.50	86.57	0.99	0.98	1.01	0.244	1.01	0.97	1.05	0.551	0.50
	High-school	6717	5864	33.80	87.30									
	University	2737	2332	13.44	85.20	0.96	0.95	0.98	<0.0010	0.96	0.92	1.01	0.09	-0.71
Paternal education	Primary	835	689	3.97	82.51	1.00	0.97	1.03	0.821					
	Secondary	5551	4845	27.93	87.28	0.99	0.98	1.00	0.21					
	High-school	7469	6570	37.87	87.96									
	University	3495	2961	17.07	84.72	0.98	0.96	0.99	0.008					
HIV		33	33	0.19	100.00	1.15	1.15	0.12	0.0251					
Diabetes		390	361	2.25	92.56	1.07	1.04	1.10	0.0007	1.04	0.94	1.16	0.442	0.10
Hypertension		243	226	1.40	93.00	1.07	1.04	1.11	0.0042	1.07	0.94	1.23	0.284	0.10
Lung diseases		14	13	0.08	92.86	1.07	0.92	1.24	0.5047					
Thyroid diseases		31	28	0.18	90.32	1.04	0.93	1.17	0.5649					
Genital herpes		3	3	0.02	100.00	1.15	1.15	1.16	0.4999					
Substance abuse		2	2	0.01	100.00	1.15	1.15	1.16	0.5818					
Other severe diseases		112	105	0.65	93.75	1.08	1.03	1.13	0.0298					
Previous still births/abortion		4022	3539	23.18	87.99	1.02	1.00	1.03	0.013					
Previous CD		17350	17350	100.00	100.00									
Abortion threads/assisted fecundation / supervision of high risk pregnancy		33	32	0.19	96.97	1.12	1.05	1.19	0.0847					

Eclampsia/ preeclampsia		140	131	0.81	93.57	1.08	1.03	1.13	0.0179	1.09	0.92	1.29	0.339	0.07
Rh-isoimmunization		142	116	0.82	81.69	0.94	0.97	1.02	0.069	0.98	0.81	1.18	0.824	-0.02
Abruptio or placenta previa or ante-partum hemorrhage		125	123	0.72	98.40	1.13	1.11	1.16	0.0001	1.17	0.98	1.40	0.082	0.12
Polyhydramnios		40	38	0.23	95.00	1.09	1.02	1.18	0.1261					
Oligohydramnios		187	159	1.08	85.03	0.98	0.92	1.04	0.4635					
Premature rupture of membranes		858	569	4.95	66.32	0.75	0.72	0.79	<0.001	0.87	0.80	0.95	0.002	-0.54
Other problems of the amnios		1	1	0.01	100.00	1.15	1.15	1.16	0.6969					
Cord prolapsed		3	3	0.02	100.00	1.15	1.15	1.16	0.4999					
Dystocia		228	144	1.31	63.16	0.72	0.66	0.80	<0.001					
Fetopelvic disproportion		184	175	1.06	95.11	1.10	1.06	1.13	0.0008	1.14	0.98	1.33	0.1	0.14
Multiple pregnancy				0.00										
Malposition and malpresentation of fetus					0.00									
Intrauterine growth retardation		306	274	1.76	89.54	1.03	0.99	1.07	0.1569					
Fetal stress		153	149	0.88	97.39	1.13	1.09	1.15	0.001					
Fetal anomalies		185	166	1.07	89.73	1.03	0.98	1.09	0.241					
Pregnancy lengh	At term	17228	14977	99.30	86.93									
	Pre-term			0.00										
	Post-term	101	72	0.58	71.29	0.82	0.72	0.93	0.002					
Infant birth weight (grams)	2500-3999	15921	13845	91.76	86.96									
	1500-2500	2	2	0.01	100.00	1.15	1.14	1.16	<0.001	1.04	0.26	4.15	0.959	0.00
	<1500	363	333	2.09	91.74	1.05	1.02	1.09	0.001	1.04	0.93	1.16	0.471	0.09
	>4000	1055	876	6.08	83.03	0.95	0.93	0.98	0.001	0.96	0.89	1.03	0.261	-0.24
Pluriparity														
Type of hospital	Teaching	4843	4131	27.91	85.30	0.98	0.96	0.99	0.0002					
	Non teaching	12507	10934	72.09	87.42									
Volumes	100-500	834	782	4.81	93.76	1.13	1.11	1.16	<0.001	1.08	0.97	1.20	0.162	0.38
	501-799	1861	1660	10.73	89.20	1.07	1.05	1.10	<0.001	1.03	0.94	1.13	0.526	0.32
	800-999	1694	1402	9.76	82.76	1.00	0.97	1.02	0.841	0.96	0.87	1.06	0.396	-0.39
	1000-2499	8707	7691	50.18	88.33	1.06	1.05	1.08	<0.001	1.04	0.97	1.12	0.263	2.04
	>2500	4254	3530	24.52	82.98									
Delivery on non-working days		1913	1249	11.03	65.29	0.73	0.71	0.75	<0.001	0.71	0.67	0.76	<0.001	-3.32
Delivery between 7 pm and 7 am		3082	1892	17.76	61.39	0.70	0.67	0.72	<0.001	0.68	0.65	0.72	<0.001	-5.79
Total		17350	15065	100	86.83									

Deliveries occurring on non-working days and between 7 pm and 7 am show the highest population attributable fractions.

Models B and C explain respectively the 54% and the 65% of the inter-hospital variability. The LR test indicates that model A and B differ significantly; whereas, the latter does not significantly differ from model C. The variables of both model B and C explain less than 1% of the total variance (Table 29).

Table 29. Variance, PCV and LR test in models in the V subgroup (n = 17341).

	Null (2 levels) Model A	Patient level Model B	Patient and hospital level Model C
Hospital variance	0.0067687	0.0031174	0.0023386
Hospital PCV vs. null model		-53.94	-65.45
Hospital PCV vs. previous model			-24.98
Pseudo R^2		0.0085278	0.0088663
LR test vs. previous model		P<0.001	0.2296

The adjusted RR of CD for the organizational variables estimated using model E and F (see Table 30) are similar with those estimated using model C.

Table 30. aRR of CD for type of hospital and volumes after adjustment with model E and F.

		Model E				Model F			
		aRR	IC		P	aRR	IC		P
Type of hospital									
	Teaching	0.99	0.90	1.09	0.848	0.99	0.91	1.09	0.865
	Non teaching								
Volumes	100-500	1.11	0.98	1.27	0.106	1.11	0.98	1.27	0.100
	501-799	1.04	0.93	1.17	0.466	1.04	0.93	1.16	0.454
	800-999	0.97	0.86	1.09	0.603	0.97	0.86	1.09	0.619
	1000-2499	1.06	0.96	1.16	0.266	1.06	0.96	1.16	0.258
	>2500								
Delivery on non-working days		0.71	0.67	0.76	<0.001	0.71	0.67	0.76	<0.001
Delivery between 7 pm and 7 am		0.68	0.65	0.72	<0.001	0.68	0.65	0.72	<0.001

The graphs (Figure 9, 10) show that in group V variation in adjusted CD rates is greater at low than at high birth volumes.

Figure 9. Funnel plot with adjusted CD rates in the V group.

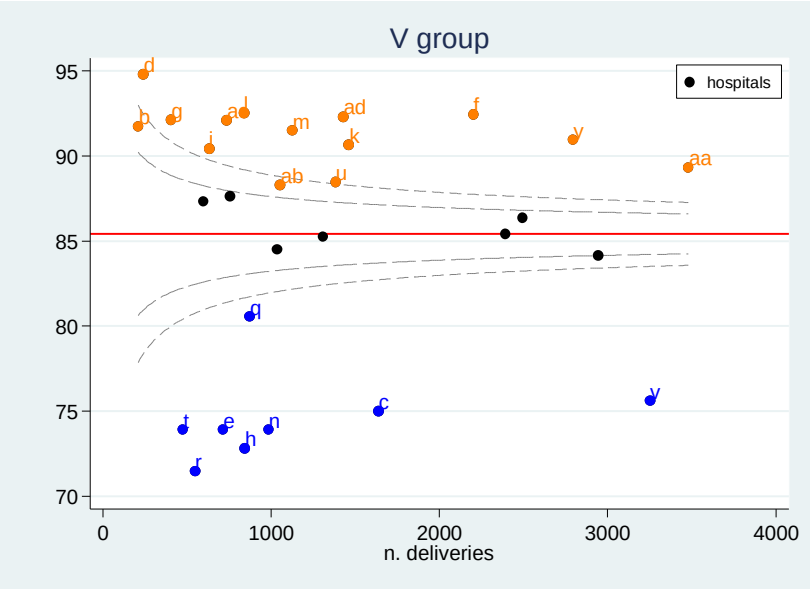
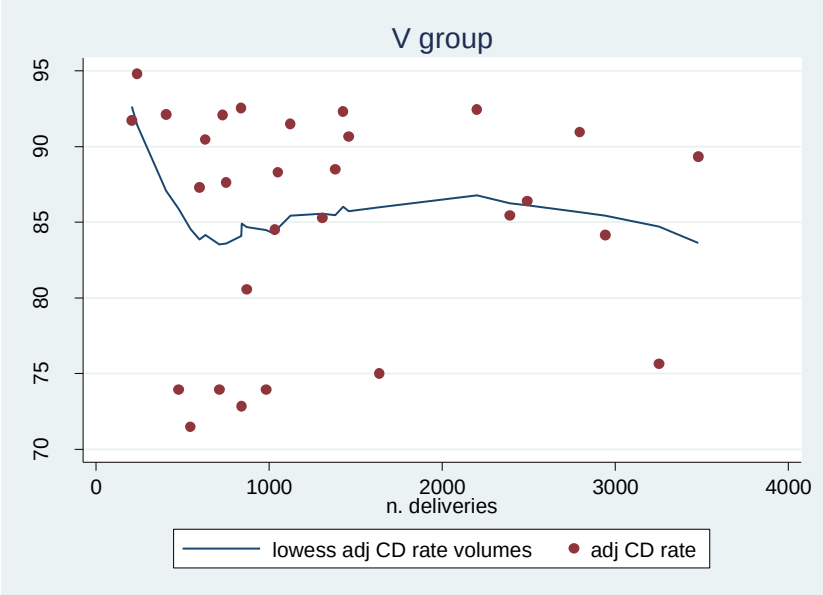


Figure 10. Scatter plot of adjusted CD rates and birth volumes with lowess curve (V group).



Deliveries after spontaneous labour

Table 31 presents the deliveries with spontaneous labour by clinical and organizational characteristics, the crude and adjusted RR (with their relative 95% CI) and the population attributable risk.

Of the 28 significant variables included in model C, the greatest RR were found for a previous CD (RR 10,23; 95% CI: 9,72-8,88), cord prolapse (RR 5,24; 95% CI: 4,17-6,59), HIV (RR 5,00; 95% CI: 3,25-7,70), malposition/malpresentation (RR 5,39; 95%CI: 5,13-6,65). As far as the organizational variable is concerned, in multivariate analyses only deliveries occurring on non-working days and between 7 pm and 7 am are significantly ($p<0.001$) associated with a reduced risk of CD.

Previous CD, malposition and malpresentation and teaching hospitals show the highest population attributable fractions.

The models explain between 39 and 47% of inter-hospital variability. The LR test indicates the two models are significantly different ($p<0.001$). The model explains less than 9% of the total variance (Table 32).

By using model E and F we obtain similar results as with model C in terms of aRR of CD for organizational variables (Table 33).

Table 31. Frequency, crude, adjusted RR and population attributable risk (PAR) for sociodemographic, clinical and organizational characteristics in women who delivered after spontaneous labour.

		N. deliveries	N. CD	Proportion of the population	% CD	Crude RR	IC		P	aRR	IC		P	PAR
							Low	High			Low	High		
Age	<18	512	38	0.40	7.42	0.73	0.53	0.99	0.04	0.63	0.46	0.87	0.005	-0.17
	18-24	16266	1307	12.56	8.04	0.79	0.74	0.83	<0.001	0.72	0.67	0.76	<0.001	-3.89
	24-29	31101	2958	24.01	9.51	0.93	0.89	0.97	0.001	0.92	0.88	0.96	<0.001	-1.98
	30-34	46867	4795	36.18	10.23	1.00				1.00				
	35-39	29159	3445	22.51	11.81	1.15	1.11	1.20	<0.001	1.12	1.07	1.17	<0.001	2.83
	>39	5634	777	4.35	13.79	1.35	1.26	1.45	<0.001	1.36	1.26	1.47	<0.001	1.55
Citizenship	Italiana	95371	10056	73.62	10.54	1.00								
	High income	1299	119	1.00	9.16	0.87	0.73	0.03	0.11					
	Low income	32869	3145	25.37	9.57	0.91	0.87	0.94	<0.001					
Marital status	Single	32549	3788	25.13	11.64	1.20	1.16	1.24	<0.001	1.08	1.03	1.12	<0.001	2.00
	Married	87113	8462	67.25	9.71	1.00				1.00				
	Divorced/separated	2780	351	2.15	12.63	1.30	1.18	1.44	<0.001	1.16	1.04	1.30	0.006	0.37
	Widow	174	351	0.13	201.72	1.01	0.64	1.58	0.98	1.16	0.72	1.87	0.541	0.36
	not declared	6923	702	5.34	10.14	1.04	0.97	1.12	0.249	1.06	0.94	1.19	0.341	0.29
Maternal education	Primary	5875	570	4.54	9.70	0.95	0.88	1.03	0.249					
	Secondary	35247	3659	27.21	10.38	1.02	0.98	1.06	0.322					
	High-school	58769	5982	45.37	10.18	1.00								
	University	29648	3109	22.89	10.49	1.03	0.99	1.07	0.155					
Paternal education	Primary	3959	394	3.06	9.95	0.94	0.85	1.04	0.229					
	Secondary	41790	4275	32.26	10.23	0.97	0.93	1.01	0.1					
	High-school	49347	5213	38.09	10.56	1.00								
	University	20441	2072	15.78	10.14	0.96	0.91	1.01	0.093					
HIV		26	21	0.02	80.77	7.87	6.52	9.50	<0.001	5.00	3.25	7.70	<0.001	0.13
Diabetes		901	192	0.70	21.31	2.09	1.84	2.37	<0.001	1.29	1.11	1.49	0.001	0.32
Hypertension		884	206	0.68	23.30	2.29	2.03	2.58	<0.001	1.61	1.40	1.85	<0.001	0.58
Llung diseases		51	19	0.04	37.25	3.63	2.54	5.18	<0.001	2.46	1.57	3.87	<0.001	0.08
Thyroid diseases		165	27	0.13	16.36	1.59	1.13	2.25	<0.001					
Genital herpes		3	3	0.00	100.00	9.73	9.57	9.88	<0.001					
Substance abuse		24	4	0.02	16.67	1.62	0.66	3.97	<0.001					
Other severe diseases		386	95	0.30	24.61	2.40	2.02	2.86	<0.001	1.54	1.26	1.89	<0.001	0.25
Previous still births/abortion		20699	2266	15.98	10.95	1.08	1.03	1.12	<0.001					
Previous CD		3863	2429	2.98	62.88	7.26	7.04	7.48	<0.001	10.23	9.72	10.77	<0.001	16.45
Abortion threads/assisted fecundation/supervision of high risk pregnancy		261	106	0.20	40.61	3.97	3.43	4.61	<0.001	0.98	0.80	1.20	0.816	-0.02
Eclampsia/ preeclampsia		390	168	0.30	43.08	4.23	3.77	4.75	<0.001	2.51	2.15	2.94	<0.001	0.76
Rh-isoimmunization		1142	73	0.88	6.39	0.62	0.50	0.77	<0.001	0.83	0.67	1.05	0.121	-0.11
Abruptio or placenta previa or ante-partum hemorrhage		430	356	0.33	82.79	8.25	7.87	8.63	<0.001	4.46	4.06	5.08	<0.001	2.08

Polyhydramnios		103	41	0.08	39.81	3.88	3.06	4.92	<0.001	1.42	1.04	1.94	0.029	0.09
Oligohydramnios		879	192	0.68	21.84	2.14	1.89	2.43	<0.001	1.90	1.64	2.19	<0.001	0.68
Premature rupture of membranes		18976	2014	10.61	14.65	1.04	0.99	1.09	<0.001					
Other problems of the amnios		63	31	0.05	49.21	1.04	0.99	1.09	<0.001	3.06	2.15	4.37	<0.001	0.16
Cord prolapse		79	77	0.06	97.47	9.53	9.16	9.91	<0.001	5.24	4.17	6.59	<0.001	0.47
Dystocia		3525	1484	2.72	42.10	9.53	9.16	9.91	<0.001					
Fetopelvic disproportion		861	490	0.66	56.91	5.71	5.37	6.06	<0.001	3.96	3.58	4.39	<0.001	2.75
Multiple pregnancy		791	512	0.61	64.73	6.51	6.16	6.87	<0.001	2.12	1.91	2.36	<0.001	2.03
Malposition and malpresentation of fetus		3234	2389	2.50	73.87	8.54	8.31	8.77	<0.001	5.39	5.13	5.65	<0.001	14.61
Intrauterine growth retardation		1844	357	1.42	19.36	1.91	1.74	2.10	<0.001	1.19	1.07	1.34	0.002	0.44
Fetal stress		2422	2007	1.87	82.87	9.31	9.08	9.55	<0.001					
Fetal anomalies		1042	193	0.80	18.52	1.81	1.59	2.06	<0.001	1.47	1.27	1.70	<0.001	0.46
Pregnancy lengh	At term	121244	11438	93.60	9.43	1.00			<0.001					
	Pre-term	6345	1679	4.90	26.46	2.80	2.68	2.93	<0.001	1.10	1.02	1.18	0.012	1.10
	Post-term	1798	187	1.39	10.40	1.10	0.96	1.26	0.162	1.11	0.96	1.28	0.171	0.14
infant birth weight (grams)	2500-3999	115750	10879	89.36	9.40	1.00								
	1500-2500	3848	1062	2.97	27.60	5.57	5.13	6.05	<0.001	0.89	0.77	1.03	0.113	-0.99
	<1500	531	278	0.41	52.35	2.94	2.78	3.10	<0.001	1.23	1.13	1.34	<0.001	0.39
	>4000	9291	1087	7.17	11.70	1.24	1.17	1.32	<0.001	1.20	1.12	1.28	<0.001	1.34
Pluriparity		13,987	969	10.80	6.93	0.65	0.61	0.69	<0.001	0.35	0.34	0.37	<0.001	-13.50
Type of hospital	Teaching	34394	4756	26.55	13.83	1.54	1.49	1.59	<0.001	1.27	0.94	1.71	0.12	7.56
	Non teaching	95145	8564	73.45	9.00									
Volumes	100-500	4330	543	3.34	12.54	1.34	1.18	1.53	<0.001	1.33	0.91	1.96	0.143	1.02
	501-799	13949	1394	10.77	9.99	1.12	1.05	1.20	0.732	1.22	0.86	1.73	0.275	1.86
	800-999	12299	1071	9.49	8.71	0.94	0.88	1.00	<0.001	1.07	0.74	1.57	0.71	0.56
	1000-2499	58745	6250	45.35	10.64	1.04	1.00	1.07	0.01	1.14	0.84	1.54	0.399	5.68
	>2500	40216	4062	31.05	10.10									
Delivery on non-working days		38780	3795	29.94	9.79	0.93	0.90	0.97	0.0001	0.94	0.90	0.98	0.003	-1.89
Delivery between 7 pm and 7 am		70439	6756	54.38	9.59	0.90	0.87	0.93	0.0001	0.94	0.90	0.98	0.003	-3.20
		129539	13320	100	10,28									

Table 32. Variance, proportional change in variance (PCV) and LR test in models in deliveries after spontaneous labour (n. = 129268).

	Null (2 levels) Model A	Patient level Model B	Patient and hospital level Model C
Hospital variance	0.123	0.074	0.065
Hospital PCV vs. null model	-	-39.30	-46.86
Hospital PCV vs. previous model			-12.45
Pseudo R^2	-	0.080	0.085
LR test vs. previous model		P<0.001	0.6306

Table 33. aRR of CD for type of hospital and volumes after adjustment with model E and F

		Model E				Model F			
A		aRR	IC		P	aRR	IC		P
Type of hospital									
	Teaching	1.08	0.86	1.35	0.528	1.16	0.88	1.54	0.292
	Non teaching								
Volumes	100-500	1.18	0.81	1.70	0.383	1.26	0.87	1.82	0.223
	501-799	1.09	0.78	1.52	0.615	1.12	0.81	1.57	0.491
	800-999	0.95	0.66	1.37	0.801	0.98	0.68	1.41	0.922
	1000-2499	1.05	0.78	1.42	0.733	1.07	0.79	1.44	0.673
	>2500								
delivery on non-working days		0.94	0.90	0.98	0.003	0.94	0.90	0.98	0.002
delivery between 7 pm and 7 am		0.94	0.90	0.98	0.003	0.94	0.90	0.98	0.003

The graphs (Figure 11 and 12) show, a U shaped curve of the adjusted CD rates.

Figure 11. Funnel plot with adjusted CD rates after spontaneous labour.

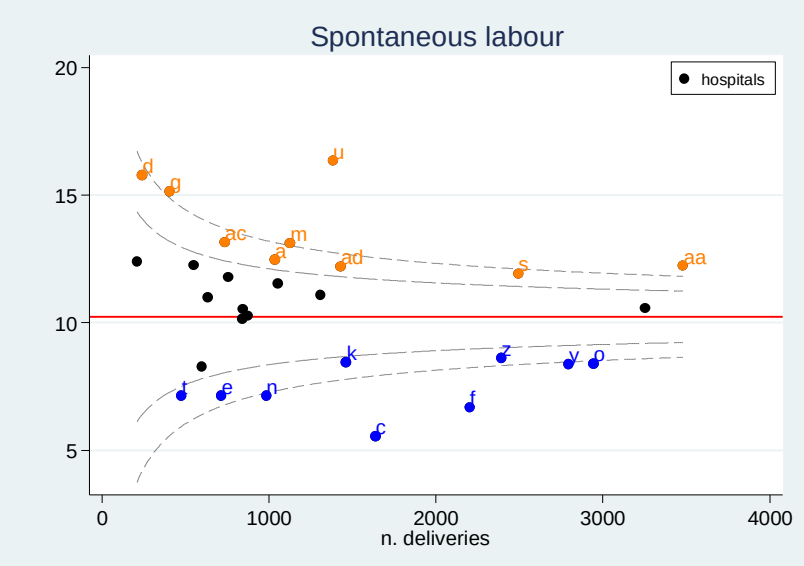
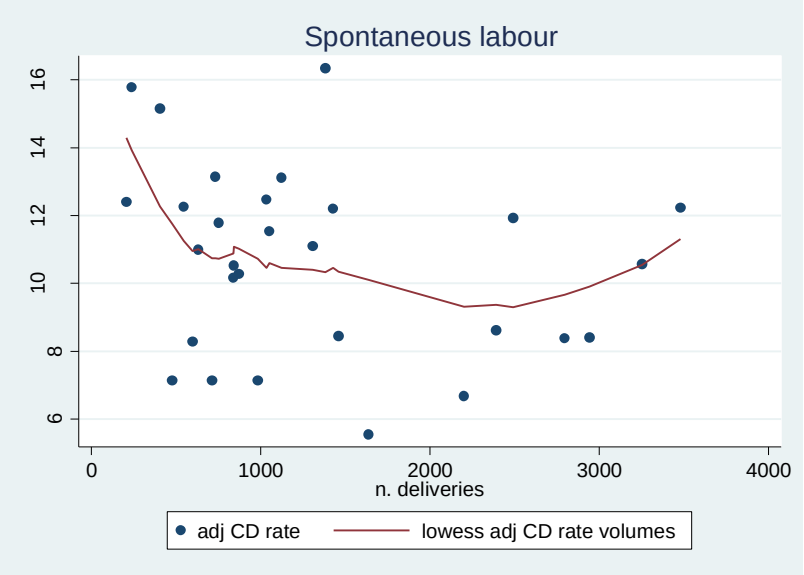


Figure 12. Scatter plot of adjusted CD rates and volumes with lowess curve (deliveries after spontaneous labour)



Deliveries after induced labour

Table 34 presents the deliveries with induced labour by clinical and organizational characteristics, the crude and adjusted RR (with their relative 95% CI) and the population attributable risk.

Of the 25 significant variables included in the model (Model C) the highest RR were found for previous CD (RR 3,88; 95% CI: 3,32-4,54) cord prolapse (RR 3,87; 95% CI: 2,58-5,79) and abruption or placenta previa or antepartum hemorrhage (RR 3,26; 95% CI: 2,79-3,81).

As far as the organizational variables are concerned, in univariate analyses teaching hospitals and performing between 1000 and 2499 deliveries per year are significantly associated with a higher risk of CD. In multivariate analyses only deliveries occurring between 7 pm and 7 am are significantly ($p<0.001$) associated with a reduced risk of CD.

Pluriparity, age, delivering between 7 am and 7 pm and teaching hospitals, show the highest population attributable fractions.

Table 34. Frequency, crude, adjusted RR and population attributable risk (PAR) for sociodemographic, clinical and organizational characteristics in deliveries with induced labour.

		N. deliveries	N. CD	Prop of the population %	% CD	Crude RR	IC		P	aRR	IC		p	PAR
							Low	High			Low	High		
Age	<18	143	24	0.34	16.78	0.74	0.51	1.06	0.101	0.51	0.34	0.77	0.001	-0.24
	18-24	4860	1009	11.63	20.76	0.91	0.86	0.97	0.003	0.73	0.68	0.79	<0.001	-4.02
	24-29	10001	2169	23.94	21.69	0.95	0.91	1	0.038	0.86	0.81	0.91	<0.001	-3.74
	30-34	14912	3401	35.69	22.81									
	35-39	9698	2206	23.21	22.75	0.99	0.95	1.05	0.912	1.10	1.04	1.16	0.001	2.07
	>39	2164	519	5.18	23.98	1.05	0.97	1.14	0.221	1.28	1.17	1.41	<0.001	1.22
Citizenship	Italian	31211	7057	74.71	22.61									
	High income	344	74	0.82	21.51	0.95	0.78	1.17	0.63	0.95	0.76	1.20	0.667	-0.04
	Low income	10223	2197	24.47	21.49	0.95	0.91	0.99	0.019	1.13	1.07	1.19	<0.001	2.74
Narital status	Single	10993	2811	26.31	25.57	1.2	1.16	1.25	<0.001	1.03	0.98	1.08	0.24	0.83
	Married	27639	5884	66.16	21.29	1								
	Divorced/separated	1020	226	2.44	22.16	1.04	0.93	1.17	0.504	1.17	0.99	1.40	0.072	0.36
	Widow	66	18	0.16	27.27	1.28	0.86	1.9	0.219	1.25	0.78	1.99	0.349	0.04
	Not declared	2060	389	4.93	18.88	0.89	0.81	0.97	0.011	1.00	0.87	1.16	0.95	0.02
Maternal education	Primary	2003	2184	4.79	109.04	0.81	0.74	0.9	<0.001	1.10	0.97	1.24	0.14	2.04
	Secondary	11446	2561	27.40	22.37	1.01	0.96	1.05	0.794	1.10	1.05	1.16	<0.001	2.60
	High-school	18748	4219	44.88	22.50	1				0.95	0.90	1.00	0.069	-1.18
	University	9581	2184	22.93	22.80	1.02	0.97	1.07	0.467					
Paternal education	Primary	6645	1495	15.91	22.50	0.85	0.007	0.76	0.96					
	Secondary	13662	3056	32.70	22.37	1.04	0.087	0.99	1.08					
	High-school	16087	3733	38.51	23.21	1								
	University	6645	1495	15.91	22.50	1.01	0.835	0.95	1.06					
HIV		2	0	0.00	0.00									
Diabetes		1050	289	2.51	27.52	1.24	1.12	1.37	<0.001	1.23	1.09	1.39	0.001	0.58
Hypertension		1839	525	4.40	28.55	1.3	1.2	1.4	<0.001	1.21	1.10	1.32	<0.001	0.97
Lung diseases		25	12	0.06	48.00	2.15	1.43	3.24	0.002	1.61	0.91	2.85	0.101	0.05
Thyroid diseases		81	20	0.19	24.69	1.11	0.76	1.62	0.6091					
Genital herpes		0	0	0.00										
Substance abuse		7	2	0.02	28.57	1.28	0.4	4.13	0.6916					
Other severe diseases		213	59	0.51	27.70	1.24	1	1.54	0.0591					
Previous still births/abortion		7020	1488	16.80	27.70	0.94	0.89	0.99	0.0126					
Previous CD		349	168	0.84	48.14	2.17	1.95	2.43	<0.001	3.88	3.32	4.54	<0.001	1.34

Abortion threads/assisted fecundation/supervision of high risk pregnancy		72	20	0.17	27.78	1.24	0.86	1.81	0.2664					
Eclampsia/ preeclampsia		1046	413	2.50	39.48	1.8	1.7	1.95	<0.001	1.67	1.51	1.85	<0.001	1.78
Rh-isoimmunization		367	62	0.88	16.89	0.76	0.6	0.95	0.012	0.99	0.76	1.27	0.919	-0-01
Abruptio or placenta previa or ante-partum hemorrhage		216	164	0.52	74.93	3.44	3.19	3.72	<0.001	3.26	2.79	3.81	<0.001	1.22
Polyhydramnios		190	76	0.45	40.00	1.8	1.51	2.14	<0.001	1.76	1.40	2.21	<0.001	0.35
Oligohydramnios		5439	1144	13.02	21.03	0.93	0.88	0.99	0.014					
Premature rupture of membranes		7703	1426	18.44	18.51	0.8	0.76	0.84	<0.001	0.81	0.76	0.86	<0.001	-3.64
Other problems of the amnios		48	24	0.11	50.00	2.24	1.69	2.98	<0.001	2.26	1.51	3.38	<0.001	0.14
Cord prolapsed		25	24	0.06	96.00	4.3	3.97	4.68	<0.001	3.87	2.58	5.79	<0.001	0.19
Dystocia		3105	1677	7.43	54.01	2.73	2.63	2.84	<0.001					
Fetopelvic disproportion		712	412	1.70	57.87	2.67	2.5	2.85	<0.001	2.19	1.97	2.44	<0.001	2.40
Multiple pregnancy		172	57	0.41	33.14	1.49	1.2	1.84	0.0006	1.54	1.18	2.00	0.001	0.21
Malposition and malpresentation of fetus		695	455	1.66	65.47	3.03	2.86	3.21	<0.001	2.70	2.46	2.98	<0.001	3.07
Intrauterine growth retardation		1870	454	4.48	24.28	1.09	1.01	1.19	0.0382					
Fetal stress		1952	1736	4.67	88.93	4.67	4.55	4.79	<0.001					
Fetal anomalies		490	108	1.17	22.04	0.99	0.83	1.17	0.8782					
Pregnancy lengh	At term	38052	8396	91.08	22.06	1								
	Pre-term	1997	448	4.78	22.43	1.02	0.94	1.11	0.698	0.96	0.87	1.07	0.482	-0.19
	Post-term	1679	470	4.02	27.99	1.27	1.17	1.37	<0.001	1.19	1.09	1.31	<0.001	0.81
Infant birth weight (grams)	2500-3999	35647	7607	85.32	21.34	1								
	1500-2500	1826	525	4.37	28.75	1.39	0.78	2.48	0.269	1.66	0.82	3.35	0.159	2.23
	<1500	27	8	0.06	29.63	1.35	1.25	1.45	<0.001	1.29	1.17	1.42	<0.001	0.02
	>4000	4256	1183	10.19	27.80	1.3	1.24	1.37	<0.001	1.30	1.22	1.39	<0.001	2.94
Pluriparity		3,843	348	9.20	9.06	0.38	0.35	0.42	<0.001	0.27	0.26	0.29	<0.001	0.00
Type of hospital	Teaching	29738	6340	71.18	21.32	1.16	1.12	1.21	<0.001	1.14	0.89	1.47	0.308	8.36
	Non teaching	12040	2988	28.82	24.82									
Volumes	100-500	1052	231	2.52	21.96	1.01	0.88	1.15	0.88	1.24	0.88	1.75	0.211	0.49
	501-799	3898	827	9.33	21.22	0.98	0.9	1.05	0.538	1.08	0.80	1.46	0.623	0.64
	800-999	3964	856	9.49	21.59	0.99	0.92	1.07	0.868	1.10	0.80	1.51	0.567	0.82
	1000-2499	18803	4358	45.01	23.18	1.07	1.02	1.11	0.006	1.16	0.90	1.49	0.251	6.41
	>2500	14061	3056	33.66	21.73									
Delivery on non working days		11448	2562	22.38	27.40	1	0.96	1.04	0.8756					
Delivery between 7 pm and 7 am		16368	3546	21.66	39.18	0.95	0.92	0.99	0.009	0.92	0.87	0.94	<0.001	-3.94
Total		41778	9328	100	22.33									

Model C explains the 5% of the inter-hospital variability. The LR test indicates differences between model A and B but not between model B and C (Table 35).

Table 35. Variance, proportional change in variance (PCV) and LR test in models in deliveries after induced labour (n. = 41706).

	Null (2 levels) Model A	Patient level Model B	Patient and hospital level Model C
Hospital variance	0.050	0.052	0.048
Hospital PCV vs. null model	-	4.59	-4.61
Hospital PCV vs. previous model			-8.79
Pseudo R^2	-	0.0457	0.048
LR test vs. previous model)		P<0.0001	0.7287

In this subgroup of women, volumes and teaching hospitals are not significant risk factors when using model E or F. As in the previous cohorts of women, delivery in non-working days and between 7 pm and 7 am are significant (Table 36).

Table 36. aRR of CD for type of hospital and volumes after adjustment with model E and F.

		Model E				Model F			
		aRR	IC		P	aRR	IC		P
Type of hospital									
	Teaching	1.04	0.87	1.24	0.706	1.08	0.87	1.36	0.448
	Non teaching								
Volumes	100-500	1.15	0.84	1.58	0.375	1.18	0.86	1.62	0.293
	501-799	1.02	0.77	1.33	0.907	1.03	0.78	1.34	0.846
	800-999	1.04	0.77	1.39	0.802	1.06	0.79	1.42	0.701
	1000-2499	1.11	0.87	1.41	0.388	1.11	0.88	1.41	0.376
	>2500								
Delivery on non-working days		0.94	0.90	0.99	0.027	0.94	0.89	0.99	0.016
Delivery between 7 pm and 7 am		0.88	0.84	0.93	<0.001	0.88	0.84	0.93	<0.001

The funnel plot (Figure 13) shows more outliers in the upper part of the graphs than in the lower. The lowess curve (Figure 14) appears less U shaped than in other subgroups of women.

Figure 13. Funnel plot with adjusted CD rates in deliveries after induced labour.

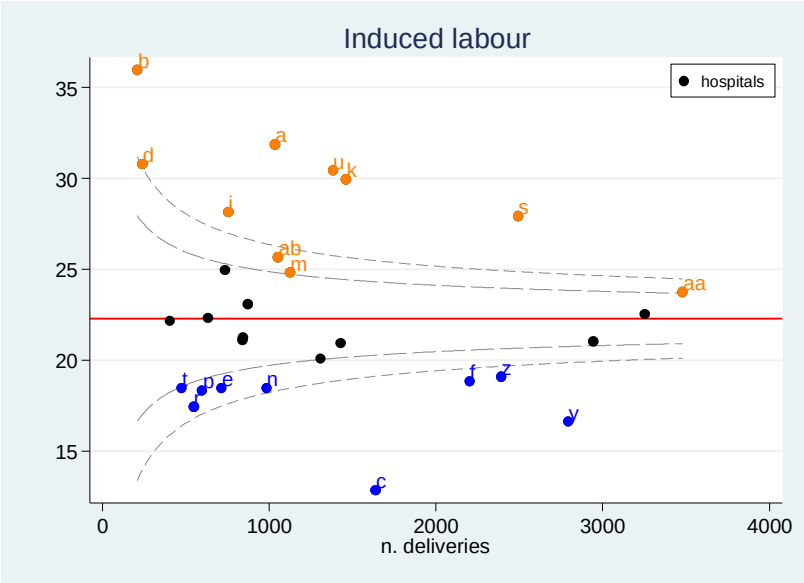
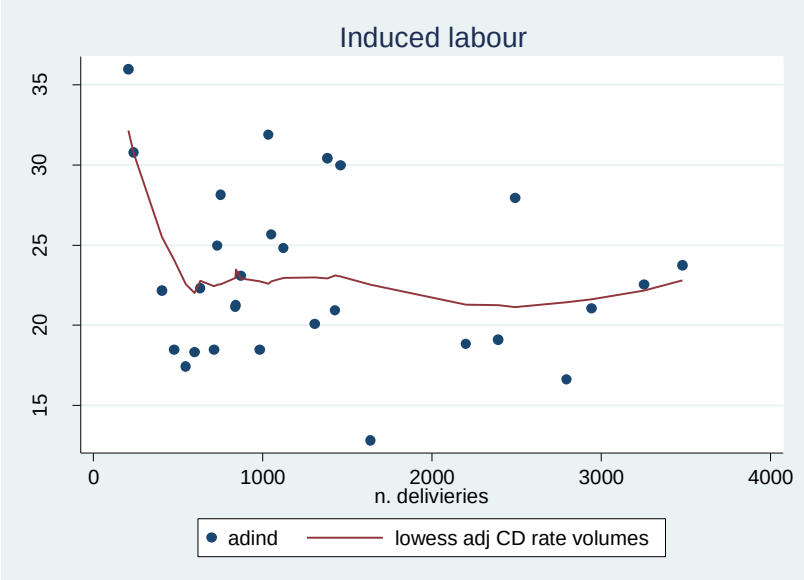


Figure 14. Scatter plot of adjusted CD rates and birth volumes with lowess curve (deliveries after induced labour).



Deliveries without labour

During the study period, 42222 women delivered without labour. Previous CD, malposition and malpresentation and preterm were frequent conditions in this population.

The frequency of most conditions differs significantly between women who had a labour and women who delivered without labour as table 37 shows. The latter group is older and, as expected, is more frequently affected by pathologies except for rh-isoimmunization, oligohydramnios, premature rupture of membrane and dystocia. These factors are more frequent in women who delivered after labour. Deliveries without labour occur more frequently in teaching hospital and, as expected, during working days and between 7 am and 7 pm.

Table 37. Frequency of sociodemographic, clinical and organizational characteristics in deliveries with and without labour.

		N deliveries without labour	Prop. of total population	N. deliveries with labour	Prop. of total population	P
Age	<18	52	0.12	655	0.38	<0.001
	18-24	2551	6.04	21126	12.33	<0.001
	24-29	7334	17.37	41102	23.99	<0.001
	30-34	14814	35.09	61779	36.06	<0.001
	35-39	13408	31.76	38857	22.68	<0.001
	>39	4063	9.62	7798	4.55	<0.001
Citizenship	Italian	33397	79.10	126582	73.89	<0.001
	High income	354	0.84	1643	0.96	<0.021
	Low income	8471	20.06	43092	25.15	<0.001
Marital status	Single	9453	22.39	43542	25.42	<0.001
	Married	29401	69.63	114752	66.98	<0.001
	Divorced/separated	1333	3.16	3800	2.22	<0.001
	Widow	106	0.25	240	0.14	<0.001
	Not declared	1929	4.57	8983	5.24	<0.001
Maternal education	Primary	1871	4.43	7878	4.60	0.141
	Secondary	11968	28.35	46693	27.26	<0.001
	High-school	19034	45.08	77517	45.25	0.537
	University	9349	22.14	39229	22.90	0.001
Paternal education	Primary	1262	2.99	10604	6.19	0.067
	Secondary	13470	31.90	55452	32.37	<0.001
	High-school	15625	37.01	65434	38.19	0.368
	University	6751	15.99	27086	15.81	<0.001
HIV		154	0.36	28	0.02	<0.001
Diabetes		1154	2.73	1951	1.14	<0.001

Hypertension		1475	3.49	2723	1.59	<0.001
Lung diseases		114	0.27	76	0.04	<0.001
Thyroid diseases		96	0.23	246	0.14	<0.001
Genital herpes		14	0.03	3	0.00	<0.001
Substance abuse		20	0.05	31	0.02	0.001
Other severe diseases		597	1.41	599	0.35	<0.001
Previous still births/abortion		8954	21.21	27719	16.18	<0.001
Previous CD		19484	46.15	4212	2.46	<0.001
Abortion threads / assisted fecundation / supervision of high risk pregnancy		335	0.79	333	0.19	<0.001
Eclampsia/ preeclampsia		1739	4.12	1436	0.84	<0.001
Rh-isoimmunization		362	0.86	1509	0.88	0.662
Abruptio or placenta previa or ante-partum hemorrhage		2029	4.81	646	0.38	<0.001
Polyhydramnios		198	0.47	293	0.17	<0.001
Oligohydramnios		1232	2.92	6318	3.69	<0.001
Premature rupture of membranes		2292	5.43	26679	15.57	<0.001
Other problems of the amnios		65	0.15	111	0.06	<0.001
Cord prolapsed		34	0.08	104	0.06	<0.001
Dystocia		424	1.00	6630	3.87	<0.001
Fetopelvic disproportion		941	2.23	1573	0.92	<0.001
Multiple pregnancy		2259	5.35	963	0.56	<0.001
Malposition and malpresentation of fetus		9036	21.40	3929	2.29	<0.001
Intrauterine growth retardation		2888	6.84	3714	2.17	<0.001
Fetal stress		1347	3.19	4374	2.55	<0.001
Fetal anomalies		777	1.84	1532	0.89	<0.001
Pregnancy lengh	At term	34597	81.94	159296	92.98	<0.001
	Pre-term	7322	17.34	8342	4.87	<0.001
	Post-term	256	0.61	3477	2.03	<0.001
Infant birth weight (grams)	2500	34035	80.61	151397	88.37	<0.001
	1500-2500	4959	11.75	5674	3.31	<0.001
	<1500	1225	2.90	558	0.33	<0.001
	>4500	1924	4.56	13547	7.91	<0.001
Pluriparity		23578	55.84	13987	8.16	<0.001
Type of hospital	Teaching	12166	28.81	46434	27.10	<0.001
	Non teaching	30056	71.19	124883	72.90	<0.001
Volumes	1	1904	4.51	5382	3.14	<0.001
	2	4025	9.53	17847	10.42	<0.001
	3	3176	7.525	16263	9.49	<0.001
	4	18792	44.51	77548	45.27	0.005
	5	14325	33.93	54277	31.68	<0.001
Delivery on non-working days		5046	11.95	50228	29.32	<0.001
Delivery between 7 pm and 7 am		5086	12.05	65524	38.25	<0,0001

Urgent and elective CD

The following table (38) reports the frequency of clinical and organizational variables for urgent and elective CD performed after 2006. The comparison between women who underwent elective and urgent CD shows that elective CDs are significantly associated with a higher frequency of pathologies such as HIV, diabetes, lung diseases, other severe diseases, previous CD, malposition and malpresentation, multiple pregnancy. Urgent CD are significantly associated with a higher frequency of eclampsia, abruptio or placenta previa or ante-partum hemorrhage, olygohydramnios, cord prolapse, other problems of the amnios, fetopelvic disproportion, dystocia and fetal stress.

Table 38. Frequency of sociodemographic, clinical and organizational characteristics in deliveries with elective and urgent CD (2007-mid 2010).

		Elective CD		Urgent CD		
		N deliveries	Prop of total population	N. deliveries	Prop. of total population	P
Age	<18	19	0.08	52	0.30	<0,0001
	18-24	1,347	5.56	1,749	9.94	<0.001
	24-29	4,003	16.51	3,736	21.22	<0.001
	30-34	8,385	34.59	6,217	35.32	0.122
	35-39	8,028	33.11	4,623	26.26	<0.001
	>39	2,461	10.15	1,226	6.96	<0.001
Citizenship	Italian	18,920	78.04	13,005	73.88	<0.001
	High income	200	0.82	151	0.86	0.745
	Low income	5,123	21.13	4,447	25.26	<0.001
Marital status	Single	5,571	22.98	5,343	30.35	<0.001
	Married	16,655	68.70	10,942	62.16	<0.001
	Divorced/separated	780	3.22	419	2.38	<0.001
	Widow	65	0.27	22	0.12	0.001
	not declared		0.00	877	4.98	<0.001
Maternal education	Primary	1054	4.35	1,010	5.74	<0.001
	Secondary	662	2.73	4,732	26.88	<0.001
	High-school	10791	44.51	7,697	43.73	0.111
	University	5,736	23.66	4,164	23.66	<0.001
Paternal education	Primary	766	3.16	480	2.73	0.991
	Secondary	7820	32.26	5,517	31.34	0.010
	High-school	9207	37.98	6,786	38.55	0.048
	University	4031	16.63	2,683	15.24	0.237
HIV		92	0.38	15	0.09	<0.001
Diabetes		742	3.06	434	2.47	<0.001
Hypertension		670	2.76	791	4.49	<0.001

Lung diseases		53	0.22	48	0.27	0.269
Thyroid diseases		56	0.23	42	0.24	0.919
Genital herpes		5	0.02	3	0.02	1
Substance abuse		13	0.05	7	0.04	0.652
Other severe diseases		350	1.44	153	0.87	<0.001
Previous still births/abortion		5,287	21.81	3106	17.64	<0.001
Previous CD		12,343	50.91	2202	12.51	<0.001
Abortion threads / assisted fecundation /supervision of high risk pregnancy		187	0.77	113	0.64	0.127
Eclampsia/ preeclampsia		601	2.48	865	4.91	<0.001
Rh-isoimmunization		201	0.83	116	0.66	0.052
Abruptio or placenta previa or ante-partum hemorrhage		860	3.55	855	4.86	<0.001
Polyhydramnios		116	0.48	86	0.49	<0.001
Oligohydramnios		484	2.00	1114	6.33	0.887
Premature rupture of membranes		1123	4.63	2616	14.86	<0.001
Other problems of the amnios		22	0.09	53	0.30	<0.001
Cord prolapsed		7	0.03	77	0.44	<0.001
Dystocia		240	0.99	1989	11.30	<0.001
Fetopelvic disproportion		540	2.23	554	3.15	<0.001
Multiple pregnancy		1381	5.70	536	3.04	<0.001
Malposition and malpresentation of fetus		5439	22.44	2253	12.80	<0.001
intrauterine growth retardation		1246	5.14	1097	6.23	<0.001
Fetal stress		404	1.67	2349	13.34	<0.001
Fetal anomalies		435	1.79	272	1.55	0.055
Pregnancy lengh	At term	20,712	85.43	14258	81.00	<0.001
	Pre-term	3,357	13.85	2887	16.40	<0.001
	Post-term	137	0.57	434	2.47	<0.001
infant birth weight (grams)	2500-4000	20,373	84.04	13561	77.04	<0.001
	1500-2500	415	1.71	598	3.40	<0.001
	<1500	2,304	9.50	1938	11.01	<0.001
	>4000	1,127	4.65	1468	8.34	<0.001
Pluriparity		14916	61.53	4585	26.05	<0.001
Type of hospital	Teaching	16,831	69.43	5731	32.56	
	Non teaching	7,412	30.57	11872	67.44	<0.001
Volumes	1	1069	4.41	602	3.42	<0.001
	2	2,536	10.46	1384	7.86	<0.001
	3	1,844	7.61	1398	7.94	<0.001
	4	11,224	46.30	7936	45.08	0.208
	5	7,570	31.23	6283	35.69	0.014
Delivery in non-working days		2,360	9.73	4849	27.55	<0.001
Delivery between 7 pm and 7 am		2,143	8.84	5924	33.65	<0.001

Elective CDs are more often conducted in teaching hospitals, whereas urgent CD are more often conducted in non-teaching hospitals. Elective CD are more frequently performed during working days and between 7 am and 7 pm, than are urgent deliveries.

Classification tree

The classification regression tree (CRT) yielded a segmentation of women into subgroups with a different likelihood of CD. Variables discriminating subgroups at increased risk of CD included previous CD, fetal presentation, abruptio, previa and ante-partum-hemorrhage, fetal weight and pluriparity (Figure 15).

The combination of these variables allowed the identification of the following subgroups (the so-called terminal nodes of the tree):

Node 6 (N=2148) women without a previous CD, without malpresentation but with abruption or placenta previa or ante-partum hemorrhage: CD rate=94,2%

Node 1 (N=23696) women with a previous CD: CD rate=93,1%

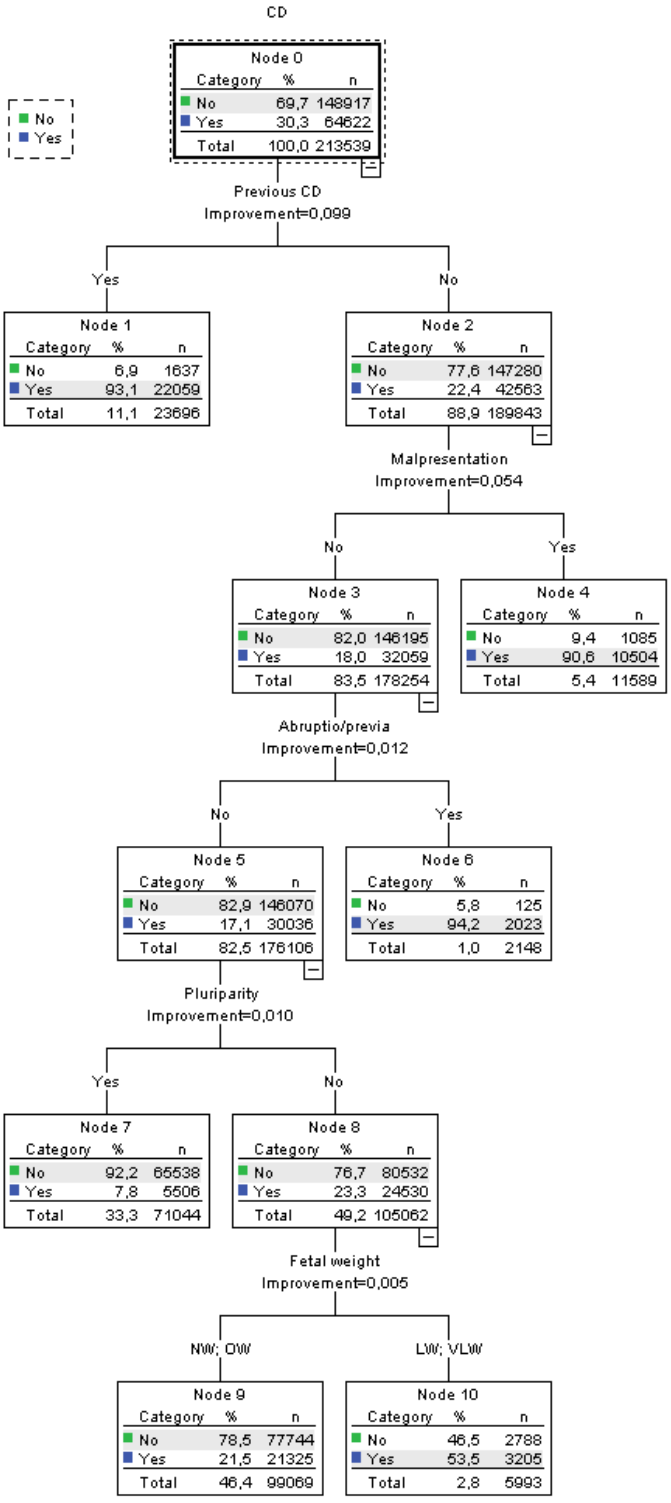
Node 4 (N=11589) women without a previous CD, with malpresentation: CD rate = 90,6%

Node 10 (N=5993) women without a previous CD, without malpresentation, without abruption or placenta previa or ante-partum hemorrhage, nulliparous with a fetus of low or very low weight: CD = 53,5%

Node 9 (N=99069) women without a previous CD, without malpresentation, without abruption or placenta previa or ante-partum hemorrhage, nulliparous with a fetus with a normal weight or overweight: CD rate = 21,5%

Node 7 (N=71044) women without a previous CD, without malpresentation, without abruption or placenta previa or ante-partum hemorrhage, pluriparous: CD rate = 7,8%.

Figure 15. Classification tree showing subgroups with different risk of CD-



Discussion

Major findings and literature

The objective of this thesis is to describe the current cesarean delivery practice and to identify the determinants of CD, including procedure volumes, type of hospital (teaching or non), time of delivery and day of the week delivery. This dissertation is based on data concerning all deliveries in RER between 2005 and June 2010 (> 210.000 deliveries).

Description of the CD practice

- During the study period, 64622 CDs were performed, amounting to 30.26% of all deliveries of the period. Most deliveries were preceded by spontaneous labour and more than half of these CDs were elective. Only 42% of CDs were urgent and occurred slightly more often during spontaneous labour, but also after induced labour or without labour. The CD rate in RER is in line with the mean Italian CD rate. Although lower than the CD rate of some Southern Italian regions, it is still far above the CD rate of other European countries (HFA-DB, 2012).
- As expected, the highest CD rates are found in the last six TGCS groups, where CD is more frequently elective. However as in Brennan et al. (2009), I found that breech (groups VI and VII), multiple pregnancy (group VIII), and preterm deliveries (group X) contribute relatively little to overall CD rates and indeed represent a fairly constant proportion of each population, despite much attention from the published literature in the recent past in relation to the timing and mode of twin deliveries (Lee, 2008, Cleary-Goldman, 2005; Simoes, 2006) vaginal breech delivery (Rietberg, 2003; Hannah, 2000), and the optimum mode of delivery for preterm, growth-restricted fetuses (Wylie, 2008; Kayem, 2008; Riskin, 2008). I also found that the highest proportion of CD among deliveries and among CD in general pertains to the V and the I and II groups. In the V group, both deliveries and CD are very high, while in the first two groups the high number of deliveries contrasts the relatively low CD rate (24%). These results are in line with the results of other studies

(Ciriello, 2012; Brennan, 2009; Howell, 2009; Regione Emilia Romagna, 2012). As a consequence, some authors (Main, 2008; Brennan, 2009; Stivanello, 2011) recommended to monitor CD rates in these groups, in particular in NTCS (I and II TGCS group) given the controversy about the safety of vaginal birth after a cesarean versus repeat CD.

- In no hospital CD rates were lower than 20%, and most rates were much higher. The 15% recommended level by the WHO in the 1980s (2009) is by far overcome, and probably not realistically achievable in the short term.
- I found that inter-hospital variation in CD rates is significant and substantial. Only within the V group inter-hospital variability is less relevant. The observed inter-hospital variation in term of CD rates has already been discussed in our studies (Fantini, 2006; Stivanello, 2011) and by other Authors in Italy or abroad (Di Lallo, 1996; Brennan, 2009; Bailit, 1999; Bragg, 2010; Rabilloud, 1998).
- The frequency of elective CD is also very different across hospitals while the variability in urgent CD rate is more modest. This suggests that inappropriateness lies more in elective than in urgent CD. In the UK, considering only singleton, Bragg et al. (2010) found more variability in urgent CD. We could argue that the reasons for inappropriateness in the UK are not the same as in RER. In some hospitals of RER factors like maternal preferences, organizational structures or legal issues could play a role as determinants of CD already during pregnancy and before labor.

Determinants of CD

- I found that previous CD, HIV, cord prolapse, fetopelvic disproportion, malpresentation and abrution, placenta previa or ante-partum hemorrhage are associated with a significant higher risk of CD after controlling for all other variables in the study population and in all the subgroups, but the V TGCS subgroup. In addition, in all subgroups, except the V, I found that mothers with older age, lower education (only secondary school vs high school degree) nulliparous show a higher risk of CD.

  These findings are in line with the literature, the above-mentioned characteristics have already been identified as risk factors for CD in many

studies (Peipert, 1993; Shearer, 1993; Signorelli, 1995; Aron, 1998; Gregory, 2000; Ecker, 2001; Bailit, 2004; Khawaja, 2004; Lin, 2004; Fantini, 2006; Scioscia, 2008; Giani, 2011; Qin, 2011; Ciriello, 2012).

- Previous CD and malpresentation of the fetus account for the highest proportion of CDs. This is confirmed by the classification tree, where these two variables are the most discriminatory and are followed by abruptio, previa and ante-partum-hemorrhage, fetal weight and pluriparity; namely variables to define TGCS groups and some additional clinical variable. This corroborates the results of Colais et al. study (2012) that indicate that TGCS should be used to control for the hospital case mix in terms of previous CD, parity, presentation, gestational age and multiple pregnancy but that there is a residual variability accounted by other clinical or socio-demographic confounders when using TGCS.
- The inter-hospital variability is only partially explained by demographic, clinical and organizational variables. This is particularly evident in deliveries with induced labour but also in the I-IIa-III-IV group and in NTCS. This was already underscored in a previous study on NTCS (Stivanello 2011) in the same region but also in singleton births in the UK and USA, where variability in CD rates is not cancelled out by adjusting for maternal and fetal risk factors (Keeler, 1997; Brag, 2010). This further suggests that other, non-considered factors determine this variability.
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Delivery during the weekend and between 7pm and 7am .

- I found that deliveries during the weekend and between 7 pm and 7 am are associated with a lower risk of CD in all subgroups. In RER hospitals, elective CDs are mostly performed during the day and during working days, and therefore in the groups of women that include a high proportion of elective CDs (e.g V to VIII TGCS groups), I expect to find that working days and daytime are risk factors and that non working days and night are protective CD factors. However, in this study, weekends and nights are protective CD factors in all subgroups and also in the subgroups where the number of elective CDs is very low (women with spontaneous labour or in the I, IIa, III, IVa group) and most CDs are urgent. Only in the subgroup of women who

delivered after induction, delivery during non-working days is not a significant CD risk factor when adjusting with the full model (model C). This is consistent with the fact that the risk of CD after induction is less dependent on non-clinical factors.

- The role of time and days of the week as determinants of clinical outcome has been analysed in some studies with mixed results. Bendavid et al. (2007) found that rates of newborn complications and obstetric trauma are marginally higher during the weekend than during the week days, although most studies did not find differences in term of neonatal outcomes (Stewart, 1998; Gould, 2003; Stephannson, 2003; Gijsen, 2012). Findings concerning time of delivery are inconsistent. Sleep deprivation has been quoted as an important risk factor (Jha, 2001; Weinger, 2002; Landrigan, 2004) and some studies reported increased risks for births during the evening or the night (De Graaf, 2010; Pasupathy, 2010;Gijesn, 2012) others do not find differences in some outcomes according to the time of the day (Bailit, 2006; Caughey, 2008; Woodhead, 2012). As far as CD rate is concerned, Mossialos et al. (2005) and Signorelli et al. (1991) in Greece and in Italy, respectively, observed that CD rates are higher during week days than during the weekend; this suggesting a possible high proportion of planned CDs during the working days. Woodhead et al. (2012) did not find differences according to the time of delivery. On the contrary Goldstick et al. (2010) indicate a marked diurnal variation in urgent operative deliveries and Caughey et al (2008) found a significantly higher CD rate in women with low risk during the evening than during the day or the night (13.5% vs 12.4 or 12.2% respectively).
- My findings indicate that the decision to perform a CD and the approaches to CD are taken differently according to the time of delivery as if the definition of “urgent” during the day is different from the night. A study conducted in the US indicated that financial mechanisms could lead to this situation (Spetz, 2001). However, in Italy there are no financial incentives according to days or nights. Other non-clinical factors are likely to play an important role: during the night or the weekend a surgical intervention might be perceived as more risky by health care professionals and the mother who puts less pressure on

having a CD, or the organization and re-opening of the operating theatre during the night may be more cumbersome and, thus, considered acceptable only in case of a true emergency.

- Interestingly, when I tested for an interaction between hospital type and time of delivery, I found that in the subgroups of women where urgent CDs are highest (I, IIa, III, IVa) the protective effect of night or holidays is significant only in non-teaching hospitals. This suggests that in teaching hospitals, surgical activities are carried out as during the day and are not considered at a greater risk. Teaching hospitals are all high volume hospitals, with adequate nursing staff 24 hours a day. The labour and delivery unit is run by a team that is in house, there are in-house anesthesiologists 24 hours a day. While in smaller and non-teaching hospital these facilities are not always available 24 hours a day.

Affiliation and birth volumes

- Our study does not provide clear evidence that affiliation and birth volumes are important CD risk factors.
- In univariate analyses these organizational variables were significant, but not in multivariate analyses. Hospitals with less than 500 deliveries a year are associated with a greater risk of CD only in the study population and in the group without previous CD when I applied the model without fetal growth retardation and cephalopelvic disproportion.
- My findings show that at low birth volumes there is a higher variability in CD rates. In addition data suggest that the best performing hospitals in term of CD rates undergo an intermediate number of deliveries per year.
- The analyses of the multivel models shows that these hospital-level variables contribute to explain a certain amount of variability but are not significant.

As far as affiliation is concerned the literature provides mixed results. Higher quality of care measures (Rosenthal, 1997; Allison, 2000; Patel, 2007) and lower complication and mortality rates (Keeler, 1992; Rosentthal, 1997; Allison, 2000; Polanczyk, 2002; Dimick, 2004; Kupersmith, 2005; Bianchi, 2012) were observed in patients treated at academic institutions. On the other hand, other authors (Khun, 1994; Ayanian, 2002; Thornlow, 2006; Vartak, 2008; Juillard, 2009) have

also reported no difference or worse outcomes at academic institutions However, as Bianchi et al. (2012) observed, the lack of multivariable adjustment may have precluded these findings. In univariate analyses the CD rate is higher in teaching hospitals, as in the study of Zhang (2011) because more complex cases go to teaching hospitals but after adjusting for clinical variables, affiliation is not significant any longer. On the contrary, Garcia et al. (2001) found that academic hospitals had significantly lower risk of CD both in univariate and multivariate analyses than community hospitals. Nicholson et al (2009) found that primary cesarean delivery rates among women with diabetes did not vary across different settings. A comparison of my results with the literature's results is very difficult. In the USA, there are great differences in the population attending different types of hospitals and in the financial aspects of the two institutions. In the RER these differences are not as evident. Our results suggest that in the RER, the teaching environment, does not influence the risk of CD directly or indirectly. It is likely that maternal preferences, obstetrician decision-making, mother-physician communication and other organizational factors do not vary substantially between teaching and non teaching hospital.

The relation between volumes and outcomes has been studied extensively. For many surgical procedures, patients at hospitals with high procedure volumes have lower mortality rates (Dudley, 2000; Hannan, 2001; Begg, 2002; Birkmeyer, 2002; Halm, 2002). A recent update of a systematic review show that in many fields there is an association between volumes and outcomes (Davoli, 2012), while in some fields there is no association. In 2005, Davoli et al. concluded that there was no evidence between volumes and CD complications.

Some studies (Moster, 1999; Heller, 2002; Snowden, 2012) have found that perinatal outcomes, such as neonatal mortality and asphyxia, are less prevalent in high birth volume hospitals, while others (Tracy, 2006; Chang, 2008; Hemminki, 2011) found no strong evidence of an association between hospital VBAC volume and the likelihood of adverse outcomes in VBAC after adjusting for patient case mix. Nevertheless, by considering only the subgroup of women with gestational or diabetes, Nicholson et al. (2009) found that some clinical outcomes change after adjustment.

Considering the CD rate as the outcome, findings are also mixed. Garcia (2001) found that high-volume hospitals are associated with a lower risk of CD, in comparison to very high volume hospitals, but medium and low volume hospitals do not have different risks between them. The risk of CD does not change with volumes after adjusting for other risk factors in women with diabetes (Nicholson, 2009).This effect may be different from that observed for other medical procedures, where high volumes correspond to 50-100 procedures per year (Garcia, 2001). Concerning delivery, in Emilia Romagna low volumes are never less than 200 deliveries and in each unit there is a dedicated obstetric service that provides care to a significant number of patients. Maybe instead of considering hospital volumes, obstetric volumes or doctor volumes should be analysed.

Strengths and limits

This has been a large population study, with recent data that covers an entire region of Italy. The thesis relies on administrative databases. In order to achieve the objective of this thesis no other source of data nor an ad hoc study would have been feasible. Multiple issues regarding the validity of administrative data remain largely unexplored (Powell, 2003). Problems in accuracy, completeness and quality might differ from hospital to hospital according to their affiliation or volumes; for example, errors in coding may occur and omissions of ICD codes identifying risk factors may be more likely in the group without a CD. Previous work (Korst, 2005) suggests that administrative data may be as reliable as data extracted from clinical charts with respect to key outcomes. In Emilia Romagna, the administrative databases proved to have a high degree of completeness and quality and have already been used in other studies (Stivanello, 2010).

In this type of retrospective study it is not possible to determine the reliability of diagnostic codes. Audit activities are based on these diagnostic codes and some diagnoses might be used improperly. In my thesis, I excluded some variables because of this problem, and I hypothesised that intrauterine growth retardation and cephalopelvic disproportion could also be used improperly. Therefore, I performed sensitive analyses without these factors, with some estimates changing by more than 10%. A recent study (De Martino, 2012) found large

differences in the frequency of some type of malpresentation across hospitals of some Italian Regions and suggested the possibility of improper or clearly opportunistic use of this variable as well. Future studies should further ascertain the reliability of the codes of these variables before using them for inter-hospital comparisons.

In addition, risk factors for CD, such as body mass index, gestational weight gain and height (Smith, 2004; Ciriello, 2012;) have not been included in the analysis because this information is not recorded in our databases.

Conclusions

- The results of the thesis support the recommendation of monitoring CD rates in NTCS women (i.e. the I and II TGCS group) during audit or inter-hospital comparisons.
- In addition to socio-demographic, clinical and the considered organizational factors, other non studied factors should be explored to understand CD variability.
- These results do not provide clear evidence that small hospitals always perform bad in terms of CD rate, they show in fact a great variability. In the absence of clear evidence, the reduction in CD rates is therefore not a strong argument for the policy of closing small hospitals. Other clinical, economic or organizational issues should be taken into account.
- In addition to exploring hospital volumes as CD risk factors, the next research step is to consider obstetric and doctor volumes, as well.
- These results also indicate that academic hospitals fare no better nor worse than non-teaching hospitals in terms of CD rate, but they are more consistent in the use of this procedure; though consistency is not *per se* a positive aspect.
- These results suggest that strategies to reduce CDs could be found by focusing more attention on the differences in the obstetric approach between day and night and between working and no-working day deliveries.

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