



**HAL**  
open science

## Lower gestational age is associated with severe maternal morbidity of preterm cesarean delivery

Delphine Sirgant, Noémie Ressayguier, Claude D'ercole, Pascal Auquier,  
Barthélémy Tosello, Julie Blanc

### ► To cite this version:

Delphine Sirgant, Noémie Ressayguier, Claude D'ercole, Pascal Auquier, Barthélémy Tosello, et al.. Lower gestational age is associated with severe maternal morbidity of preterm cesarean delivery. *Journal of Gynecology Obstetrics and Human Reproduction*, 2020, 49 (7), pp.101764. 10.1016/j.jogoh.2020.101764 . hal-02972064

**HAL Id: hal-02972064**

**<https://hal.science/hal-02972064>**

Submitted on 22 Aug 2022

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial 4.0 International License

## TITLE PAGE

### **Lower gestational age is associated with severe maternal morbidity of preterm cesarean delivery**

Delphine Sirgant<sup>1</sup> MD, Noémie Ressaygues<sup>2</sup> MD, PhD, Claude d'Ercole<sup>1,2</sup> MD, PhD, Pascal Auquier<sup>2</sup> MD, PhD, Barthélémy Tosello<sup>3,4</sup> MD, PhD, Julie Blanc<sup>1,2</sup> MD

<sup>1</sup> Department of Obstetrics and Gynecology, Nord Hospital, APHM, chemin des Bourrely, 13015 Marseille, France

<sup>2</sup> EA3279, CEReSS, Health Service Research and Quality of Life Center, Aix-Marseille University, 13284 Marseille, France

<sup>3</sup> Department of Neonatology, North Hospital, Assistance Publique des Hôpitaux de Marseille, France

<sup>4</sup> Aix-Marseille Univ, CNRS, EFS, ADES, Marseille, France

Correspondence: Dr Julie Blanc, MD, Department of Obstetrics and Gynecology, Nord Hospital, APHM, chemin des Bourrely, 13015 Marseille, France.

Phone number +334 91 96 46 72

Fax number +334 91 96 46 93

Electronic address: [julie.blanc@ap-hm.fr](mailto:julie.blanc@ap-hm.fr)

ORCID: 0000-0002-1542-504X

#### **Short title:**

Preterm cesarean and severe maternal morbidity

1 **Lower gestational age is associated with severe maternal morbidity of preterm cesarean**  
2 **delivery**

3

4 **Abstract**

5 ***Objective***

6 To evaluate whether gestational age was associated with the severe maternal morbidity  
7 (SMM) of preterm cesarean delivery between 22 and 34 weeks of gestation (weeks).

8 ***Material and Methods***

9 We performed an observational retrospective cohort study in two tertiary university hospitals  
10 in 2018. We included all mothers of preterm infants born by caesarean delivery between 22  
11 and 34 weeks, excluding mothers with multiple births greater than two, with pregnancy  
12 terminations or stillbirths, and who died unrelated to obstetrical causes. The principal  
13 endpoint, SMM, was a composite outcome (classical uterine incision, postpartum hemorrhage  
14 defined by blood loss  $\geq 500$  mL, blood transfusion, any injury to adjacent organs, unplanned  
15 procedure/need for reintervention, Intensive Care Unit (ICU) stay longer than 24 hours,  
16 postpartum fever , and/or death).

17 ***Results***

18 Among the 252 women, SMM occurred in 89 (35.3%) cases. After multivariate analysis,  
19 gestational age was independently associated with SMM (adjusted Odds Ratio [aOR] 0.87;  
20 95% Confidence Interval [CI] 0.78-0.97). The other variables statistically associated with  
21 SMM were type of pregnancy with a negative association with twin pregnancy (aOR, 0.44;  
22 95% CI, 0.20-0.93) and a positive association with general anesthesia (aOR, 2.52; 95% CI,  
23 1.25-5.13). A sensitivity analysis was performed and found an association, at the limit of  
24 significance, between gestational age  $< 28$  weeks and SMM (aOR, 1.80; 95% CI, 0.99-3.27,  $p$   
25 = 0.05).

26 ***Conclusion***

27 Lower gestational age was associated with the risk of SMM for preterm cesarean delivery  
28 between 22 and 34 weeks. Obstetricians should integrate this knowledge into their shared  
29 decision-making processes with parents.

30 ***Key words***

31 Cesarean delivery, gestational age, prematurity, severe maternal morbidity, shared decision-  
32 making

### 33 **Introduction**

34 The survival of preterm infants born between 22 and 28 weeks of gestation (weeks) has  
35 increased worldwide in the past few decades.<sup>1-3</sup> In France, a national population-based cohort  
36 study “EPIPAGE 2” reported a 14.4% increase in global neonatal survival without adverse  
37 outcomes between 1997 and 2011.<sup>4</sup>

38 The improvement in the survival of these extremely preterm infants is related to the  
39 development of neonatal proactive management as well as active antenatal care, such as  
40 caesarean delivery in the case of fetal indications.<sup>5,6</sup> Preterm caesarean delivery rates have  
41 regularly increased, particularly before 26 weeks.<sup>1,2,7,8</sup> However, European and American  
42 cohorts of preterm infants reported variable rates of caesarean delivery before 26 weeks.<sup>1,2,4,6,7</sup>  
43 These heterogeneous care practices can be observed across and within countries<sup>5</sup> and can be  
44 associated with disagreements in team care.<sup>9</sup> A shared decision-making process is essential in  
45 situations at risk of extremely preterm delivery and should take into account available data  
46 regarding neonatal and maternal morbidity. Many studies have reported on neonatal morbidity  
47 in relation to the mode of delivery, but there is currently a paucity of data regarding maternal  
48 morbidity in relation to preterm caesarean delivery.<sup>10-13</sup> In the case of term delivery, a severe  
49 maternal morbidity (SMM) associated with caesarean delivery is higher compared to SMM  
50 after vaginal delivery.<sup>14-16</sup> Few studies have assessed the SMM of extremely preterm  
51 caesarean delivery as well as the association between gestational age and SMM.<sup>17,18</sup> We have  
52 recently reported a secondary analysis of a population-based cohort study, demonstrating that  
53 mothers undergoing a caesarean delivery before 26 weeks experienced more than a two-fold  
54 increase in the risk of SMM compared with those undergoing a caesarean delivery between 26  
55 and 34 weeks.<sup>19</sup> The strength of this previous study was its specific prospective population-  
56 based cohort design, with its main limitation being the evaluation of SMM (defined as the  
57 occurrence of severe postpartum hemorrhage defined by the use of a blood transfusion,

58 intensive care unit admission, or death) using available maternal variables from this cohort of  
59 preterm infants.

60 To confirm the hypothesis that lower gestational age is associated with a greater risk of SMM  
61 of preterm caesarean delivery, we performed as a sensitivity analysis, a recent retrospective  
62 cohort study in local tertiary care centers.

63 **Material and Methods**

64 *Study population and setting*

65 We performed an observational retrospective cohort study in two tertiary university hospitals  
66 in Marseille, France between January and December 2018.

67 We included all the mothers of preterm infants born by caesarean delivery between 22 and 34  
68 weeks, excluding mothers with multiple births greater than two, mothers with a history of  
69 pregnancy terminations or stillbirths, and case of maternal death unrelated to an obstetrical  
70 cause.

71

72 *Data collection*

73 Maternal, obstetrical, and neonatal data were collected retrospectively from each mother's  
74 and infants' electronic medical files.

75 D.S. entered the data and the accuracy of the database was validated by J.B. and N.R..

76

77 *Outcomes and studied factors*

78 The principal endpoint, Severe Maternal Morbidity (SMM), was a composite outcome  
79 defined as the occurrence of at least one of the following complications:

- 80 - classical uterine incision (referring to an incision in the upper uterine segment and  
81 because classical incision leads to a caesarean delivery upon the next pregnancy and  
82 therefore increases the global maternal morbidity rate);
- 83 - postpartum hemorrhage defined as blood loss  $\geq 500$  mL (as defined by the World  
84 Health Organization and French clinical guidelines <sup>20</sup>);
- 85 - blood transfusion;
- 86 - any injury of adjacent organs (gastrointestinal, urological, or vascular),
- 87 - unplanned procedure/need for reintervention;

- 88 - Intensive Care Unit (ICU) stay longer than 24 hours in duration;
- 89 - postpartum fever;
- 90 - and/or death.

91 This composite endpoint was chosen as a synthesis of prior definitions of severe maternal  
92 morbidity in these clinical situations literature and depending on available data during the stay  
93 of the mother.<sup>18,19,21-23</sup>

94 The main studied factor was gestational age at caesarean delivery. As a sensitivity analysis,  
95 gestational age was also studied as a binary variable with the threshold of 26 and 28 weeks,  
96 the usual thresholds defining extreme and very high prematurity, respectively. Gestational age  
97 was routinely determined by the first trimester ultrasound and verified before any extremely  
98 early caesarean delivery. If the first trimester ultrasound was not performed (less than 5% of  
99 the women), gestational age was best estimated based on the last menstrual period and its  
100 consistency with the measured head circumference of the earliest prenatal ultrasound.

101 The other studied factors were as follows: maternal age, parity, scarred uterus, Body Mass  
102 Index (BMI) (calculated based on pre-pregnancy weight), active smoking during pregnancy,  
103 pregestational diabetes, notable maternal pathologies, previous preterm delivery, known  
104 uterine malformations, type of pregnancy (singleton or twin), type of prematurity  
105 (spontaneous or induced), type of anesthesia, uterine injury during extraction, any difficulty  
106 during fetal extraction, and a five-minute Apgar score. Indications of caesarean delivery were  
107 also collected depending on the principal identified cause reported in the medical files and  
108 divided into six mutually exclusive groups, as previously published in cohort EPIPAGE 2:<sup>24</sup>  
109 preterm labor without preterm premature rupture of membranes, preterm premature rupture of  
110 membranes, hypertensive disorders without suspected fetal growth restriction, hypertensive  
111 disorders with suspected fetal growth restriction, placental abruption after an uncomplicated  
112 pregnancy, and suspected fetal growth restriction without hypertensive disorders. Suspected

113 fetal growth restriction was defined by an estimated fetal weight in less than the 5<sup>th</sup> centile on  
114 customized birth weight curves.<sup>25</sup>

115 The Data Protection Authority (*General Data Protection Regulation / AP-HM no. 2018-89*)  
116 approved this study. According to French regulations, this study is exempt from institutional  
117 board review, because it is an observational and retrospective investigation using anonymized  
118 data from medical records. The mothers were informed that their records would be used for  
119 the evaluation of medical practices and that they could opt out of these studies.

120

### 121 *Statistical analysis*

122 We first described the principal characteristics of our study population. Categorical variables  
123 were presented as effectives, percentages, and continuous variables, were shown as mean  $\pm$   
124 standard deviation (SD).

125 We then performed a univariate analysis to compare maternal, obstetrical, and neonatal  
126 characteristics depending on the occurrence of SMM. Categorical variables were compared  
127 with a  $\chi^2$  test or Fisher exact test when appropriate. For the continuous variables, the data  
128 were analyzed using *t* tests or a Mann-Whitney test when appropriate.

129 We performed a multivariate logistic regression model to quantify the association between  
130 gestational age and SMM with an adjusted odds ratio (aOR) and a 95% confidence interval  
131 (95% CI). The variables included in the multivariate model were (i) gestational age (main  
132 factor studied); (ii) notable maternal pathologies and type of prematurity (forced variables due  
133 to known prognostic interest in the literature); and (iii) variables with *p* values < 0.20 in the  
134 univariate analysis (candidate variable). A stepwise backward regression was applied in order  
135 to keep only statistically significant variables and forced adjusting variables in the final  
136 model. Firth correction was applied to take into account the small number of events.<sup>26</sup> There  
137 were no missing data concerning the main studied factors and the principal endpoint. Data

138 was analyzed using R studio V.1.2.1335, and the R package `logistf` was used. All tests were  
139 two-sided, with statistical significance defined as  $p < 0.05$ .

140 **Results**

141 *Population*

142 Among the 5401 women who delivered at the two tertiary centers, 1400 mothers had a  
143 caesarean delivery, 797 (56.9%) in Conception hospital and 603 (43.1%) in North hospital  
144 between January and December 2018, and 262 (18.7%) women had a caesarean delivery  
145 between 22 and 34 weeks. More precisely, 262 women had a cesarean delivery between 24  
146 and 34 weeks since no cesarean delivery was perform before 24 weeks during the study  
147 period. After the application of the exclusion criteria, 252 women were included in the study  
148 (Figure 1).

149 The maternal, obstetrical, and neonatal characteristics of the study population are described in  
150 Table 1. We couldn't present the results of umbilical arterial pH since we had missing data.

151 Among the 34 (13.5%) mothers presenting notable maternal pathology, eight with chronic  
152 hypertension, three with cardiac pathology (e.g., dilated cardiomyopathy with cardiac  
153 transplantation, restrictive cardiomyopathy, or rhythm troubles), three with nephropathy, two  
154 with infectious chronic diseases (e.g., VIH, VHC), three with thrombophilia, two with  
155 hemoglobin S disease, four with neurologic pathology (e.g., multiple sclerosis, epilepsy, or  
156 brachycephalic trunk hypoplasia), two with antiphospholipid syndrome or lupus, one with  
157 hematologic pathology (e.g., Willebrand), one with Crohn's disease, two with pulmonary  
158 pathology (e.g., cystic fibrosis with pulmonary transplantation), and two with venous  
159 thromboembolism were identified.

160 SMM occurred in 89 (35.3%) of the cases: 30 (12%) mothers had postpartum hemorrhage, 19  
161 (7.5%) needed blood transfusions, three (1.2%) had injuries to adjacent organs (urological or  
162 vascular), five (2%) had unplanned procedures/return to theatre (because of abscess or  
163 hematoma of abdominal wall), 11 (4.4%) were admitted to the ICU, 15 (6%) presented

164 postpartum fever, and one mother died. The death of this mother occurred during caesarean  
165 delivery performed for severe preeclampsia and was due to pulmonary embolism.  
166 The cesarean delivery was performed in 67 (26.6%) cases in the context of spontaneous  
167 prematurity. In these cases, the indications of the cesarean delivery were mostly: breech  
168 presentation in 41 (61.2%), non-reassuring fetal hearth rate in 7 (10.4%) and suspected intra-  
169 uterine infection in 7 (10.4%).

#### 170 *Univariate analysis*

171 The following factors were positively associated with SMM: gestational age ( $29.2 \pm 2.6$   
172 weeks vs  $30.1 \pm 2.5$  weeks;  $p= 0.01$ ), known uterine malformations (3(3.4%) vs 0;  $p= 0.03$ ),  
173 general anesthesia (21 (23.6%) vs 18 (11.0%);  $p= 0.01$ ), and uterine injury during extraction  
174 (6 (6.7%) vs 2 (1.2%);  $p= 0.02$ ). Twin pregnancy was negatively associated with SMM (11  
175 (12.4%) vs 37 (22.7%);  $p= 0.04$ ) (Table 2).

176

#### 177 *Multivariate analysis*

178 After multivariate analysis, gestational age was independently associated with SMM (adjusted  
179 Odds Ratio [aOR] 0.87; 95% Confidence Interval [CI] 0.78-0.97;  $p=0.01$ ) (Table 3). The  
180 other variables statistically associated with SMM were type of pregnancy with a negative  
181 association with twin pregnancy (aOR, 0.44; 95% CI, 0.20-0.93;  $p=0.03$ ) and with general  
182 anesthesia (aOR, 2.52; 95% CI, 1.25-5.13;  $p=0.01$ ). The other variables included in the  
183 multivariate analysis (e.g., notable maternal pathology and type of prematurity) were not  
184 independently associated with SMM.

185 Two sensitivity analyses were then performed with the same variables and with a gestational  
186 age according to two modalities ( $< 26$  weeks and  $\geq 26$  weeks;  $< 28$  weeks and  $\geq 28$  weeks).  
187 This analysis failed to find a significant association between gestational age  $< 26$  weeks and  
188 SMM (aOR, 2.01; 95% CI, 0.77-5.31,  $p = 0.15$ ). It did, however, find an association (at the

189 limit of significance) between gestational age < 28 weeks and SMM (aOR, 1.80; 95% CI,  
190 0.99-3.27,  $p = 0.05$ ).

191 **Discussion**

192 Our study showed that gestational age was independently and negatively associated with  
193 SMM in the case of preterm caesarean delivery between 22 and 34 weeks. More precisely,  
194 gestational age between 24 and 34 weeks was negatively associated with SMM since no  
195 caesarean delivery was performed before 24 weeks.

196 These results confirm our findings from a national population-based cohort study, EPIPAGE  
197 2.<sup>19</sup> Whereas previous articles reported a higher rate of SMM for caesarean delivery than  
198 vaginal delivery regardless of gestational age<sup>14,27-29</sup> or an association between prematurity and  
199 maternal morbidity regardless of the mode of delivery,<sup>21,30</sup> our study confirmed the  
200 association between gestational age and SMM in the case of preterm caesarean delivery.

201 Twin pregnancy, which has a high incidence within the population of preterm deliveries (19%  
202 in our study), was independently and negatively associated with SMM for preterm caesarean  
203 delivery. This result is consistent with the hypothesis that the SMM of extremely preterm  
204 caesarean delivery is related to the incision of a deepen myometrium. In fact, in the case of  
205 extremely preterm singleton delivery, the lower uterine segment is usually not yet formed. In  
206 contrast, in the case of extremely preterm twin delivery, the lower uterine segment forms  
207 earlier, and the incision takes place in a thinner myometrium. This is consistent with previous  
208 published results about the increased risk of intraoperative adverse events in the case of  
209 singleton pregnancy.<sup>18</sup>

210 We did not find an independent association between SMM and notable maternal pathology,  
211 even if highly heterogeneous, or between SMM and the type of prematurity (spontaneous or  
212 induced). This is an additional concept to consider that the SMM of preterm caesarean  
213 delivery is related to the surgical act itself. General anesthesia was significantly associated  
214 with SMM. This could be explained because of the maternal indication of general anesthesia  
215 in most cases (hellp syndrome for example).

216 We reported SMM in 89 (35.3%) of the cases in our cohort, which is substantial. This finding  
217 should be included in shared decision-making process between parents, neonatologists, and  
218 obstetricians, particularly if vaginal delivery could be considered as an option (e.g.,  
219 spontaneous preterm labor without abnormal fetal heart rate). In accordance with a patient-  
220 centered approach,<sup>31</sup> shared decision-making aims to enable patients “to take an active role in  
221 deciding about and planning their health care”. The shared decision-making process, and  
222 particularly the agreement between obstetricians and neonatologists, is essential, as previously  
223 reported by Guinsburg et al..<sup>9</sup> In fact, disagreement in the proactive management of extreme  
224 prematurity has been associated with an increased risk of death of 2.39 times in the first day  
225 of the neonates.<sup>9</sup> In ten European regions between 2003 and 2012, the lowest gestational age  
226 at which maternity units reported performing a caesarean delivery for the acute distress of a  
227 singleton non-malformed fetus significantly decreased when parents were in favor of active  
228 management (from an average of 24.7 weeks in 2003 to 24.1 weeks in 2012) and when  
229 parents were against of active management (from an average of 26.1 weeks in 2003 to 25.2  
230 weeks in 2012).<sup>32</sup> The shared decision-making process should take into account these practice  
231 evolutions, the wishes of parents, and available data.<sup>33</sup> As recently suggested by Sandall et al.,  
232 the key message of the information delivered to the parents could be “a caesarean section is a  
233 life-saving intervention for specific complications during pregnancy and childbirth that should  
234 be available for all women in need” and “a caesarean section also confers an increased risk of  
235 maternal morbidity, severe acute morbidity, and adverse outcomes in subsequent pregnancies  
236 when compared with vaginal delivery”.<sup>34</sup>

237 The strength of our study was its evaluation of SMM. Despite the retrospective design of the  
238 study, the prospective filling of each electronic medical file allowed us to obtain reliable data  
239 and define a composite outcome with consistent variables. In the literature, the definition of  
240 SMM is not standardized, but we chose to generate a “synthesis” of each identified definition.

241 In fact, SMM is sometimes defined as a blood transfusion and/or hysterectomy to define  
242 severe postpartum hemorrhage, ICU admission, death, and length of hospitalization exceeding  
243 seven days.<sup>35</sup> Other studies have defined SMM as the occurrence of an infection, surgical  
244 injury, endometritis, readmission, or reopening or an unexpected procedure.<sup>21,23</sup> The threshold  
245 of 500 mL and not 1000 mL was chosen to define postpartum hemorrhage in our cohort of  
246 cesarean deliveries and could be discussed. We chose to follow French and international  
247 definition<sup>20</sup> and think that this is not a limit since we only compared women having cesarean  
248 deliveries and not women having vaginal delivery versus cesarean delivery. We did not  
249 choose maternal hospital stays exceeding seven days in our composite outcome, because, in  
250 this case, the length of stay could be related to neonatal hospitalization.

251 The main limitation of our study was its small size. Although our study took place in only two  
252 centers, the recency of the collection of data (2018) optimizes the external validity of our  
253 results. Furthermore, the short duration of the inclusion period allowed us to avoid bias  
254 related to the evolution of practices over time, as it was in previous published retrospective  
255 studies.<sup>18</sup> The aOR of the gestational age < 26 weeks is close to the aOR we reported in our  
256 previous study.<sup>19</sup> Due to a lack of power, we failed to find a significant association between  
257 gestational age < 26 weeks and SMM in the present analysis.

258 Our study suggests that lower gestational age is related to a greater risk of SMM for preterm  
259 caesarean delivery between 22 and 34 weeks. These results should encourage reflection,  
260 research, and teamwork between neonatologists and obstetricians to improve agreement and  
261 shared decision-making processes with parents.

262 **Acknowledgements:** none

263 **Declaration of interest statement:** The authors report no conflict of interest.

264 **Funding:** This research did not receive any specific grant from funding agencies in the

265 public, commercial, or not-for-profit sectors.

266 **Author contributions**

267 **Delphine Sirgant:** Data curation, Writing – original draft, Formal analysis, Final approval;

268 **Noémie Ressayguier:** Conceptualization, Methodology, Supervision analysis, Writing –

269 review and editing, Final approval; **Claude d’Ercole:** Conception, Supervision, Revision and

270 Validation the work, Final approval; **Pascal Auquier:** Design, Methodology, Revision and

271 Validation the work, Final approval; **Barthélémy Tosello:** Interpretation of data for the work,

272 Writing – review and editing, Validation, final approval; **Julie Blanc:** Conceptualization,

273 Formal analysis, Writing – original draft, Final approval.

274 **References**

- 275 1 Stoll BJ, Hansen NI, Bell EF, Shankaran S, Laptook AR, Walsh MC *et al.* Neonatal  
276 outcomes of extremely preterm infants from the NICHD Neonatal Research Network.  
277 *Pediatrics* 2010; **126**: 443–456.
- 278 2 Costeloe KL, Hennessy EM, Haider S, Stacey F, Marlow N, Draper ES. Short term  
279 outcomes after extreme preterm birth in England: comparison of two birth cohorts in  
280 1995 and 2006 (the EPICure studies). *BMJ* 2012; **345**: e7976.
- 281 3 Ishii N, Kono Y, Yonemoto N, Kusuda S, Fujimura M, Neonatal Research Network,  
282 Japan. Outcomes of infants born at 22 and 23 weeks' gestation. *Pediatrics* 2013; **132**:  
283 62–71.
- 284 4 Ancel P-Y, Goffinet F, EPIPAGE-2 Writing Group, Kuhn P, Langer B, Matis J *et al.*  
285 Survival and morbidity of preterm children born at 22 through 34 weeks' gestation in  
286 France in 2011: results of the EPIPAGE-2 cohort study. *JAMA Pediatr* 2015; **169**: 230–  
287 238.
- 288 5 Diguisto C, Goffinet F, Lorthe E, Kayem G, Roze J-C, Boileau P *et al.* Providing  
289 active antenatal care depends on the place of birth for extremely preterm births: the  
290 EPIPAGE 2 cohort study. *Arch Dis Child Fetal Neonatal Ed* 2017; **102**: F476–F482.
- 291 6 Perlberg J, Ancel PY, Khoshnood B, Durox M, Boileau P, Garel M *et al.* Delivery  
292 room management of extremely preterm infants: the EPIPAGE-2 study. *Arch Dis Child*  
293 *Fetal Neonatal Ed* 2016; **101**: F384–390.
- 294 7 EXPRESS Group, Fellman V, Hellström-Westas L, Norman M, Westgren M, Källén  
295 K *et al.* One-year survival of extremely preterm infants after active perinatal care in  
296 Sweden. *JAMA* 2009; **301**: 2225–2233.
- 297 8 Ancel P-Y, Goffinet F, EPIPAGE 2 Writing Group. EPIPAGE 2: a preterm birth  
298 cohort in France in 2011. *BMC Pediatr* 2014; **14**: 97.
- 299 9 Guinsburg R, Branco de Almeida MF, Dos Santos Rodrigues Sadeck L, Marba STM,  
300 Suppo de Souza Rugolo LM, Luz JH *et al.* Proactive management of extreme prematurity:  
301 disagreement between obstetricians and neonatologists. *J Perinatol* 2012; **32**: 913–919.
- 302 10 Riskin A, Gonen R, Kugelman A, Maroun E, Ekhilevitch G. Does cesarean section  
303 before the scheduled date increase the risk of neonatal morbidity? *Isr Med Assoc J* 2014;  
304 **16**: 559–563.
- 305 11 Kayem G, Combaud V, Lorthe E, Haddad B, Descamps P, Marpeau L *et al.* Mortality  
306 and morbidity in early preterm breech singletons: impact of a policy of planned vaginal  
307 delivery. *Eur J Obstet Gynecol Reprod Biol* 2015; **192**: 61–65.
- 308 12 Tucker Edmonds B, McKenzie F, Macheras M, Srinivas SK, Lorch SA. Morbidity  
309 and mortality associated with mode of delivery for breech periviable deliveries. *Am J*  
310 *Obstet Gynecol* 2015; **213**: 70.e1–70.e12.
- 311 13 Običan SG, Small A, Smith D, Levin H, Drassinower D, Gyamfi-Bannerman C. Mode  
312 of delivery at periviability and early childhood neurodevelopment. *Am J Obstet Gynecol*  
313 2015; **213**: 578.e1–4.
- 314 14 Deneux-Tharaux C, Carmona E, Bouvier-Colle M-H, Bréart G. Postpartum  
315 maternal mortality and cesarean delivery. *Obstet Gynecol* 2006; **108**: 541–548.
- 316 15 Allen VM, O'Connell CM, Liston RM, Baskett TF. Maternal morbidity associated  
317 with cesarean delivery without labor compared with spontaneous onset of labor at term.  
318 *Obstet Gynecol* 2003; **102**: 477–482.
- 319 16 Burrows LJ, Meyn LA, Weber AM. Maternal morbidity associated with vaginal  
320 versus cesarean delivery. *Obstet Gynecol* 2004; **103**: 907–912.
- 321 17 Kawakita T, Reddy UM, Grantz KL, Landy HJ, Desale S, Iqbal SN. Maternal

322 outcomes associated with early preterm cesarean delivery. *Am J Obstet Gynecol* 2017;  
323 **216**: 312.e1-312.e9.

324 18 Bertholdt C, Menard S, Delorme P, Lamau M-C, Goffinet F, Le Ray C. Intraoperative  
325 adverse events associated with extremely preterm cesarean deliveries. *Acta Obstet*  
326 *Gynecol Scand* 2018; **97**: 608–614.

327 19 Blanc J, Resseguier N, Goffinet F, Lorthe E, Kayem G, Delorme P *et al.* Association  
328 between gestational age and severe maternal morbidity and mortality of preterm  
329 cesarean delivery: a population-based cohort study. *Am J Obstet Gynecol* 2019.  
330 doi:10.1016/j.ajog.2019.01.005.

331 20 Sentilhes L, Vayssière C, Deneux-Tharoux C, Aya AG, Bayoumeu F, Bonnet M-P *et*  
332 *al.* Postpartum hemorrhage: guidelines for clinical practice from the French College of  
333 Gynaecologists and Obstetricians (CNGOF): in collaboration with the French Society of  
334 Anesthesiology and Intensive Care (SFAR). *Eur J Obstet Gynecol Reprod Biol* 2016; **198**:  
335 12–21.

336 21 Reddy UM, Rice MM, Grobman WA, Bailit JL, Wapner RJ, Varner MW *et al.* Serious  
337 maternal complications after early preterm delivery (24-33 weeks' gestation). *Am J*  
338 *Obstet Gynecol* 2015; **213**: 538.e1–9.

339 22 Hesselman S, Jonsson M, Råssjö E-B, Windling M, Högberg U. Maternal  
340 complications in settings where two-thirds of extremely preterm births are delivered by  
341 cesarean section. *J Perinat Med* 2017; **45**: 121–127.

342 23 Thomas PE, Petersen SG, Gibbons K. The influence of mode of birth on neonatal  
343 survival and maternal outcomes at extreme prematurity: A retrospective cohort study.  
344 *Aust N Z J Obstet Gynaecol* 2016; **56**: 60–68.

345 24 Delorme P, Goffinet F, Ancel P-Y, Foix-L'Hélias L, Langer B, Lebeaux C *et al.* Cause  
346 of Preterm Birth as a Prognostic Factor for Mortality. *Obstet Gynecol* 2016; **127**: 40–48.

347 25 Ego A. [Definitions: small for gestational age and intrauterine growth  
348 retardation]. *J Gynecol Obstet Biol Reprod (Paris)* 2013; **42**: 872–894.

349 26 Firth D. Bias reduction of maximum likelihood estimates. *Biometrika* 1993; **80**:  
350 27–38.

351 27 Hall MH, Bewley S. Maternal mortality and mode of delivery. *Lancet* 1999; **354**:  
352 776.

353 28 Esteves-Pereira AP, Deneux-Tharoux C, Nakamura-Pereira M, Saucedo M,  
354 Bouvier-Colle M-H, Leal M do C. Caesarean Delivery and Postpartum Maternal Mortality:  
355 A Population-Based Case Control Study in Brazil. *PLoS ONE* 2016; **11**: e0153396.

356 29 Kilpatrick SJ, Abreo A, Gould J, Greene N, Main EK. Confirmed severe maternal  
357 morbidity is associated with high rate of preterm delivery. *Am J Obstet Gynecol* 2016;  
358 **215**: 233.e1–7.

359 30 Rossi RM, DeFranco EA. Maternal Complications Associated With Periviable Birth.  
360 *Obstet Gynecol* 2018; **132**: 107–114.

361 31 Weston WW. Informed and shared decision-making: the crux of patient-centered  
362 care. *CMAJ* 2001; **165**: 438–439.

363 32 Bonet M, Cuttini M, Piedvache A, Boyle EM, Jarreau PH, Kollée L *et al.* Changes in  
364 management policies for extremely preterm births and neonatal outcomes from 2003 to  
365 2012: two population-based studies in ten European regions. *BJOG: An International*  
366 *Journal of Obstetrics & Gynaecology* 2017; **124**: 1595–1604.

367 33 Lantos JD. Ethical Problems in Decision Making in the Neonatal ICU. *N Engl J Med*  
368 2018; **379**: 1851–1860.

369 34 Sandall J, Tribe RM, Avery L, Mola G, Visser GH, Homer CS *et al.* Short-term and  
370 long-term effects of caesarean section on the health of women and children. *The Lancet*

371 2018; **392**: 1349–1357.  
372 35 Villar J, Carroli G, Zavaleta N, Donner A, Wojdyla D, Faundes A *et al.* Maternal and  
373 neonatal individual risks and benefits associated with caesarean delivery: multicentre  
374 prospective study. *BMJ* 2007; **335**: 1025.  
375

376

377 **Figure caption list**

378 **Figure 1.** Flow chart of the study population

## Tables

**Table 1.** Maternal, obstetrical, and neonatal characteristics of the study population

Characteristics	N = 252
<b>Maternal characteristics</b>	
Maternal age, years	31.2 ± 6.0
Parity	1.15 ± 1.47
Preconceptional BMI, kg/m <sup>2</sup>	25.6 ± 6.2
Active smoking	42 (16.9)
Pregestational diabetes	3 (1.2)
Notable maternal pathology <sup>a</sup>	34 (13.5)
Previous preterm delivery	26 (10.3)
Known uterine malformation	3 (1.2)
Scarred uterus	70 (27.8)
<b>Characteristics of pregnancy</b>	
Assisted Reproductive Technology	28 (11.1)
Type of pregnancy	
Singleton	204 (81.0)
Twin	48 (19.0)
<b>Characteristics of delivery</b>	
Gestational age, weeks	29.8 ± 2.6
Gestational age < 28 weeks	64 (25.4)
Gestational age ≥ 28 weeks	188 (74.6)
Type of prematurity	
Spontaneous	67 (26.6)
Induced	185 (73.4)

<b>Indications of caesarean delivery</b>	
Spontaneous preterm labour	64 (25.4)
Preterm premature rupture of membranes	48 (19.0)
Hypertensive disorders without suspected foetal growth restriction	36 (14.3)
Hypertensive disorders with fetal growth restriction group	28 (11.1)
Placental abruption after uncomplicated pregnancy	11 (4.4)
Suspected foetal growth restriction without hypertensive disorders	56 (22.2)
Other	9 (3.6)
General anaesthesia	39 (15.5)
Uterine injury during extraction	8 (3.2)
Difficulty of foetal extraction	15 (6.0)
<b>Severe Maternal Morbidity</b>	
Classical incision	45 (18.2)
Postpartum haemorrhage	30 (12.0)
Transfusion	19 (7.5)
Any injury to adjacent organs <sup>b</sup>	3 (1.2)
Postpartum fever	15 (6.0)
Unplanned procedure/return to theatre	5 (2.0)
Intensive Care Unit (ICU) stay longer than 24 hours	11 (4.4)
Death	1 (0.4)
<b>Neonatal characteristics</b>	
Antenatal corticosteroids	199 (79.3)
Magnesium sulfate	169 (67.9)
Birth weight, g	1228.7 ± 500.7
5-min Apgar score	7.8 ± 2.1

- 379 BMI, Body Mass Index
- 380 weeks, weeks of gestation
- 381 ICU, Intensive Care Unit
- 382 <sup>a</sup>Chronic hypertension, cardiac pathology, nephropathy, infectious chronic disease,
- 383 thrombophilia, hemoglobine S disease, neurologic pathology, antiphospholipid syndrome,
- 384 lupus, hematologic pathology, Crohn's disease, pulmonary pathology, or venous
- 385 thromboembolism
- 386 <sup>b</sup>urological (1) or vascular (2)
- 387 Data is n (%) or mean  $\pm$  standard deviation

**Table 2.** Association between maternal and neonatal characteristics and Severe Maternal Morbidity: Univariate Analysis

<b>Characteristics</b>	<b>SMM group n= 89</b>	<b>Whitout SMM group n=163</b>	<b><i>P</i></b>
<b>Maternal characteristics</b>			
Maternal age, years	31.7 ± 6.4	30.9 ± 5.8	0.35
Parity	1.3 ± 1.7	1.1 ± 1.3	0.42
Preconceptional BMI, kg/m <sup>2</sup>	26.0 ± 6.6	25.3 ± 6.0	0.39
Active smoking	14 (15.9)	28 (17.4)	0.79
Pregestational diabetes	2 (2.3)	1 (0.6)	0.27
Notable maternal pathology <sup>a</sup>	12 (13.5)	22 (13.5)	0.97
Previous preterm delivery	9 (10.1)	17 (10.4)	0.98
Known uterine malformation	<b>3 (3.4)</b>	<b>0</b>	<b>0.03</b>
Scarred uterus	24 (27.0)	46 (28.2)	0.85
<b>Characteristics of pregnancy</b>			
Assisted Reproductive Technology	9 (10.1)	19 (11.7)	0.75
Type of pregnancy			<b>0.04</b>
Singleton	<b>78 (87.6)</b>	<b>126 (77.3)</b>	
Twin	<b>11 (12.4)</b>	<b>37 (22.7)</b>	
<b>Characteristics of delivery</b>			
Gestational age, weeks	<b>29.2 ± 2.6</b>	<b>30.1 ± 2.5</b>	<b>0.01</b>
Gestational age < 28 weeks	29 (32.6)	35 (21.5)	0.05
Gestational age ≥ 28 weeks	60 (67.4)	128 (78.5)	
Type of prematurity			0.90

Spontaneous	24 (27.0)	43 (26.4)	
Induced	65 (73.0)	120 (73.6)	
General anaesthesia	<b>21 (23.6)</b>	<b>18 (11.0)</b>	<b>0.01</b>
Uterine injury during extraction	<b>6 (6.7)</b>	<b>2 (1.2)</b>	<b>0.02</b>
Difficulty during foetal extraction	8 (9.0)	7 (4.4)	0.14
<b>Neonatal characteristics</b>			
Birth weight, g	1177.1 ± 532.3	1256.9 ± 481.9	0.23
5 min Apgar score <7	<b>27 (31.4)</b>	<b>29 (18.0)</b>	<b>0.02</b>

388 BMI, Body Mass Index

389 SMM, Severe Maternal Morbidity

390 <sup>a</sup>Chronic hypertension, Cardiac pathology, nephropathy, infectious chronic disease,

391 thrombophilia, hemoglobine S disease, neurologic pathology, antiphospholipid syndrome,

392 lupus, hematologic pathology, Crohn's disease, pulmonary pathology, or venous

393 thromboembolism

394 Data are n (%) or mean ± standard deviations

395 Boldface type indicates significance ( $p < 0.05$ )

396 **Table 3.** Association between Severe Maternal Morbidity (SMM) and maternal  
 397 characteristics: multivariate analysis  
 398

Variables	Adjusted OR (CI 95%)	399
Gestational age, weeks	<b>0.87 (0.78-0.97)</b>	400
Notable maternal pathology <sup>a</sup>	1.13 (0.50-2.46)	401
Type of pregnancy		402
Singleton	1	403
Twin	<b>0.44 (0.20-0.93)</b>	404
Type of prematurity		405
Induced	1	406
Spontaneous	1.15 (0.60-2.17)	407
General anaesthesia	<b>2.52 (1.25-5.13)</b>	408
		409

410 OR, Odds Ratio (adjusted for gestational age, notable maternal pathology, type of pregnancy,  
 411 type of prematurity and general anaesthesia)

412 CI, Confidence Interval

413 weeks, weeks of gestation

414 <sup>a</sup>Chronic hypertension, Cardiac pathology, nephropathy, infectious chronic disease,  
 415 thrombophilia, hemoglobine S disease, neurologic pathology, antiphospholipid syndrome,  
 416 lupus, hematologic pathology, Crohn's disease, pulmonary pathology, or venous  
 417 thromboembolism

418 Boldface type indicates significance ( $p < 0.05$ )

419

420 **Table 3 bis.** Association between Severe Maternal Morbidity (SMM) and maternal  
 421 characteristics: multivariate analysis  
 422

Variables	Adjusted OR (CI 95%)
Gestational age < 28 weeks	<b>1.80 (0.99-3.27)</b>
Notable maternal pathology <sup>a</sup>	1.00 (0.45-2.13)
Type of pregnancy	
Singleton	1
Twin	<b>0.44 (0.20-0.91)</b>
Type of prematurity	
Induced	1
Spontaneous	1.20 (0.64-2.25)
General anaesthesia	<b>2.58 (1.29-5.24)</b>

434 OR, Odds Ratio (adjusted for gestational age, notable maternal pathology, type of pregnancy,  
 435 type of prematurity and general anaesthesia)

436 CI, Confidence Interval

437 weeks, weeks of gestation

438 <sup>a</sup>Chronic hypertension, Cardiac pathology, nephropathy, infectious chronic disease,  
 439 thrombophilia, hemoglobine S disease, neurologic pathology, antiphospholipid syndrome,  
 440 lupus, hematologic pathology, Crohn's disease, pulmonary pathology, or venous  
 441 thromboembolism

442 Boldface type indicates significance ( $p < 0.05$ )

443

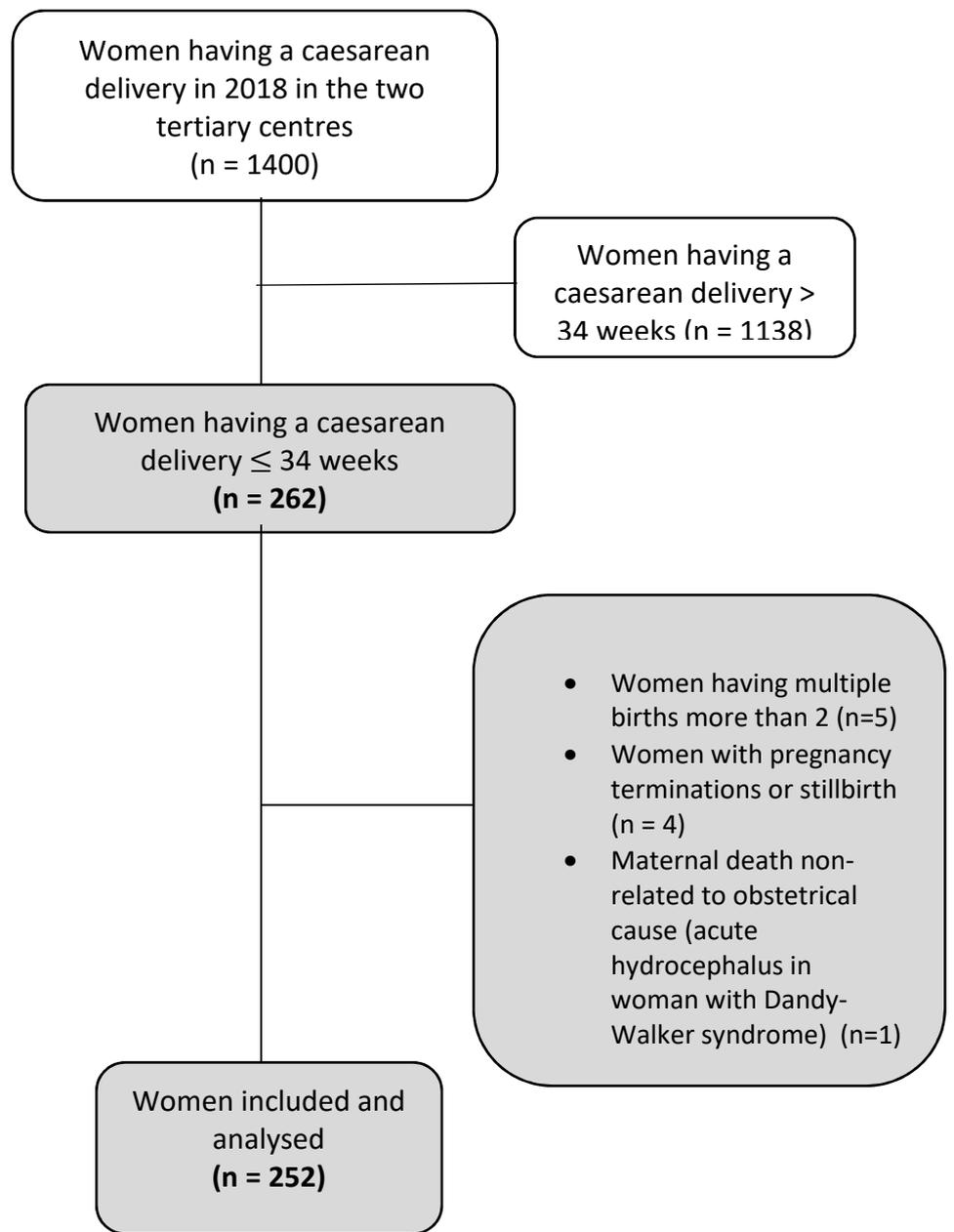


Figure 1 Flow chart of the study population