1 **Title**: Delivery and neonatal outcomes in women with antepartum severe maternal morbidity:

2 a population-based study.

3

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22 **Running Title:** Antepartum severe maternal morbidity

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24

25

Abstract

- **Objectives**: To assess the incidence, causes, risk factors and adverse outcomes of antepartum severe maternal morbidity (SMM)

- **Design**: Population-based case–control study

- **Setting**: 119 Maternity hospitals, 6 French regions

- **Population:** All women with antepartum SMM (cases, N=601), a randomly selected control sample of women who gave birth without SMM in the same hospitals during the same period (controls, N=3650)

- **Methods**: Uni- and multivariable logistic regression with multiple imputation

- **Main outcomes measure**: Antepartum SMM, defined as a morbid event occurring from 22 weeks of gestation and before the onset of labour

- **Results**: Antepartum SMM complicated 0.33% of pregnancies (95%CI, 0.30-0.36). Rates of prematurity, neonatal mortality, and transfer to the neonatal intensive care unit were 10 times higher for babies whose mothers had antepartum SMM than for the control mothers. Similarly, emergency caesarean and general anaesthesia were more frequent in women with antepartum SMM. Risk factors for antepartum SMM were maternal age >35 (aOR 1.55; 95% CI, 1.22-1.97), increased body mass index (aOR for 5kg/m^2 increase, 1.24; 95% CI, 1.14-1.36), maternal birth in sub-Saharan Africa (aOR, 1.80; 95% CI, 1.29-2.53), pre-existing medical condition (aOR, 2.56; 95% CI, 1.99-3.30), nulliparity (aOR, 2.26; 95% CI, 1.83-2.80), previous pregnancy-related hypertensive disorders (aOR, 4.94; 95% CI, 3.36-7.26), multiple pregnancy (aOR, 5.79; 95% CI, 3.75-7.26), irregular prenatal care (aOR, 1.86; 95% CI, 1.27-2.72).

- **Conclusion**: Antepartum SMM is rare but associated with a massively higher incidence of adverse delivery and neonatal outcomes.

- **Keywords**: antepartum, perinatal morbidity, pregnancy-related hypertensive disorders, prematurity, severe maternal morbidity

51   **Tweetable abstract**: Antepartum severe maternal morbidity is rare but associated with a

52   massively higher incidence of adverse delivery and neonatal outcomes.

53 **Introduction**

54   Severe maternal morbidity (SMM), defined as a potentially life-threatening

55 complication occurring during pregnancy or just afterwards, is a major indicator of maternal

56 health. Data about the incidence of SMM are increasingly available: it ranges from 0.5 to 1.5%

57 of deliveries in the most recent population-based studies.[1,2,3,4] SMM is generally explored

58 globally, without consideration of the timing of the morbid event relative to the delivery. But

59 as the most frequent cause of SMM is postpartum haemorrhage (at least half of all SMM

60 events),[5,6] results from studies exploring SMM mostly reflect postpartum SMM. The study of

61 antepartum SMM—before labour—remains inadequate, as information about the timing of the

62 morbid event is rarely available. It may, however, have specific characteristics, with a different

63 profile of causes, risk factors, and adverse consequences. Additionally, its management presents

64 a unique challenge, in its need to optimize the risk-benefit balance for both mother and the

65 child.[7] Better knowledge of antepartum SMM might help to anticipate the occurrence of this

66 complex situation and prevent its adverse outcomes.

67   EPIMOMS is a French population-based study specifically designed to explore SMM.[8]

68 Its prospective inclusion allows the separate exploration of antepartum SMM.

69   Our objectives were to use this population-based data to assess the incidence, causes,

70 and risk factors of antepartum SMM and the adverse outcomes associated with it for both

71 mother and baby.

72

73 **Methods**

74

75   Data came from the EPIMOMS prospective population-based study, conducted in 6

76 French regions (May 2012 - November 2013).[9] The EPIMOMS study was funded with support

77 from the French National Research Agency (*Agence Nationale de la Recherche* (ANR), Paris

78   France; grant no. ANR-10-BLAN-1134-01) and the Ile de France Regional Health Agency

79   (*Agence Régionale de Santé Ile de France*, Paris, France; grant no. PPS784). The first step of

80   EPIMOMS was to define SMM through an extensive national Delphi expert consensus process.

81   This definition of SMM combined 6 diagnostic criteria (major obstetric bleeding, eclampsia,

82   severe preeclampsia, pulmonary embolism, stroke, or psychiatric disorder), 6 organ dysfunction

83   criteria (cardiovascular, respiratory, renal, neurologic, hepatic, or hematologic), and 2

84   intervention criteria (admission to an intensive care unit (ICU) or laparotomy after delivery), as

85   well as maternal death (Appendix S1).

86   The source population included 182,309 women who gave birth in the 119 maternity

87   units of 6 French regions, which account for one fifth of all deliveries in France. The

88   characteristics of women and maternity units were similar to the national profile.[10] All women

89   who experienced a morbid event meeting the EPIMOMS SMM definition between 22 weeks

90   of gestation and 42 days after delivery were prospectively included (N=2540). The prospective

91   inclusion allowed to take into account the timing of the morbid event relative to the delivery,

92   and to make the distinction between antepartum, intrapartum, and postpartum SMM. Besides,

93   a 2% unmatched control sample of women without SMM was randomly selected among women

94   who gave birth in the same maternity units during the same time period (control group, n=3651

95   women).

96   This analysis excludes among the women with SMM those for whom the date of the

97   morbid event was missing (n=3) and those with intrapartum or postpartum (or both) SMM only

98   (N=1936). Finally, we included all women who experienced SMM in the antepartum period,

99   defined as a morbid event occurring from 22 weeks of gestation and before the onset of labour.

100 Women with antepartum SMM but also intrapartum and/or postpartum SMM were included in

101 the study population. Furthermore, this analysis included the entire group of control women

102 (N=3651).

103   The causes of antepartum SMM, gestational age at occurrence of the morbid event and

104   at delivery (in weeks) were prospectively collected by the clinician responsible for the woman.

105   Data about women's social and demographic characteristics, pre-existing medical and obstetric

106   conditions, pregnancy and delivery characteristics, and neonatal and maternal outcomes, were

107   collected from a manual review of all available medical files by research midwives trained for

108   this study; they were entered into an electronic case report form specifically designed for this

109   study and used for the women in both the case and control groups.

110

111   Statistical analysis

112   We calculated the incidence of antepartum SMM among all deliveries and the

113   proportion of antepartum SMM among all women with SMM. We described the causes of

114   antepartum SMM as well as gestational age at onset of the morbid event and at delivery. Then

115   we described and compared the characteristics of delivery and neonatal outcomes for cases and

116   controls. Categorical variables were analysed with the Chi-square test or Fisher's exact test,

117   and continuous variables with Student's t-test or the Kruskal–Wallis test, as appropriate.

118   Using univariate and multivariable logistic regression models, we explored risk factors for

119   antepartum SMM first globally and then for the most frequent causes of antepartum SMM,

120   among social and demographic characteristics, medical and obstetric pre-existing conditions,

121   and features of current pregnancy. BMI was the only continuous variable included in the final

122   model. The selection of the variables included in the multivariable model was based on the

123   available literature and on the results of the univariate analysis.

124   The proportion of women with missing data in the multivariable model was 32.1%. As

125   the comparison of the characteristics of women with and without missing data supported the

126   missing-at-random hypothesis, we performed multiple imputation with chained equations for

127   missing data according to Rubin's rule (30 datasets, Appendix S2).[11] Results are presented with

128   imputed data. Analyses were also performed with non-imputed data.

129   STATA software was used for all analyses (Version 13; Stata Corp, College Station,

130   TX). Statistical significance was set at a two-tailed value of *P*<.05.

131

132   **Results**

133   Among the source population of 182,109 deliveries, 601 women experienced

134   antepartum SMM (0.33% of all deliveries, 95% CI, 0.30-0.36). They accounted for 23.1% (95%

135   CI, 23.1-24.1) of all women with SMM (601/2540).

136   Severe pregnancy-related hypertensive disorders were the leading cause of antepartum SMM

137   (52.1%), followed by exacerbation of chronic somatic conditions, psychiatric disorders (de

138   novo or decompensation of a chronic psychiatric condition), and obstetric haemorrhage, each

139   accounting for 8.7% to 9.6% of the cases (Table 1).

140   Compared with controls, women with antepartum SMM gave birth significantly more

141   frequently by emergency caesarean (69.4% vs 13.6%) and with general anaesthesia (29.7% vs

142   1.2%), as well as before 37 weeks (73.0% vs 7.3%) and before 32 weeks (50.3% vs 1.4%). The

143   proportion of induced prematurity among infants born to mothers with antepartum SMM was

144   also higher than among controls (93.3% vs 49.6%) (Table 2).

145   Neonatal adverse outcomes were all significantly more frequent in women with antepartum

146   SMM than in controls, with a significantly higher rate of stillbirths (9.6% versus 0.8%), and

147   among live births, significantly higher rates of transfer to the NICU (65.4% versus 4.8%) and

148   of neonatal mortality within the first 7 days of life (2.7% versus 0.1%). The median gestational

149   age at birth was 32.9 weeks in babies born to mothers with antepartum SMM, compared to 39.3

150   weeks in controls, with median birth weights of 1890 g and 3266 g respectively.

151 Gestational ages at occurrence of the morbid event and at delivery differed according to the

152 cause of SMM. In women with antepartum SMM due to pregnancy-related hypertensive

153 disorders, both morbid event and delivery occurred before 32 weeks in more than 80% of the

154 women. In contrast, among women with antepartum SMM from psychiatric disorders, the

155 morbid event occurred before 28 weeks in 50% of women, but 80% of them gave birth after 37

156 weeks (Table 3).

157 In the multivariable analysis, risk factors for antepartum SMM were maternal age >35, higher

158 BMI, maternal birth in sub-Saharan Africa, pre-existing medical condition, nulliparity, prior

159 pregnancy-related hypertensive disorders, multiple pregnancy, and irregular prenatal care

160 (Table 4). The same risk factors were found for antepartum SMM due to pregnancy-related

161 hypertensive disorders (Appendix S3).

162 Analysis with non-imputed data provided similar results (Appendix S4).

163

164 **Discussion**

165 *Main findings*

166 In this population-based study, antepartum SMM complicated 0.33% of pregnancies and

167 accounted for a quarter of all SMM cases. Half of the antepartum SMM cases were secondary

168 to pregnancy-related hypertensive disorders. The other main causes of antepartum SMM were

169 exacerbation of chronic somatic conditions, psychiatric disorders, and obstetrical

170 haemorrhages. Women with antepartum SMM had much more severe and much higher rates of

171 adverse neonatal outcomes than women without SMM; their preterm birth rate was 10 times

172 higher, and half of their babies were born before 32 weeks. Moreover, their prevalence of

173 interventions at risk of postpartum maternal morbidity, such as emergency caesareans and

174 general anaesthesia for delivery, was also much higher than among the control group.

175

176   *Strengths and limitations*

177   Our study has several strengths. The prospective design of the EPIMOMS study provided

178   detailed information, particularly on the timing of both the antepartum morbid event and the

179   delivery and neonatal outcomes. We used a standardized definition of SMM, obtained by a

180   consensus of national experts. This comprehensive definition is not limited to interventions or

181   diagnostic criteria that might be influenced by local practices, but also includes severe clinical

182   presentations such as organ dysfunctions. Consequently, the selection bias of women with

183   antepartum SMM was minimized. The population-based design and the large source

184   population, with characteristics similar to the national profile,[10] provided good external validity.

185   This study also has some limitations. For the study of antepartum SMM risk factors, controls

186   should have included all the women without antepartum SMM, i.e., not only women without

187   SMM overall, but also women with intrapartum or postpartum SMM. These women were not

188   included in the EPIMOMS' control group. However, as they accounted for 1.1% of all

189   deliveries,[4] their omission from the control group probably had little, if any, impact on the

190   associations we observed. The incidence of antepartum SMM we report does not include severe

191   morbidity before 22 weeks, which may result in an underestimate for the entire duration of

192   pregnancy. Data were missing for at least one variable included in the multivariable analysis in

193   32% of women. But because the characteristics of women with and without missing data were

194   similar, we were able to apply multiple imputations.

195

196   *Interpretation*

197   Only one previous study, a retrospective population-based study from Canada, reported data

198   about the incidence of antepartum SMM. Using national hospital database (2004-2015), the

199   authors reported that antepartum SMM concerned 0.30% of all deliveries, very close to our

200   results from prospective data.[12]

201   The profile of causes of antepartum SMM we report here differs from that of causes of

202   SMM globally. As expected, pregnancy-related hypertensive disorders were the main cause of

203   antepartum SMM. However, non-obstetric diseases, such as exacerbation of a chronic disease

204   or psychiatric disorders, also account for significant proportions of antepartum SMM. As the

205   prevalence of chronic diseases among pregnant women is increasing over time,[13] this result

206   highlights the importance of multidisciplinary care for these women, including in the pre-

207   conceptional and antenatal periods, to prevent acute decompensation and antepartum SMM.[14]

208   Similarly, recent studies reported that antepartum psychiatric disorders, severe or not, concern

209   5% to 10% of pregnant women.[15] Our study, specifically focusing on the severe end of the

210   continuum of psychiatric disorders, emphasizes their contribution to SMM. It highlights the

211   need for women with psychiatric disease to receive multidisciplinary care, as well as the

212   importance of regularly assessing maternal mental health during prenatal care for those with de

213   novo psychiatric disorders.

214   Our study shows that severe adverse neonatal outcomes, mostly severe prematurity and

215   perinatal mortality, were much higher among babies of women with antepartum SMM. High

216   rates of preterm birth have previously been noted in studies focusing on pregnancy-related

217   hypertensive disorders,[16,17] not among women with antepartum SMM overall and with non-

218   obstetric conditions. Additionally, we were able to describe specifically other adverse

219   outcomes, such as neonatal death <7 days, low birth weight, low pH, low Apgar score, and

220   NICU admission. Preterm births were particularly prevalent in our study among women with

221   antepartum SMM from pregnancy-related hypertensive disorders (94.6%), but not only:

222   exacerbation of chronic diseases or antepartum obstetrical haemorrhage also led to preterm

223   birth very frequently (63.6% and 70.6% respectively). Our approach also added information to

224   the current literature about antepartum SMM from pregnancy-related hypertensive disorders,

225   because the EPIMOMS definition of SMM focused on the severity of maternal outcomes. In

226   particular, women with severe preeclampsia and foetal extraction before 32 weeks were

227   included only if the preterm delivery was performed for a main maternal indication.

228   Our study reports a high proportion of at-risk interventions for delivery among women

229   with antepartum SMM, including caesarean deliveries, in particular emergency caesareans, and

230   general anaesthesia. Although these interventions may be indicated in this context to improve

231   maternal condition, they also constitute well-known risk factors for SMM.[18] Caesarean delivery

232   is an independent risk factor for intrapartum and postpartum SMM[8] and for severe postpartum

233   haemorrhage.[19,20] A recent population-based study with propensity score analysis reported that

234   the risk of serious maternal complications rose quite significantly among women who had

235   general anaesthesia without clinical indication for a caesarean as compared to women who had

236   neuraxial anesthesia.[21] Preventing the occurrence of the antepartum SMM event may also

237   prevent these interventions at risk for intra/postpartum morbidity.

238   In our study, risk factors for antepartum SMM and for antepartum SMM from severe

239   pregnancy-related hypertensive disorders were very similar. These results may be explained by

240   the fact that severe pregnancy-related hypertensive disorders are the most frequent cause of

241   antepartum SMM. Interestingly, these risk factors for SMM due to pregnancy-related

242   hypertensive disorders are also quite similar to those described for pregnancy-related

243   hypertensive disorders overall, i.e., severe or not severe.[22,23,24] These results suggest that,

244   among these disorders, the specific phenotype of severe maternal complications is associated

245   with the same at risk subgroups, such as multiple pregnancy and previous hypertensive disorder.

246   Finally, women with non-obstetric risk factors, as well as those with obstetric risk factors for

247   antepartum SMM we reported here, such as multiple pregnancy, deserve to receive prenatal

248   care and to give birth in a maternity unit with all appropriate resources for mother and child.

249

250   **Conclusion**

251   Antepartum severe maternal morbidity presents a specific profile of causes dominated

252   by pregnancy-related hypertensive disorders, but non-obstetric conditions also make a notable

253   contribution and should be taken into account in the management of pregnant women. Although

254   antepartum SMM is rare, it is frequently associated with severe outcomes for both mother and

255   children, dominated by severe induced prematurity. Better knowledge of antepartum SMM

256   would help to prevent, or at least anticipate, these adverse events and their harmful

257   consequences, probably by optimizing pre-conceptional and prenatal care. Additionally, the

258   identification of antepartum SMM risk factors should permit to focus on women or subgroups

259   at risk of antepartum SMM. Then, individualized risk stratification could be applied to these

260   groups and improve their care.

261   Further research, with a prospective design, is needed to explore the morbidity continuum and

262   identify the specific individual and care-related factors associated with the occurrence of

263   antepartum SMM among women with chronic conditions or non-severe pregnancy-related

264   hypertensive disorders. Moreover, even though caesarean delivery or general anaesthesia are

265   often justified in an antepartum SMM, careful assessment of the clear indications of these

266   interventions and decision-making processes should improve perinatal care and help optimize

267   clinical decisions in these complex situations.

268

288

Disclosure of interests

MPB, who works in Armand Trousseau Hospital, (Paris), reports personal fees from Vifor
Pharma Group, outside the submitted work. No other external funding or competing interests
declared.

Contribution to authorship:

CDT, MPB, MR had full access to all the data in the study and take responsibility for the
integrity of the data and the accuracy of the data analysis. CDT, MPB and MG conceptualized
the study and wrote the manuscript. MR and AS performed the statistical analysis. CDT
obtained funding and supervised the study. All authors contributed to the analysis plan and
interpretation of the results and reviewed and approved the final manuscript. All authors accept
responsibility for the papers as published. CDT is the guarantor.

301

Details of Ethics Approval

303 The *Commission Nationale de l'Informatique et des Libertés* (CNIL, no 912210), the French

304 data protection agency, approved the EPIMOMS study. The requirement for written informed

305 consent was waived, in accordance with French legislation at that time, because all women

306 received standard care and all data were anonymized. All women included were informed about

307 the study and did not indicate their objection to the use of their data.

308

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387 **Tables caption list**

388 Table 1. Causes of antepartum severe maternal morbidity

389 Table 2. Delivery characteristics and neonatal outcomes in women with antepartum severe

390 maternal morbidity and in controls

391 Table 3. Time of occurrence of the morbid event and of delivery in women with antepartum

392 severe maternal morbidity, overall and by causes

393 Table 4. Risk factors of antepartum severe maternal morbidity

394

395 **Supporting Information**

396 Appendix S1. EPIMOMS multicriteria standardized definition of severe maternal morbidity

397 Appendix S2. Characteristics of women with and without missing data

398 Appendix S3. Risk factors of antepartum SMM due to pregnancy-related hypertensive disorders

399 Appendix S4. Risk factors for-all cause antepartum SMM, analysis with non-missing data

400 (N=399 women with antepartum SMM and 2529 control women)

401

402   **Table 1.** Causes of antepartum severe maternal morbidity

Causes*	Women with antepartum SMM (N = 601)	
	n	**%**
Severe pregnancy-related hypertensive disorder [a]	313	52.1
Exacerbation of a chronic somatic disease *including*:	58	9.6
- Hematologic disease	14	24.1
- Nephropathy	8	13.8
- Cardiopathy	7	12.1
- Diabetes	5	8.6
- Chronic infection	5	8.6
- Neurologic disease	5	8.6
- Other[b]	14	24.1
Psychiatric disorder	52	8.7
- De novo	30	57.7
- Exacerbation of chronic disease	22	42.3
Severe antepartum obstetrical haemorrhage	52	8.7
Severe hepatic disease	33	5.5
Sepsis	24	4.0
Stroke	14	2.3
Pulmonary embolism	11	1.8
Other[c]	47	7.8

403

404   * Non-exclusive categories

405   [a]: including eclampsia, severe preeclampsia, HELLP associated with splenic rupture or

406   hematoma

407   [b]: thromboembolic disease, autoimmune disease, inflammatory bowel disease, pulmonary

408   disease, neoplasia

409   [c]: Gestational thrombopenia, thrombotic thrombocytopenic purpura, trauma, acute pulmonary

410   oedema, PRESS, peripartum cardiomyopathy, cardiac arrhythmia, hypoglycaemic coma,

411   hyperemesis gravidarum, acute undernutrition, acute intoxication, Guillain-Barre syndrome

412 **Table 2.** Delivery characteristics and neonatal outcomes

	Women with antepartum SMM N = 601		Controls N = 3651		*p*
	n	**%**	**n**	**%**	
Delivery characteristics					
Delivery mode					
Vaginal delivery	131	22.7	2906	79.6	
Caesarean during labour	48	8.3	357	9.8	**<0.001**
Caesarean before labour	399	69.0	386	10.6	
Emergency caesarean	353	88.5 [a]	139	36.0 [a]	
General anaesthesia for delivery	171	29.7	43	1.2	**<0.001**
Neonatal outcomes					
Gestational age at birth (mean, SD), WG + days	32.9	4.8	39.3	2.1	**<0.001**
22 – 27+6	84	14.6	26	0.7	
28 – 31+6	206	35.7	26	0.7	**<0.001**
32 – 36+6	131	22.7	214	5.9	
≥ 37	156	27.0	3382	92.7	
Induced prematurity among preterm deliveries	393	93.3	132	49.6	**<0.001**
Status at birth					
Alive	562	90.5	3680	99.2	
Per partum death	10	1.6	4	0.1	**< 0.001**
Intrauterine foetal death	49	7.9	25	0.7	
Birth weight (mean, SD), g	1889.7	1025.0	3265.8	580.3	**< 0.001**
< 1500	264	46.2	55	1.5	
1500 – 2499	134	23.4	207	5.7	**< 0.001**
≥ 2500	174	30.4	3385	92.8	
Apgar <7 at 5 min [b]	92	16.4	52	1.4	**< 0.001**
Arterial umbilical pH < 7.0 [b]	22	3.9	13	0.3	**< 0.001**
Neonatal ICU transfer [b]	376	66.9	187	5.1	**< 0.001**
Neonatal death < 7 days [b]	17	3.0	3	0.1	**< 0.001**

413   [a] : among women with caesarean before labour

414   [b] : among live births

415 **Table 3.** Gestational age at the occurrence of the morbid event and at delivery in women with antepartum SMM, overall and by causes

416

Gestational age (WG + days)	Antepartum SMM overall		Antepartum SMM from pregnancy-related hypertensive disorder		Antepartum SMM from exacerbation of chronic somatic disease		Antepartum SMM from psychiatric disorder		Antepartum SMM from obstetrical haemorrhage	
	N = 601		N = 313		N = 58		N = 52		N = 52	
	SMM event	Delivery	SMM event	Delivery	SMM event	Delivery	SMM event	Delivery	SMM event	Delivery
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
22-27+6	147 (25.1)	84 (14.6)	80 (25.7)	73 (23.5)	14 (24.1)	3 (5.5)	20 (47.6)	0 (0.0)	8 (16.7)	7 (13.7)
28-31+6	234 (40.0)	206 (35.7)	173 (55.6)	176 (56.6)	17 (29.3)	8 (14.5)	3 (7.1)	0 (0.0)	13 (25.5)	11 (21.6)
32-36+6	148 (25.3)	131 (22.7)	43 (13.8)	45 (14.5)	19 (32.8)	24 (43.6)	16 (38.1)	8 (19.1)	16 (31.4)	18 (35.3)
37-42	56 (9.6)	156 (27.0)	15 (4.8)	17 (5.5)	8 (13.8)	20 (36.4)	3 (7.1)	34 (80.9)	14 (27.4)	15 (29.4)

417

418 WG: weeks of gestation

419   **Table 4.** Risk factors for antepartum SMM

	Women with antepartum SMM N = 601		Controls N = 3651		cOR	95% CI	aOR	95% CI
	n	%	n	%				
Age (years)								
< 35	426	70.9	2915	79.9	1		1	
35 – 39	130	21.6	599	16.4	1.49	[1.20-1.84]	1.55	[1.22-1.97]
≥ 40	45	7.5	137	3.7	2.25	[1.58-3.19]	2.01	[1.35-3.00]
BMI (mean, SD) **(**/5 kg/m^2)	25.6	6.2	23,9	5.0	1.29	[1.20-1.40]	1.24	[1.14-1.36]
Maternal place of birth								
France or other European country	369	70.3	2419	79.0	1		1	
North Africa	71	13.5	353	11.5	1.27	[0.96-1.68]	1.30	[0.97-1.73]
Sub-Saharan Africa	69	13.1	172	5.6	2.43	[1.81-3.26]	1.80	[1.29-2.53]
Other [a]	16	3.0	119	3.9	0.89	[0.51-1.57]	0.90	[0.49-1.62]
Living alone	41	7.5	135	4.0	1.88	[1.30-2.71]	1.34	[0.89-2.01]
Pre-existing medical condition [b]	127	21.7	274	7.5	3.31	[2.62-4.17]	2.56	[1.99-3.30]
Nulliparous	301	50.9	1517	41.8	1.49	[1.25-1.77]	2.26	[1.83-2.80]
Previous pregnancies [c]								
Prior pregnancy-related-hypertensive disorder	66	23.9[c]	102	4.8[c]	4.47	[3.23-6.17]	4.94	[3.36-7.26]
Prior caesarean	87	31.4[c]	441	21.2[c]	1.26	[0.99-1.63]	1.01	[0.73-1.38]
Prior postpartum haemorrhage	10	3.6[c]	83	3.9[c]	/	/	/	/
In vitro fertilization	30	5.1	76	2.1	2.51	[1.64-3.87]	1.34	[0.81-2.22]
Multiple pregnancy	47	8.0	59	1.6	5.20	[3.51-7.72]	5.79	[3.75-7.26]
Irregular prenatal follow-up	40	8.4	151	4.6	1.72	[1.22-2.44]	1.86	[1.27-2.72]

420   Univariate and multivariable logistic regression models with multiple imputation, including all

421   variables listed in the table except prior postpartum haemorrhage.

422   [a] : Asia (Japan, China, India, Southeast Asia) and North, Central, and South America

423   [b] : pre-existing medical condition were defined as a binary variable by the presence of at least

424   one of the following conditions: chronic hypertension, diabetes, dyslipidaemia, constitutional

425   bleeding disorders, asthma, allergy, psychiatric disorder, thromboembolic disease, stroke,

426   transient ischemic attack, coronary heart disease, severe trauma, heart disease, epilepsy,

427   hemoglobinopathy, hepatopathy, thyroid dysfunction, systemic lupus erythematosus,

428   autoimmune disease, inflammatory bowel disease, nephropathy, cancer, myasthenia gravis,

429   myopathy, multiple sclerosis, respiratory disease.

430   [c] : among parous pregnant women

431   cOR: crude odds ratio

432   aOR: adjusted odds ratio

433   95% CI: 95% confidence interval

434   BMI: body mass index