1 **Postpartum hemorrhage due to uterine atony after vaginal delivery:**

2 **Factors associated with severity**

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27

28 **Précis**

29

30 Risk of severe blood loss in women with postpartum hemorrhage increases with delayed initiation of

31 care and specific aspects of labor, delivery, and their management.

ABSTRACT

Objective- To identify factors associated with severity of postpartum hemorrhage (PPH) among characteristics of women and their delivery, the components of initial PPH management, and the organizational characteristics of maternity units.

Methods- This population-based cohort study included women with PPH due to uterine atony after vaginal delivery in 106 French hospitals between November 2004 and October 2006 (N=4,550). Severe PPH was defined by a peripartum change in hemoglobin (Δ[Hgb]) of 4 g/dL or more. A multivariable logistic model was used to identify factors independently associated with PPH severity.

Results- Severe PPH occurred in 952 women (20.9%). In women with PPH, factors independently associated with severity were: primiparity, previous PPH, previous cesarean delivery, cervical ripening, prolonged labor, and episiotomy; delay in initial care for PPH and specifically, administration of oxytocin more than 10 minutes after PPH diagnosis (10-20 minutes after, adjusted OR 1.38, 95% CI 1.03-1.85; more than 20 minutes after, 1.86, CI 1.45-2.38), manual examination of the uterine cavity more than 20 minutes after (adjusted OR 1.83, 95% CI 1.42-2.35), call for additional assistance more than 10 minutes after (adjusted OR 1.61, 95% CI 1.23-2.12 for an obstetrician and 1.51, 95% CI 1.14-2.00 for an anesthesiologist); and delivery in a public non-university hospital. Epidural analgesia was found to be a protective factor against severe blood loss in women with PPH.

Conclusion- Aspects of labor, delivery, and their management, delay in initial care, and place of delivery are independent risk factors for severe blood loss in women with PPH caused by atony.

51 **INTRODUCTION**

52 Postpartum hemorrhage (PPH) remains the leading cause of maternal mortality worldwide and the

53 main component of severe maternal morbidity in western countries.[1-4] Most PPHs are due to uterine

54 atony. Although pharmacological prevention of uterine atony in the third stage of labor significantly

55 decreases the incidence of PPH[5] and is now recommended in international and national guidelines,[6-11]

56 reports from developed countries indicate a recent rise in the PPH rate.[12-15] This increase is especially

57 troubling because severe PPH, even when not fatal, jeopardizes the woman's fertility, exposes her to

58 the risks of transfusion and intensive care, and incurs costs. In this context, decreasing the prevalence

59 of severe PPH constitutes a major current obstetrical challenge.

60 The likelihood of a continuum of morbidity between simple and severe PPH makes the identification

61 of factors that modulate the course of PPH from excessive bleeding to severe hemorrhage an important

62 approach for increasing our understanding of the women and situations most at risk of severe PPH. To

63 our knowledge, no previous study has specifically addressed this question.

64 Two categories of explanatory factors can be considered: the individual characteristics of women and

65 deliveries, and factors related to medical care, that is, both the content of care and the organization of

66 healthcare services. Various characteristics of women and deliveries have been reported to be risk

67 factors for PPH,[16-18] but whether they are associated with an increased risk of severe PPH once early

68 PPH has occurred is not known. On the other hand, focusing on prevention requires identifying the

69 potential risk factors associated with medical care because they are most amenable to change. Clinical

70 guidelines for management of early PPH are based mainly on expert consensus, a low level of

71 evidence. Data documenting the components of initial care that significantly influence the course of

72 PPH would be useful, making it possible to define the most relevant recommendations and thus

73 perhaps increase their translation into practice.

74 The Pithagore6 trial, because it ascertained all cases of PPH in 106 French maternity units during one

75 year and collected detailed data on them, provides unique data for studying the various factors

76 modulating the continuum of severity in PPH-related maternal morbidity.

77 The aim of this study was to identify factors associated with PPH severity among characteristics of

78 women and deliveries, components of initial PPH management, and organizational characteristics of

79 maternity units, in women with PPH due to uterine atony after vaginal delivery.

80

81 **MATERIALS AND METHODS**

82 **Population**

83 The study population was a cohort of women with PPH selected from the Pithagore6 trial population.

84 The Pithagore 6 trial was a cluster randomized controlled trial in 106 French maternity units operating

85 as 6 perinatal networks. The main objective of this trial was to evaluate a multifaceted educational

86 intervention for reducing the rate of severe PPH. No significant difference in the rate of severe PPH

87 was found between the two groups of hospitals (details of this trial available elsewhere[19]).

88 A 1998 French statute aimed at optimizing the organization of obstetric care made it mandatory for all

89 maternity units to belong to a perinatal network,[20] organized around one or more level 3 units

90 (reference centers with an onsite neonatal intensive care unit) and including units rated as level 1 (no

91 facilities for non-routine neonatal care) and 2 (with a neonatal care unit), both public and private. The

92 six perinatal networks involved in the Pithagore 6 trial were the Perinat Centre network around Tours

93 (23 units), the Port-Royal St Vincent de Paul network in Paris (22 units), and the 4 networks of the

94 Rhône-Alpes region: the Aurore network around Lyon (33 units), the Savoie network around

95 Chambery (14 units), the Grenoble network (5 units), and the St-Etienne network (9 units). The 106

96 Pithagore6 maternity units represented 17% of all French maternity units and covered 20% of

97 deliveries nationwide. Data were collected from December 2004 through November 2005 in the

98 Aurore network, and from December 2005 through November 2006 in the other five. PPH was

99 clinically assessed by the caregivers if the estimated postpartum blood loss was greater than 500 ml or

100 defined by a peripartum change in hemoglobin (Hb) greater than 2 g/dL (considered equivalent to the

101 loss of more than 500 mL of blood). Prepartum hemoglobin was collected as part of routine prenatal

102 care during the last weeks of pregnancy; postpartum hemoglobin was the lowest hemoglobin level

103 found in the three days after delivery. Birth attendants in each unit prospectively identified all

104 deliveries with PPH and reported them to the research team. In addition, a research assistant reviewed

105   the delivery suite logbook of each unit monthly, as well as computerized patient charts when available.

106   For every delivery with a mention of PPH, uterine cavity examination, or manual removal of the

107   placenta, the patient's obstetric file was further checked to verify the PPH diagnosis. During the one-

108   year data collection period, 9,365 cases of PPH (defined either by estimated blood loss or drop in Hb)

109   occurred among 146,876 deliveries in the 106 Pithagore6 units, for a total PPH incidence of 6.4% of

110   deliveries.

111   For the present analysis, a specific definition of PPH cases was used. We excluded cases of PPH

112   where no excessive bleeding was clinically identified and that were identified only by a decreased

113   hemoglobin level, because, by definition, these cases did not receive any specific care for PPH, and

114   one major objective was to study the association between components of initial care for PPH and the

115   risk of severe PPH within this cohort of PPH. The cohort was further restricted to PPH due to uterine

116   atony after vaginal delivery, a more homogeneous situation that is the leading cause of PPH and the

117   main target of clinical guidelines. Finally, the study population included 4,550 women. Figure 1 shows

118   the process of selection of the study population.

119

120   **Data collection**

121   Characteristics of the patient, pregnancy, labor, delivery, and PPH management were collected on a

122   case report form from the chart of every delivery with confirmed PPH. The procedures for PPH

123   management were considered to have been performed only if they were specifically mentioned in the

124   chart.

125

126   **Study variables**

127   The outcome was severe PPH, defined by a peripartum change in hemoglobin of 4 g/dL or more

128   (considered equivalent to the loss of 1000 mL or more of blood).

129   Three groups of potential risk factors for severe PPH were examined: characteristics of the women and

130   aspects of labor and delivery before PPH; components of initial PPH management; and organizational

131   characteristics of the units. The individual preexisting characteristics were as follows: age in years at

132   delivery in 3 categories: <25, 25-35, >35; body mass index (BMI) at conception in 4 categories: ≤18,

133 >18-25, >25-30, and >30; parity and previous cesarean delivery, categorized as: primiparous,

134 multiparous without previous cesarean delivery, and multiparous with previous cesarean delivery (one

135 or more). History of PPH, multiple pregnancy, hydramnios, epidural analgesia, prolonged labor

136 (defined as an active phase of labor > 6 h without expulsive efforts), prolonged expulsive efforts

137 (defined as a duration of pushing > 30 minutes), and prophylactic oxytocin after delivery were

138 analyzed as dummy variables. Onset of labor was categorized as spontaneous, induced by oxytocin,

139 and induced cervical ripening. Gestational age at delivery in weeks was categorized as preterm (<37),

140 term (37-41), or post-term delivery (>41). Episiotomy and delivery were categorized as spontaneous

141 delivery without episiotomy, spontaneous delivery with episiotomy, operative delivery without

142 episiotomy, and operative delivery with episiotomy. Birth weight in grams was studied in 3 categories:

143 < 2,500, 2,501-3,999, and 4,000 or more. Data were missing for no more than 3% of women for all

144 variables, except BMI (13.2%) and prolonged expulsive efforts (14.3%); a specific missing data class

145 was added for them.

146 Four components of initial care for PPH were studied. For all of them, the reference category was the

147 performance within 10 minutes of PPH diagnosis, as recommended by the 2004 French national

148 guidelines.[11] Oxytocin administration and manual examination of the uterine cavity were both

149 classified as performed in ≤10 minutes, >10-20 minutes, >20 minutes, done but delay unknown, and

150 not done. The calls for assistance from a senior obstetrician and an anesthesiologist were classified as:

151 present or called in ≤10 minutes, >10 minutes, called but delay unknown, and not called.

152 The organizational characteristics of the units included: status, classified as university public, other

153 public, or private; number of annual deliveries, categorized as <1,500, 1,500-2,500, or >2,500; level of

154 neonatal care, categorized into 1, 2, or 3; 24/24 onsite presence of an obstetrician, and of an

155 anesthesiologist, studied as dummy variables.

156

157 **Analysis**

158 The characteristics of women, labor, delivery, and initial PPH management were described as

159 proportions in all PPH deliveries meeting the study case definition. The percentage of PPH deliveries

160 meeting severity criteria was calculated overall and by pregnancy characteristics. The crude

161   associations of severe PPH with these variables were tested with χ^2 statistics and quantified with

162   unadjusted odds ratios (ORs) and their 95% confidence intervals. Multivariable logistic regression

163   modeling was used to assess the independent effect of each variable. Given the hierarchical structure

164   of our data, level 1: women, level 2: centers ("clusters"), we took into account the intraclass (or intra-

165   cluster) correlation for outcomes of women cared for at a given center by using random-intercept

166   hierarchical logistic regression models [21]. Such modeling provides a more accurate estimation of

167   associations and makes it possible to study explanatory variables at both levels. In a first step, a

168   logistic regression analysis including all relevant characteristics of women, labor, and delivery before

169   PPH was performed to determine whether these characteristics were independently associated with

170   PPH severity. Then, separate multilevel models tested the association of each component of initial

171   PPH care with PPH severity, after adjustment for the significant characteristics of women, labor, and

172   delivery. Finally, the association of each organizational characteristic with PPH severity was

173   examined after adjustment for characteristics of women, labor, delivery, and components of initial

174   care.

175   Cases with one or more missing value among the characteristics of women, labor, and delivery were

176   not included in the multivariate analyses (n= 151 women, 3.3% of total). Cases with missing data for

177   the timing of procedures were included in a specific category "done but unknown delay".

178   Organizational characteristics were available for all units.

179   Based on a sample size of 4,500 women with PPH delivery that met the study definition and an

180   expected 20% prevalence of severe PPH in this group, we estimated that the power of the study would

181   be more than 80% to detect a relative risk of 2.0 between exposed and unexposed women for variables

182   with a prevalence of 2% or more of deliveries and to detect a relative risk of 1.5 for variables with a

183   prevalence of 6% or more of deliveries.

184   Statistical analysis used Stata v.10 software (Stata Corporation, College Station, TX).

185   Approval for the study was obtained from the Sud Est III Institutional Review Board and from the

186   French Data Protection Agency (CNIL).

187

188   **RESULTS**

189   Among 4,550 women with PPH in the study population, 952 (20.9%) had severe PPH.

190

191   **Characteristics of women, labor, and delivery**

192   Table 1 reports the distributions of the characteristics of women, labor, and delivery in the cohort of

193   women with PPH and their association with severe PPH. After adjustment for other individual

194   potential risk factors, the risk of severe PPH for women with PPH was significantly higher in

195   primiparas, multiparas with previous cesarean delivery, women with previous PPH, women who had

196   induced cervical ripening, prolonged labor, episiotomy (for both spontaneous and instrumental

197   delivery), and women who received prophylactic uterotonics.

198   Epidural analgesia was associated with a significantly reduced risk of severe PPH.

199

200   **Initial PPH management**

201   The distribution of the components of initial PPH management in the cohort is shown in Table 2, as

202   well as their crude associations with severe PPH.

203   Oxytocin was administered late or not at all to 24.5% of women with PPH, who therefore did not

204   receive the recommended care. Manual examination of the uterine cavity was inappropriate (late or

205   not done) for 33.2%. In this cohort, 40.6% of women with PPH were managed with no senior

206   obstetrician called or present, and 63.2% with no anesthesiologist called or present.

207   Delayed care, compared with the recommended management, was associated with an increased risk of

208   severe PPH (Table 2), and the associations remained significant when controlling for characteristics of

209   women, labor, and delivery before PPH (Table 3). After adjustment for preexisting factors, the risk of

210   severe PPH was 1.4 times higher in women who received oxytocin between 10 and 20 minutes after

211   PPH diagnosis, and 1.9 times higher when it was administered more than 20 minutes after diagnosis

212   compared with those who received it within the first 10 minutes (Table 3 model 1), and 1.8 times

213   higher in women who had a manual examination of the uterine cavity more than 20 minutes after

214   diagnosis compared to the first 10 minutes (Table 3 model 2). Similarly, a delayed call for obstetric

215   assistance was associated with a 1.6 times higher risk of severe PPH, compared with cases where a

216   senior obstetrician was present or called within 10 minutes (Table 3 model 3). The same was true for a

217 delayed call for an anesthesiologist (Table 3 model 4). Associations between delayed management and

218 severe PPH remained when several components of care were included in the same model (models 5

219 and 6 in Table 3), except for the obstetrician call. When all four components of care were included,

220 only delayed administration of oxytocin remained significantly associated with severe PPH (table 3,

221 model7).

222 Women in the category "done but delay unknown" were at lower risk of severe PPH than those for

223 whom the procedure was performed within 10 minutes for oxytocin administration and manual

224 examination (Table 3 Model 1 and 2).

225 The risk of severe PPH was lower when the obstetrician or the anesthesiologist was absent and not

226 called than when they were called promptly (Table 3 Model 3 and 4). We performed a secondary

227 analysis restricted to the population of PPH women who received sulprostone (second-line

228 pharmacological treatment) to test the hypothesis that an indication bias might explain these

229 associations, given that midwives and junior doctors manage the most minor cases of postpartum

230 bleeding alone. In this population, the obstetrician "not called, not present" category was associated

231 with an increased risk of severe PPH (adjusted OR 2.01 95%CI 1.44-2.84); no significant association

232 was found between the presence of an anesthesiologist and the risk of severe PPH (data not shown).

233

234 **Characteristics of the units**

235 The distribution of hospital-of-birth characteristics among the PPH deliveries is shown in Table 2. The

236 risk of severe PPH was 1.5 times higher for PPH in non-teaching public hospitals compared with

237 university hospitals, and this significant association remained after adjustment for the characteristics

238 of the women, labor, delivery, and components of early PPH management (Table 4). When we

239 controlled for the characteristics of women, labor, and delivery, severe PPH was not significantly

240 associated with the annual number of deliveries, the level of care, or the onsite presence of an

241 obstetrician or an anesthesiologist (Table 4).

242

243 **DISCUSSION**

244   This study is the first, to our knowledge, to document the factors that modulate the course from simple

245   to severe PPH. Our results suggest that various specific characteristics are independent determinants

246   of PPH aggravation. These include the woman's obstetric history, aspects of delivery before PPH,

247   delay in initial care for PPH, and hospital status.

248

249   We found that several characteristics of the woman and her pregnancy, previously described as risk

250   factors for PPH,[16-18] also are associated with a higher risk of severity once PPH has occurred.

251   Although any PPH requires immediate management, for women with a history of PPH or cesarean, or

252   having a first baby, or whose labor was managed with induced cervical ripening or was prolonged, or

253   who had an episiotomy, excessive but not severe postpartum bleeding requires even more careful

254   attention because they are at higher risk of severe hemorrhage. Interestingly, several of these

255   characteristics -previous cesarean, cervical ripening, and episiotomy- are related to the management of

256   labor and delivery, and the associations found here provide additional evidence to be considered in

257   balancing the risks and benefits of those procedures. In our cohort of 4550 women with PPH, 2314

258   (51%) had at least one of these 3 characteristics; efforts to decrease the rate of these procedures may

259   actually reduce the importance of this group and possibly the incidence of severe PPH.

260   Interestingly, episiotomy is associated with a higher risk of severe PPH, although the study population

261   was restricted to PPH due to uterine atony, with PPH due to bleeding episiotomy excluded. This

262   finding suggests that the existence of multiple sources of blood loss, even in physiological range,

263   increases the risk of severe PPH and reinforces the relevance of policies for limited use of episiotomy

264   at vaginal birth.

265   An unexpected result was the increased risk of severe PPH in women who received preventive

266   oxytocin, as compared to women with PPH who had no prophylaxis. This may reflect an indication

267   bias, prophylaxis being more likely in women with risk factors, although these risk factors were taken

268   into account in our analysis. Alternatively, excessive postpartum bleeding occurring after and despite

269   prevention may be more likely to be severe, since, by definition, prophylactic oxytocin was not able to

270   prevent it. Another possible explanation is that the surveillance of postpartum blood loss may be less

271   intense when prophylaxis has been done, leading to delayed diagnosis.

272   Epidural anesthesia had a protective effect here. It has previously been discussed as a risk factor for

273   PPH,[17, 22] presumably by lengthening labor or negatively affecting the endogenous oxytocin level or

274   both, but evidence for such an effect is weak so far. Our results suggest that regardless of the effect of

275   the epidural on the occurrence of PPH, women diagnosed with PPH who already have an epidural are

276   at a smaller risk of severe bleeding. This unexpected result illustrates the importance of analyzing the

277   role of risk factors at different levels of the continuum of severity. The presence of the epidural

278   catheter likely facilitates immediate management of PPH since some procedures, such as examination

279   of the uterine cavity, manual removal of the placenta, or instrumental examination of the vagina and

280   cervix, are usually done under anesthesia. Inversely, the need for anesthesia may delay initial care for

281   PPH and thus increase the risk of severe PPH in women who delivered without epidural: in our study

282   population, this group had a significantly higher proportion of women with no or delayed examination

283   of the uterine cavity than did the women with epidurals.

284   Delay in initial PPH care (manual examination of the uterine cavity, oxytocin administration, and call

285   for extra help) was associated with an increased risk of severe PPH. These results might appear

286   expected or even obvious. However, gathering evidence to support clinical practice recommendations

287   is the principle of evidence-based medicine and an essential task, for it increases their level of proof

288   and thus their legitimacy, both factors that may improve their translation into practice.[23] The content

289   of PPH-related guidelines for the initial steps is very similar in all countries. The present study is the

290   first, to our knowledge, to provide evidence to support the recommendations for immediate

291   management of excessive bleeding.

292   The risk of severe blood loss is higher for women with a PPH after vaginal birth in public non-

293   university hospitals, compared with other public university or private hospitals, and this excess risk is

294   not explained by characteristics of the women, their delivery, or the initial PPH management. We

295   hypothesize that second-line treatment for PPH may be inappropriate or delayed in these hospitals

296   because of limited human (e.g., available staff, surgical skills of obstetricians) or material (e.g.,

297   interventional radiology) resources. However, these further steps of PPH management are less

298   standardized and their appropriateness is more difficult to assess because the corresponding content of

299   guidelines is quite imprecise. That is why they were not considered in this study.

300

301 The design of the present study had several strengths. It was population-based, covering all maternity

302 units and consequently all deliveries in a given area. This feature ensures the external validity of its

303 results. The prospective identification of deliveries with PPH and the characterization of severe PPH

304 within the cohort of women with identified PPH provided unbiased comparison groups with regard to

305 the study objectives. The large number of units and deliveries provided good power for studying the

306 independent role of multiple factors and allowed an analysis that could take the hierarchical structure

307 of the data into account and explore the role of factors at the levels of both the women and the units.

308 Finally, the definition of severe PPH was based on change in hemoglobin, a more objective criterion

309 than the clinically assessed volume of blood loss, or the need for surgery, embolization, or transfusion,

310 all dependent on practices likely to vary widely among clinicians and centers.

311 Our definition of severe PPH also has some limitations. Peripartum change in hemoglobin may not

312 always accurately reflect postpartum blood loss. It may overestimate blood loss in women who

313 received large amounts of fluids, who could then be wrongly classified as severe PPH; it may

314 underestimate the total blood loss if not performed after 48 hours of delivery. This is however unlikely

315 to bias our conclusions, as the consequence would actually be an underestimation of the strength of the

316 associations we found with severe PPH. Given our study objectives and the constraints of our data, the

317 definition of severe PPH by a maximum change in Hb appeared as the least biased option.

318 Selection by indication bias is common in observational studies assessing the role of procedures or

319 treatments on health outcomes. In the present study, some women with PPH may have received more

320 appropriate immediate management because their bleeding was considered at high risk of immediate

321 aggravation. Conversely, in women with excessive bleeding after delivery but not considered to be at

322 risk for heavy blood loss, delay in adequate management is more likely. The effect of this bias is to

323 attenuate the negative impact of inadequate care. The actual associations between delayed initial care

324 and severe PPH may therefore be stronger than we found here. As mentioned above, this bias probably

325 also explains the apparent lower risk of severe PPH in cases where an obstetrician or anesthesiologist

326 were not called promptly.

327   We cannot exclude the possibility that some procedures were performed but not recorded in the

328   medical files, although this seems unlikely for pharmacological treatments such as oxytocin or

329   invasive exams such as examination of the uterus. The relatively high proportion of missing data for

330   the timing of oxytocin administration and manual examination shows that the quality of data recording

331   in obstetrics files needs to improve. We found that the women with PPH for whom these two

332   procedures were done, but at an unknown time, were at lower risk of severe PPH. One possible

333   explanation for this finding is that the procedures were performed immediately after PPH diagnosis

334   and that the specific time was not recorded because implicitly considered simultaneous with the

335   diagnosis.

336

337   Identifying factors that influence the course of PPH from simple to severe has direct potential

338   implications for clinicians, especially for factors related to care, which have been rarely explored so

339   far. Our study shows that some aspects of the management of labor and delivery, as well as delayed

340   initial care for PPH, and place of delivery, increase the risk of heavy postpartum bleeding caused by

341   atony. More specifically, it provides evidence suggesting that reducing the use cervical ripening,

342   episiotomy, or cesarean delivery, in particular in situations where these interventions do not provide

343   clear benefits, as well improving the rapidity of first care once PPH has occurred, may reduce the

344   incidence of severe PPH.

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402   theoretic concepts, practical experience and research evidence in the adoption of clinical practice

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408 **Figure 1- Study population**

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┌─────────────────────────────────┐
│        146,781 deliveries        │
└─────────────────────────────────┘
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┌─────────────────────────────────┐
│         Women with PPH           │
│ (estimated blood loss and/or drop in Hb) │
│            N=9,365               │
└─────────────────────────────────┘
```

Excluded

```
┌─────────────────────────────────┐
│ 2,705 women with PPH assessed    │
│ only by hemoglobin measurement   │
└─────────────────────────────────┘
```

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┌──────────────────┐
│  6,660 women     │
│  with clinically │
│  assessed PPH    │
└──────────────────┘
```

```
┌─────────────────────────────────┐
│      1,432 women with            │
│  PPH not due to uterine atony    │
└─────────────────────────────────┘
```

```
┌──────────────────┐
│ 5,228 women with │
│ PPH due to uterine│
│      atony       │
└──────────────────┘
```

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┌─────────────────────────────────┐
│      678 women with              │
│  PPH after cesarean delivery     │
└─────────────────────────────────┘
```

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┌─────────────────────────────────────────┐
│ Women with clinically assessed PPH due to │
│    uterine atony after vaginal delivery   │
│               N= 4,550                    │
└─────────────────────────────────────────┘
```
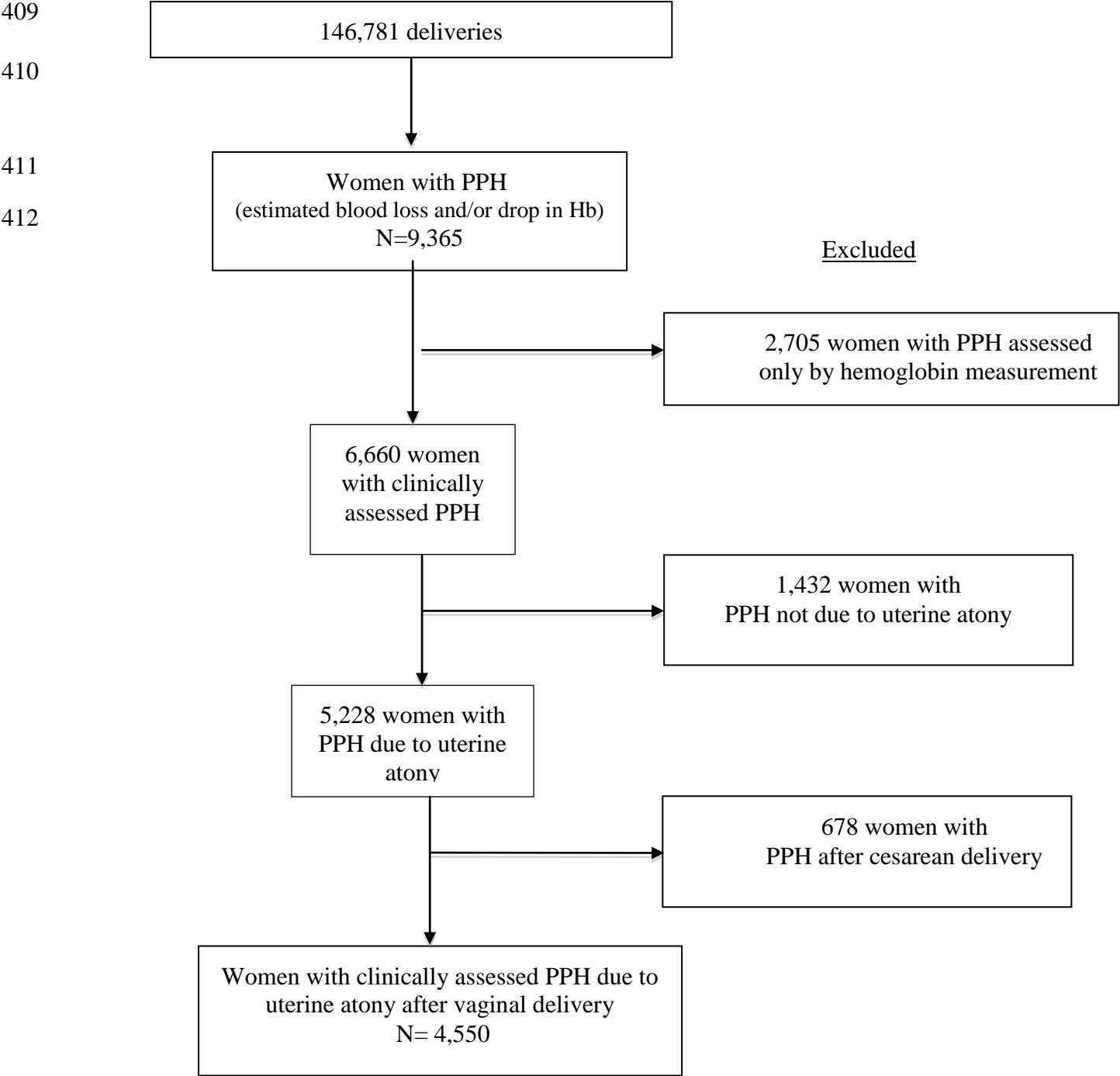
Table 1-Characteristics of women, labor, and delivery: distribution in the cohort of PPH and risk of severe PPH, univariable and multivariable analyses

		n	%	Proportion with severe PPH (%)	OR*	95% CI	aOR§	95% CI
Women and pregnancy								
Age (yrs)	<25	876	19.3	22.0	1.05	0.87-1.26	0.95	0.77-1.17
	25-35	2 970	65.3	21.3	1.00	-	1.00	-
	>35	700	15.4	18.3	0.83	0.67-1.02	0.98	0.77-1.24
BMI	≤ 18	215	5.4	24.2	1.18	0.86-1.64	1.10	0.78-1.55
	>18-25	2 864	72.5	21.1	1.00	-	1.00	-
	>25-30	595	15.1	18.7	0.85	0.68-1.06	0.85	0.67-1.08
	> 30	275	7.0	19.3	0.89	0.65-1.20	0.89	0.63-1.24
Previous PPH		249	5.5	20.9	0.99	0.73-1.37	1.47	1.02-2.13
Fibroma		33	0.7	21.2	1.02	0.44-2.35	0.74	0.29-1.98
Hydramnios		44	1.0	25.0	1.26	0.64-2.51	0.94	0.42-2.11
Parity	primiparous	2 268	49.9	26.2	1.99	1.70-2.32	1.88	1.51-2.33
	multiparous with no previous cesarean delivery	2 036	44.8	15.1	1.00	-	1.00	-
	multiparous with previous cesarean delivery	245	5.4	20.7	1.47	1.05-2.04	1.66	1.15-2.41
Multiple pregnancy		119	2.6	26.9	1.40	0.93-2.12	1.17	0.70-1.96
Labor								
Onset of labor	spontaneous	3 457	76.0	20.3	1.00	-	1.00	-
	induction	571	12.5	21.2	1.06	0.86-1.32	1.20	0.93-1.55
	induced cervical ripening	522	11.5	25.7	1.37	1.10-1.69	1.45	1.13-1.85
Epidural analgesia		3 552	78.2	20.2	0.83	0.70-0.98	0.53	0.43-0.67
Prolonged labor		1 376	31.2	24.5	1.38	1.19-1.61	1.27	1.06-1.53
Oxytocin during labor		3 029	66.7	21.7	1.15	0.98-1.34	1.04	0.85-1.28
Prolonged expulsive efforts		534	13.7	27.0	1.45	1.18-1.79	0.97	0.77-1.24
Delivery								
Gestationnal age (wks)	< 37	218	4.8	23.9	1.25	0.90-1.72	1.14	0.70-1.85
	37-41	3 565	78.5	20.1	1.00	-	1.00	-
	> 41	759	16.7	24.1	1.26	1.05-1.52	1.10	0.89-1.37
Delivery	spontaneous without episiotomy	2 444	53.7	16.3	1.00	-	1.00	-
	spontaneous with episiotomy	1 230	27.0	25.2	1.73	1.46-2.05	1.55	1.27-2.87
	operative without episiotomy	176	3.9	19.3	1.23	0.83-1.81	1.05	0.69-1.62
	operative with episiotomy	698	15.4	30.1	2.21	1.82-2.69	1.70	1.33-2.18
Prophylactic uterotonics		2 486	54.6	21.7	1.11	0.96-1.28	1.22	1.03_1.43
Birth weight (g)	≤2,500	179	3.9	23.5	1.18	0.83-1.68	0.97	0.56-1.69
	2,501-3,999	3 880	85.3	20.6	1.00	-	1.00	-
	≥4,000	486	10.7	22.4	1.11	0.89-1.40	1.21	0.95-1.58
Total		4,550	100.0	20.9			NA	

*Simple logistic regression   § Multivariable logistic regression including all variables

Table 2- Initial management of PPH and characteristics of the units: distribution in the cohort of PPH and risk of severe PPH, univariable analysis

		n	%	Proportion with severe PPH (%)	OR	95%CI
Initial management of PPH*						
Oxytocin administration	≤10 min	2,208	48.5	20.5	1.00	-
	>10-20 min	329	7.2	24.6	1.27	0.97-1.66
	>20 min	447	9.8	31.8	1.81	1.45-2.26
	done but delay unknown	1,224	27.0	17.7	0.83	0.63-1.13
	not done	342	7.5	17.8	0.8	0.70-1.00
Manual examination of the uterine cavity	≤10 min	2,114	46.5	20.7	1.00	-
	>10-20 min	326	7.2	23.9	1.21	0.92-1.59
	>20 min	490	10.8	28.2	1.50	1.20-1.88
	done but delay unknown	929	20.4	15.6	0.71	0.58-0.87
	not done	691	15.2	22.3	1.10	0.89-1.35
Call for obstetrician	present/call ≤10min	2,050	45.1	24.8	1.00	-
	call > 10 min	362	8.0	29.8	1.29	1.01-1.65
	called but delay unknown	294	6.5	24.8	1.00	0.76-1.33
	not called. not present	1,844	40.6	14.3	0.50	0.43-0.6
Call for anesthesiologist	present/call ≤10 min	999	22.0	29.9	1.00	-
	call > 10 min	356	7.8	35.1	1.27	0.98-1.64
	called but delay unknown	318	7.0	28.3	0.92	0.70-1.22
	not called. not present	2,877	63.2	15.2	0.42	0.35-0.50
Characteristics of the units**						
Status	University public	1,423	31.3	17.6	1.00	-
	Other public	2,219	48.8	23.8	1.45	1.09-1.92
	Private	908	19.9	19.2	1.07	0.77-1.50
Level of care	1	1,369	30.1	21.4	0.97	0.76-1.23
	2	2,219	48.8	21.1	1.00	-
	3	962	21.1	19.8	0.92	0.64-1.33
Number of annual of deliveries	<1,500	1,483	32.6	23.3	1.18	0.93-1.51
	1,500-2,500	1,922	42.2	19.6	1.00	-
	>2,500	1,145	25.2	20.2	1.02	0.73-1.43
24h/24 presence of obstetrician		3,318	73.0	19.7	0.80	0.64-1.00
24 h/24 presence of anesthesiologist		4,084	89.8	20.8	1.07	0.78-1.47
Total		4,550	100.0	20.9		NA

* Logistic regression

** Multilevel logistic regression

Table 3- Initial management of PPH and risk of severe PPH, multivariable analysis

		Model 1		Model 2		Model 3		Model 4		Model 5		Model 6		Model 7	
		aOR	95% CI	aOR	95% CI	aOR	95% CI	aOR	95% CI	aOR	95% CI	aOR	95% CI	aOR	95% CI
Oxytocin administration	≤10 min	1.00	-							1.00	-	1.00	-	1.00	-
	>10-20 min	1.38	1.03-1.85							1.39	1.02-1.89	1.38	1.01-1.88	1.33	0.97-1.83
	>20 min	1.86	1.45-2.38							1.63	1.26-2.11	1.60	1.23-2.08	1.49	1.14-1.94
	done but delay unknown	0.75	0.61-0.91							0.95	0.74-1.21	0.97	0.76-1.25	1.00	0.78-1.30
	not done	0.82	0.60-1.13							0.96	0.68-1.33	0.97	0.69-1.36	1.02	0.72-1.43
Manual examination of uterine cavity	≤10 min			1.00	-					1.00	-	1.00	-	1.00	-
	>10-20 min			1.30	0.97-1.76					1.12	0.82-1.55	1.04	0.75-1.43	0.87	0.62-1.20
	> 20 min			1.83	1.42-2.35					1.60	1.23-2.10	1.35	1.01-1.80	1.05	0.78-1.41
	done but delay			0.62	0.50-0.78					0.69	0.52-0.92	0.67	0.50-0.89	0.68	0.50-0.91
	not done			0.96	0.76-1.21					1.01	0.79-1.27	1.10	0.86-1.40	1.30	1.01-1.66
Call for obstetrician	present/call ≤ 10min					1.00	-					1.00	-	1.00	-
	call > 10 min					1.61	1.23-2.12					1.29	0.96-1.73	1.10	0.80-1.52
	called but unknown delay					1.14	0.84-1.56					1.32	0.96-1.82	1.24	0.87-1.76
	not called. not present					0.54	0.44-0.65					0.56	0.46-0.68	0.70	0.57-0.85
Call for anaesthesiologist	present/call ≤10 min							1.00	-					1.00	-
	call > 10 min							1.51	1.14-2.00					1.33	0.96-1.84
	called but delay unknown							0.99	0.73-1.35					1.06	0.75-1.50
	not called. not present							0.37	0.31-0.46					0.43	0.35-0.54

Models 1-7: multilevel logistic regression models adjusted for characteristics of women before PPH: previous PPH, parity/previous cesarean delivery, multiple pregnancy, onset of labor, epidural analgesia, prolonged labor, gestational age, prophylactic uterotonics, delivery/episiotomy, birth weight (N= 4 399 PPH)

Table 4-Characteristics of the units and risk of severe PPH, multivariable analysis

Variables		Adjusted OR	95% CI
Status	University public	1.00	-
	Other public	1.46	1.10-1.87
	Private	1.00	0.73-1.37
Level of care	1	0.92	0.72-1.17
	2	1.00	-
	3	0.94	0.66-1.34
Number of annual of deliveries	<1,500	1.11	0.81-1.53
	1,500-2,500	1.00	-
	>2,500	1.06	0.76-1.46
24 h/24 presence of obstetrician		0.83	0.66-1.04
24 h/24 presence of anesthesiologist		1.05	0.78–1.42

Multilevel logistic regression adjusted for characteristics of women before PPH (previous PPH, parity/previous cesarean delivery, multiple pregnancy, onset of labor, epidural analgesia, prolonged labor, gestational age, prophylactic uterotonics, delivery/episiotomy, birth weight) and early management of PPH (oxytocin administration. manual examination of the uterine cavity) (N= 4 399 PPH)