

## **Transfusion practices in postpartum hemorrhage: a population-based study.**

Marie-Pierre Bonnet, Catherine Deneux-Tharaux, Corinne Dupont,  
Rene-Charles Rudigoz, Marie-Helene Bouvier-Colle

► **To cite this version:**

Marie-Pierre Bonnet, Catherine Deneux-Tharaux, Corinne Dupont, Rene-Charles Rudigoz, Marie-Helene Bouvier-Colle. Transfusion practices in postpartum hemorrhage: a population-based study.: Transfusion in Postpartum Haemorrhage. Acta Obstetricia et Gynecologica Scandinavica, Wiley, 2013, 92 (4), pp.404-13. <10.1111/aogs.12063>. <inserm-00809169>

**HAL Id: inserm-00809169**

**<http://www.hal.inserm.fr/inserm-00809169>**

Submitted on 1 Jan 2014

**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.

1 **Transfusion Practices in Postpartum Haemorrhage: a Population-Based Study**

2

3 **Running headline:** Transfusion in Postpartum Haemorrhage

4

5 Marie-Pierre Bonnet, MD<sup>1,2,3</sup>; Catherine Deneux-Tharaux, MD, PhD<sup>1,2</sup>; Corinne Dupont,  
6 PhD<sup>4,5</sup>; René-Charles Rudigoz, MD<sup>4,5</sup>; Marie-Hélène Bouvier-Colle, PhD<sup>1,2</sup>

7

8 1: INSERM, UMR S953, Epidemiological Research Unit on Perinatal Health and Women's  
9 and Children's Health, Maternité Port Royal, Cochin Teaching Hospital, F-75014 Paris,  
10 France

11 2: UPMC Paris 06 University, UMR S953, F-75005, Paris, France

12 3: Anaesthesia and Critical Care Department, Cochin Teaching Hospital, Groupement  
13 Hospitalier Universitaire Ouest, Assistance Publique - Hôpitaux de Paris, 27, rue du faubourg  
14 Saint-Jacques 75679, Paris Cedex 14, Université Paris 05 René Descartes, Paris, France

15 4: Aurore Perinatal Network, Hôpital de la Croix Rousse, 103 Grande rue de la Croix-Rousse,  
16 69004, Lyon, Lyon 1 University, Lyon, France

17 5: Research Unit 'Health, Individuals, Societies' (EA-SIS 4129), Lyon 2 Lumière University,  
18 5 avenue Pierre Mendès-France, 69676 Bron, France

19

20 From the Institut National de la Santé et de la Recherche Médicale (INSERM), Unité Mixte  
21 de Recherche S953, Epidemiological Research Unit on Perinatal Health and Women's and  
22 Children's Health, Paris, France; and UPMC Université Paris 06, Paris, France

23

24 **Corresponding author:** Marie-Pierre Bonnet

1 INSERM UMR S953, Maternité Port Royal, 53, avenue de l'Observatoire, 75014 Paris,

2 France

3 Phone: +33 1 42 34 55 73

4 Fax: +33 1 43 56 89 79

5 E-mail: [marie-pierre.bonnet@inserm.fr](mailto:marie-pierre.bonnet@inserm.fr)

6

7

8

1 **Conflicts of interest**

2 The authors declare that they have no conflicts of interests relevant to the manuscript

3 submitted to *Acta Obstetricia et Gynecologica Scandinavica*.

4

1 **Abstract**

2

3 **Objective:** To describe transfusion practices and blood loss severity in women with

4 postpartum haemorrhage (PPH), according to the clinical context.

5 **Design:** Population-based cohort study

6 **Setting:** 106 French maternity units (146781 deliveries, December 2004-November 2006)

7 **Population:** All women with PPH (n=9365)

8 **Methods and main outcome measures:** We determined the rate of red blood cell (RBC)

9 transfusion in PPH overall and according to transfusion guidelines. Transfusion practices and

10 blood loss severity were described by mode of delivery and cause of PPH in women given

11 RBCs within 12 hours after clinical PPH diagnosis (early transfusion group).

12 **Results:** 701 women received RBCs ( $0.48 \pm 0.04\%$  of all women and  $7.5 \pm 0.5\%$  of women with

13 PPH). Half the women with clinical PPH and haemoglobin lower than 7.0 g/dL received no

14 RBCs. In the group with clinical PPH and early transfusion (n=426), operative vaginal

15 delivery was associated with a larger maximal haemoglobin drop, more frequent

16 administration of fresh-frozen plasma (FFP) and pro-haemostatic agents (OR: 3.54, 95%CI

17 1.12-11.18), transfusion of larger volumes of RBCs and FFP, a higher rate of massive RBCs

18 transfusion (OR: 5.22, 95%CI 2.12-12.82), and more frequent use of conservative surgery

19 (OR: 3.2, 95%CI 1.34-7.76), compared with spontaneous vaginal delivery.

20 **Conclusions:** Omission of RBC transfusion for PPH was observed in a large proportion of

21 women with low haemoglobin level. Compared with spontaneous vaginal delivery, operative

22 vaginal delivery is characterised by higher blood loss and more transfusions and,

23 consequently, deserves specific attention.

24

25 **Key words:** Obstetrics, practices, postpartum haemorrhage, blood transfusion

26

1 **Abbreviations**

2 95%CI: 95% confidence interval

3 DIC: disseminated intravascular coagulation

4 FFP: fresh frozen plasma

5 Hb: haemoglobin

6 ICU: intensive care unit

7 IQR: interquartile range

8 NA: not appropriate

9 OR: odd ratio

10 PPH: postpartum haemorrhage

11 RBC: red blood cell

12 SD: standard deviation

13

1 **Key message**

2

3 Blood transfusion for PPH is given in 1 of every 200 women in France. Omission of RBC  
4 transfusion for PPH was observed in a large proportion of women with low haemoglobin  
5 level. Operative vaginal delivery is characterized by higher blood loss and more transfusions  
6 than spontaneous vaginal delivery.

7

## 1 **Introduction**

2

3        Postpartum haemorrhage (PPH) is a common complication of delivery whose incidence  
4 has increased recently in several countries (1-4). PPH is associated with substantial maternal  
5 morbidity and mortality (5). In high-resource countries, PPH is the main obstetrical reason for  
6 intensive care unit (ICU) admission, and the rates of severe adverse outcomes after PPH, such  
7 as hysterectomy, have also increased recently (2, 5). Progression from excessive to severe  
8 haemorrhage is probably dependent not only on individual characteristics of women and  
9 deliveries, but also on factors related to medical care (6). Transfusion is an important part of  
10 PPH management, especially in case of on-going haemorrhage. The goals of appropriate  
11 blood product transfusion are to maintain circulating blood volume and tissue oxygenation  
12 and to prevent or reverse coagulopathy. The lack of access to blood products can result in  
13 death of the mother (7). Better knowledge of transfusion practices in PPH may help to  
14 understand the impact on maternal outcomes.

15        Several studies have evaluated transfusion practices in women with PPH (3, 8-15).  
16 However, these studies either used a single-centre retrospective design (8-11), and therefore  
17 had limited external validity, or relied on hospital discharge databases, which were not  
18 designed for clinical research (3, 15). Transfusion practices were also described in recent  
19 nationwide prospective observational studies, but only as secondary outcomes and in women  
20 requiring invasive second-line treatments for PPH (12-14). Information on transfusion  
21 practices is needed to identify situations associated with specific blood-product needs and to  
22 understand the reasons for these specific needs. This information is also necessary to optimise  
23 healthcare resource allocation and to improve PPH management.



1           Our objective here was to describe transfusion practices and blood loss severity in  
2 women with PPH, overall and in subgroups defined based on obstetrical contexts, in a large  
3 population-based cohort of women with PPH in France.

4

## 1 **Material and methods**

2

3 The Sud Est III Institutional Review Board and the French Data Protection Authority  
4 approved this study (QH 04 2005). The ethics committee waived the requirement for  
5 informed consent.

6

### 7 *Population*

8 The source population was the cohort of women included in the Pithagore6 trial, a  
9 cluster-randomised trial performed in 106 French maternity units grouped into six regional  
10 perinatal networks (16) and accounting for 20% of all deliveries in France. A 1998 French  
11 statute aimed at optimising the organisation of obstetric care requires every maternity unit to  
12 belong to a perinatal network built around one or more level-three units (reference centres  
13 with an onsite neonatal ICU) and including level-1 units (no facilities for non-routine neonatal  
14 care) and level-2 units (with a neonatal care unit), whether public or private. Among the 106  
15 maternity units in Pithagore6, 11% were in university hospitals, 56% in non-teaching public  
16 hospitals, and 33% in non-teaching private hospitals; 56% were level 1, 36% level 2, and 8%  
17 level 3. The annual number of deliveries was less than 500 in 14% of the maternity units,  
18 between 500 and 1500 in 46%, and greater than 1500 in 40%. Data were collected over 1 year  
19 in each unit, between December 2004 and November 2006. The aim of Pithagore6 was to  
20 evaluate a multifaceted educational intervention for reducing the rate of severe PPH. As no  
21 significant differences in severe PPH rates were found between the groups (16), all  
22 participants were pooled in a single cohort of women with PPH.

23 In the Pithagore6 trial, PPH was assessed clinically by the medical staff or defined as a  
24 greater than 2.0 g/dL decline in the haemoglobin level. The clinical definition of PPH was  
25 blood loss greater than 500 mL or excessive blood loss prompting manual removal of the

1 placenta or examination of the uterine cavity (or both). The prepartum haemoglobin was  
2 collected as part of routine prenatal care during the last few weeks of pregnancy. Postpartum  
3 haemoglobin was the lowest haemoglobin found within 3 days of delivery (nadir of  
4 haemoglobin), whether the woman had been transfused or not before. It was neither measured  
5 routinely, nor as part of the study protocol. Instead, the decision was left to the clinicians.  
6 Birth attendants in each unit identified all women with PPH and reported them to the research  
7 team. Additionally, a research assistant reviewed the delivery-suite logbook of each unit  
8 monthly and checked any available computerised woman charts. For each woman with a note  
9 of PPH, uterine cavity examination, or manual removal of the placenta, the obstetric ward file  
10 was reviewed to verify the diagnosis of PPH. During the study period, among 146,781  
11 deliveries, 9365 (6.4%) were complicated by PPH, including 6660 (71.1%) diagnosed  
12 clinically and 2705 (28.9%) diagnosed only on a haemoglobin decline (Figure 1).

13 By definition, women with PPH defined by a haemoglobin decline, with no clinical  
14 diagnosis of PPH, did not receive specific acute care for PPH. Consequently, in our study,  
15 these women were excluded from the analysis of transfusion practices and blood loss severity.  
16 Our analysis was thus restricted to women with clinical PPH requiring red blood cell (RBC)  
17 transfusion within 12 hours after the diagnosis (clinical PPH with early transfusion, clinical  
18 PPH with early transfusion group, n=426). Indeed, this situation indicates significant acute  
19 PPH, where transfusion is an essential part of the management and can be lifesaving.

20

### 21 *Study variables*

22 During the Pithagore6 trial, a standardised case-report form was used to extract data  
23 from the medical chart of each woman with PPH.

24 We looked at compliance with 2002 national French transfusion guidelines (17) and  
25 2004 French guidelines on PPH management (18). These guidelines indicate that RBCs

1 should be transfused when the haemoglobin level is lower than 7.0 g/dL, especially in case of  
2 acute anaemia. The haemoglobin concentration should be interpreted according to blood loss  
3 and vital signs and should be kept between 7.0 and 10.0 g/dL as long as the haemorrhage  
4 continues. RBC transfusion is usually unnecessary when the haemoglobin level is greater than  
5 10.0 g/dL (18). French transfusion guidelines are widely diffused and freely available on the  
6 websites of the French Society of Anaesthesiology  
7 (<http://www.sfar.org/article/198/hemorragies-du-post-partum-immediat-rpc-2004>) and  
8 National College of Obstetricians and Gynaecologists  
9 ([http://www.cngof.asso.fr/D\\_PAGES/PURPC\\_12.HTM](http://www.cngof.asso.fr/D_PAGES/PURPC_12.HTM)). Data on the existence of an  
10 algorithm in each maternity unit were not collected in the Pithagore6 trial. However, such  
11 algorithms are not intended to modify national guidelines but instead to describe local  
12 implementation modalities.

13 The following baseline characteristics were recorded: maternal age in years, body  
14 mass index (weight (Kg)·[height (m)]<sup>2</sup>), primiparity, prior PPH, previous caesarean section,  
15 and multiple pregnancy, all handled as binary variables; gestational age in, and prenatal  
16 haemoglobin level (g/dL). We also recorded the characteristics of the delivery: epidural or  
17 spinal analgesia/anaesthesia (binary variable); mode of delivery in four categories  
18 (spontaneous vaginal delivery, operative vaginal delivery, caesarean section before labour,  
19 caesarean section during labour); birth weight (grams), and postpartum haemoglobin  
20 measurement (binary variable). PPH was documented using the time from delivery to PPH as  
21 a continuous variable. The cause of PPH was recorded using five categories: coagulation  
22 disorders, trauma, abnormal placenta insertion, uterine atony or retained tissues, and  
23 unidentified cause. In PPH due to multiple causes, only one cause was recorded, in the order  
24 reported above.

1 Transfusion was studied during the whole postpartum hospital stay. We evaluated the  
2 nature of the blood product (RBC, fresh frozen plasma [FFP], platelets) or blood-derived  
3 product (fibrinogen concentrates) administered, use of the RBC+FFP+platelet+fibrinogen  
4 combination, and use of massive transfusion (10 or more RBC units), all studied as binary  
5 variables. The transfused volume of each blood product (in units) and the fibrinogen dose (g)  
6 administered were studied as continuous variables. In women who received both RBC and  
7 FFP, the FFP/RBC ratio was computed and analysed both as a continuous variable and as a  
8 categorical variable (FFP/RBC ratio of 0.5 or more and FFP/RBC ratio less than 0.5). The  
9 administration of pro-haemostatic agents (recombinant activated factor VII, other synthetic  
10 coagulation factors, tranexamic acid, anti-thrombin III, aprotinin) was handled as a binary  
11 variable. Time from PPH diagnosis to RBC transfusion initiation was analysed as a  
12 continuous variable. Acute adverse events of transfusion were looked for specifically in the  
13 medical chart, where they were spontaneously reported.

14 Concerning blood loss severity, the nadir of haemoglobin and the greatest haemoglobin  
15 (g/dL) drop versus baseline were studied as continuous variables. Secondary disseminated  
16 intravascular coagulation (DIC), defined as a coagulation disorder not present before the  
17 diagnosis of PPH (platelet count less than  $50 \cdot 10^3 \cdot \text{mm}^{-3}$ , or prothrombin time less than 50%, or  
18 combination of platelet count between 50 and  $100 \cdot 10^3 \cdot \text{mm}^{-3}$  and/or prothrombin time  
19 between 50% and 65% and/or fibrinogen level less than 1 g/L), was studied as a binary  
20 variable. Components of the second-line management of PPH were handled as binary  
21 variables; these components included arterial embolisation, conservative surgery (vascular  
22 ligation and/or uterine suture), hysterectomy, and ICU admission.

23

24 *Statistical analysis*

1           The rate of blood transfusion was calculated for all deliveries and for all PPH cases  
2 during the study period, overall and according to the mode of diagnosis of PPH and to the  
3 mode of delivery (vaginal or caesarean delivery).

4           We calculated the rates of haemoglobin measurements and of RBC transfusion among  
5 women with haemoglobin levels lower than 7.0 g/dL and among those with haemoglobin  
6 levels lower than 6.0 g/dL.

7           The characteristics of the women, pregnancies, and deliveries were compared between  
8 the clinical PPH with early transfusion group and the other women with clinical PPH (not  
9 transfused or transfused more than 12 hours after PPH diagnosis). In the clinical PPH with  
10 early transfusion group, we compared transfusion practices according to mode of delivery and  
11 according to cause of PPH, separately in the women with vaginal delivery and caesarean  
12 section.

13           Normality plots were constructed to assess normality of distribution of continuous data.  
14 Categorical variables were compared using the chi-square test or Fisher's exact test as  
15 appropriate. For continuous variables, parametric tests (unpaired t test or analysis of variance  
16 followed by Bartlett's test) or non-parametric tests (Mann-Whitney test or Kruskal-Wallis  
17 test) were used as appropriate. Analyses were performed using STATA v10.1 software (Stata  
18 Corporation, College Station, TX, USA).

## 1 **Results**

2

3 For the 146,781 deliveries during the study period, the RBC transfusion rate for PPH  
4 was  $0.48\pm 0.04\%$  overall,  $0.34\pm 0.03\%$  after vaginal delivery (n=117,606), and  $1.03\pm 0.11\%$   
5 after caesarean delivery (n=29,175). PPH with transfusion of at least four RBC units occurred  
6 in 0.17% of deliveries. The 701 RBC-transfusion recipients accounted for  $7.5\pm 0.5\%$  of  
7 women with PPH (n=9365), 5.5% of women with PPH after vaginal birth and 14.4% of  
8 women with PPH after caesarean delivery. The RBC transfusion rate was  $9.7\pm 0.7\%$  (n=647)  
9 among women with clinically diagnosed PPH (n=6660) (Figure 1).

10 RBC transfusion was given to less than half of the women with clinical PPH and  
11 haemoglobin levels lower than 7.0 g/dL and to three quarters of women with clinical PPH and  
12 haemoglobin levels lower than 6.0 g/dL (Table 1). Five transfusion-related adverse events  
13 were recorded. Only one was severe, with pulmonary oedema requiring ICU admission.

14 Of the 647 women with clinical PPH who required RBC transfusions, 426 (65.8%)  
15 received RBCs within 12 hours of the diagnosis (clinical PPH with early transfusion group)  
16 and 157 (24.3%) received RBCs later on. In the remaining 64 (9.9%) women, the time from  
17 PPH diagnosis to RBC transfusion was unknown. Women with clinical PPH and early  
18 transfusion were significantly older and had significantly lower prenatal haemoglobin, higher  
19 prevalences of prior PPH, prior caesarean section, multiple pregnancy, caesarean delivery, as  
20 well as younger gestational age at delivery and lower birth weight than did the other women  
21 with clinical PPH (Table 2).

22

### 23 *Transfusion practice and blood loss severity in clinical PPH with early transfusion*

24 The following results only concern women with clinical PPH and early transfusion  
25 (clinical PPH with early transfusion group, n=426). In this population, more than half of the

1 women received a combination of blood products (Table 3). In women with PPH after  
2 operative vaginal delivery, the median volumes of RBC and FFP units transfused were larger  
3 compared to the women with spontaneous vaginal delivery ( $p=0.001$  for RBC and  $p=0.004$   
4 for FFP). Overall, 11% of the women with PPH after a vaginal delivery received 10 or more  
5 RBC units, and receiving 10 or more RBC units was significantly more common after  
6 operative than after spontaneous vaginal delivery ( $p<0.001$ , OR: 5.22, 95%CI 2.12-12.82).  
7 The use of prohaemostatic agents was significantly more common in the operative vaginal  
8 delivery group ( $p=0.04$  between spontaneous and operative vaginal delivery, OR: 3.54,  
9 95%CI 1.12-11.18), with 5 out of the 9 women who received recombinant activated factor VII  
10 included in this group.

11 The maximal haemoglobin drop was significantly higher after operative than after  
12 spontaneous vaginal delivery ( $p=0.003$ ), as was the rate of conservative surgical procedures  
13 ( $p=0.006$ , OR: 3.22, 95%CI 1.34-7.76) (Table 4).

14 Uterine atony or retained tissues was the most common causes of PPH overall (47.4%)  
15 and in case of vaginal or caesarean delivery. The distribution of PPH causes significantly  
16 differed between vaginal and caesarean delivery, abnormal placenta insertion and coagulation  
17 disorders being more frequent in case of caesarean delivery. Among vaginal delivery, the  
18 distribution of PPH causes significantly differed between spontaneous and operative vaginal  
19 delivery ( $p=0.002$ ). Trauma was the leading cause of PPH requiring transfusion within the  
20 first 12 hours in operative vaginal delivery (42.6%).

21 In PPH after vaginal delivery, coagulation disorders and abnormal placenta insertion  
22 were the causes associated with the highest rates of combined blood-products transfusion and  
23 of massive transfusion, the largest blood product volumes, the greatest maximal haemoglobin  
24 drops, and the highest DIC rate (Table S1). In PPH after caesarean delivery, these two causes



1 were associated with larger RBC volumes, larger FFP volumes, and higher rates of massive  
2 transfusion (Table S2).

3

## 1 **Discussion**

2

3 This study shows that 1 woman in every 200 giving birth received a RBC transfusion  
4 for PPH in France. Contrasting with French transfusion guidelines, omission of RBC  
5 transfusion for PPH was observed in a large proportion of women with low haemoglobin  
6 level. In women with early RBC transfusion, operative vaginal delivery was associated with a  
7 higher rate of FFP transfusion, larger volumes of blood products, higher rate of massive  
8 transfusion and greater severity of haemorrhage than spontaneous vaginal delivery.

9

10 The RBC transfusion rates we reported is consistent with several findings from previous  
11 studies (2, 15, 19, 20). In a population-based retrospective study from the United States, the  
12 overall RBC transfusion rate in the obstetric population was 0.48% (1994-2004) (20). Another  
13 retrospective population-based cohort study from Canada reported a national rate of PPH with  
14 RBC transfusion of 0.39%, without any significant change over time during the study period  
15 (1991-2004) (2). In a prospective cohort study performed in several hospitals from Uruguay  
16 and Argentina, the rate of transfusion for PPH after vaginal birth was 0.35%.(19). A recent  
17 population-based Danish study from Holm and co-workers reported a RBC transfusion rate of  
18 1.92% of all deliveries (15). This higher rate may be ascribable to the inclusion of all cases of  
19 RBC transfusion --whether related to PPH or to other causes of postpartum anaemia-- and of  
20 all RBC transfusions given within 7 days after delivery.

21 Our data have documented omission of RBC transfusion in a significant proportion of  
22 PPH women with haemoglobin levels lower than the recommended trigger. These results  
23 suggest that undertransfusion may exist in this context. Moreover, our results suggest that  
24 women with PPH in our study may have received smaller volumes of RBCs compared to  
25 those in the LEMMoN study, a recent nationwide study of severe acute maternal morbidity

1 performed in the Netherlands (21). In this study, PPH with transfusion of at least four RBC  
2 units occurred for 0.6% of deliveries, three times more frequently than in our study. Failure to  
3 recognize severe haemorrhage may result in less frequent RBC transfusion. Omission of RBC  
4 transfusion for PPH with low haemoglobin level and small RBC volumes were also found in a  
5 previous study of maternal death secondary to PPH in France, where they certainly  
6 contributed to the fatal issue (7). In contrast, a trend towards over-transfusion of women has  
7 been reported in the United States (8), the United Kingdom (9) and the Netherlands (22). That  
8 the RBC transfusion rate in our study was comparable to that in other countries despite  
9 omission of transfusion for PPH with low haemoglobin level may be ascribable to the greater  
10 severity of PPH in our population. Various aspects of labour, delivery, and their management,  
11 as well as delayed PPH initial treatment and place of delivery, have been shown to increase  
12 the risk of severe blood loss in women with PPH (6), and may contribute to increase PPH  
13 severity in France. The use of a low transfusion threshold in our study may be ascribable to  
14 greater concern among physicians about the risk of maternal alloimmune reactions compared  
15 to the risk of acute anaemia in woman who usually have no history of coronary artery disease.  
16 In addition, the persistent reluctance to use blood transfusion generated in France by the  
17 human immunodeficiency virus epidemic probably made a major contribution. (23). The  
18 impacts of low haemoglobin trigger for RBC transfusion on women outcomes has to be  
19 evaluated, in order to determine if transfusion guidelines should be strictly followed or if the  
20 physicians' attitude is justified.

21 In our study, almost 20% of the women with PPH and early RBC transfusion received  
22 fibrinogen concentrates. This proportion appears to be high considering the absence of  
23 scientific evidence for an efficacy of this treatment. The use of fibrinogen concentrates could  
24 have been influenced by results from experimental laboratory and animal studies that strongly  
25 suggested a potent haemostatic effect of fibrinogen substitution (24, 25), and from few

1 observational studies. Virally inactivated fibrinogen concentrate offers rapid restoration of  
2 fibrinogen levels, with a small volume infusion and minimal preparation time (26). It is  
3 effective in treating patients with congenital hypofibrinogenemia (27), but there are very few  
4 reports of its use in obstetric hemorrhage. The 2004 French recommendations stated that the  
5 use of fibrinogen concentrates in PPH was controversial (18). Before recommending the early  
6 use of fibrinogen concentrates in PPH, prospective studies designed to assess its efficacy and  
7 tolerance, such as the FIB-TRIAL are required (28).

8 Previous studies have established operative vaginal delivery as a risk factor for PPH  
9 (19, 29, 30). Our results show that operative vaginal delivery is also a risk factor for  
10 transfusion among women with PPH. Haemorrhage after operative vaginal delivery required  
11 larger blood-product volumes compared to spontaneous vaginal delivery, as previously  
12 reported by James et al., without any clear explanation (11). Operative vaginal delivery was  
13 also associated with a significantly higher rate of invasive procedures compared with  
14 spontaneous vaginal delivery. These differences seem ascribable to greater blood loss severity  
15 in operative than in spontaneous vaginal delivery, as illustrated by the significantly greater  
16 haemoglobin drop and higher ICU admission rate. Decreased accuracy of visual blood loss  
17 assessment after operative vaginal delivery has been reported (31). Thus, delayed PPH  
18 management due to challenges in blood loss assessment, together with the high rate of  
19 secondary coagulopathy after operative vaginal delivery -- as observed in our study -- may  
20 contribute to increase blood loss severity in operative vaginal deliveries.

21 As previously reported, coagulation disorders and abnormal placenta insertion were  
22 associated with higher blood loss and more transfusion use than other causes of PPH (12, 14,  
23 32). These findings suggest that, in the event of operative vaginal delivery, coagulopathy, or  
24 abnormal placenta insertion, very close monitoring of postpartum blood loss and of its

1 consequences is particularly needed. Point-of-care tests for haemoglobin level and  
2 coagulation may be useful tools in these contexts (33).

3         Due to the paucity of data, transfusion guidelines in women are often derived from data  
4 and recommendations for trauma patients. We found several similarities in transfusion  
5 practices between trauma and obstetrical patients: as with trauma patients, the number of RBC  
6 units transfused per woman varied widely; the FFP/RBC ratio in trauma patients was similar  
7 to that in our study (34), suggesting that transfusion practices for acute haemorrhage with  
8 coagulopathy may be comparable in trauma and PPH (35). Nevertheless, most of the studies  
9 of transfusion practices in trauma patients found considerably higher transfusion rates (45% to  
10 55%) (34, 36) and larger transfused volumes of RBC (36) than in our women with PPH.  
11 Morbidity and mortality rates due to haemorrhagic shock are higher in trauma patients than in  
12 women with PPH, with severe acute haemorrhage requiring aggressive transfusion therapy  
13 being more common among trauma patients than among women with PPH. Therefore,  
14 transfusion guidelines for trauma patients may be relevant only to women with heavy  
15 haemorrhage.

16         This study has several strengths. We used a population-based cohort composed of all  
17 women who delivered in a predefined geographic area, and whose characteristics were  
18 comparable to those of the overall population of women delivering in France (37). These  
19 features support the external validity of our results. The large number of deliveries provided  
20 robust estimates of transfusion practices in women with PPH and produced sufficient  
21 statistical power for comparisons of various obstetrical situations. Moreover, contemporary  
22 French guidelines on PPH management (38) and on transfusion in patients with acute  
23 haemorrhage (17) are similar to those from other high-resource countries (39, 40), making  
24 international comparisons of transfusion practices possible. In the present study, the  
25 prospective identification of PPH cases and review of delivery-suite logbooks and

1 computerised woman charts probably ensured a high ascertainment rate. Finally, we collected  
2 detailed data on transfusion practices in PPH. Three previous prospective population-based  
3 studies described transfusion practices but were confined to women with severe PPH  
4 requiring invasive second-line treatments such as uterine compression suture, pelvic vessel  
5 ligation, interventional radiological techniques (12, 13), and/or hysterectomy (13, 14), which  
6 limited the total number of transfused women included. Moreover, in these studies, data on  
7 transfusion practices were limited, with no information on the FFP/RBC ratio, time from PPH  
8 diagnosis to transfusion, or use of fibrinogen, although these items constitute important  
9 information on the quality of transfusion management and may have a major impact on  
10 woman outcomes (23, 41).

11 This study has some limitations. The haemoglobin trigger for RBC transfusion was not  
12 directly available in the collected data. However, it could be indirectly assessed through the  
13 postpartum nadir of haemoglobin, especially among women who were not transfused. Indeed,  
14 the absence of RBC transfusion in a great proportion of women with haemoglobin nadir lower  
15 than 7g/dL -level recommended as a trigger for RBC transfusion- suggests that the actual  
16 haemoglobin trigger for RBC transfusion is frequently lower than recommended. Importantly,  
17 this trigger should be interpreted in conjunction with the clinical context. Thus, transfusion  
18 requirements differ between women with stable anaemia and those with acute haemorrhage.  
19 In the event of active haemorrhage, clinical symptoms of acute anaemia should be given more  
20 weight than the haemoglobin trigger. Consequently, using only the haemoglobin to select  
21 women for transfusion may be overly restrictive. Nevertheless, most of the studies evaluating  
22 the appropriateness of RBC transfusion both in women with stable anaemia and in those with  
23 acute haemorrhage relied on the haemoglobin (42, 43). Another limitation of our study is the  
24 absence of maternity unit-specific data on organisational features such as local blood-bank  
25 resources, blood availability, and the supply chain. Consequently, we were unable to analyse

1 the differences in transfusion practices according to local organisation. We used data from the  
2 Pithagore6 trial, which evaluated the impact of an educational intervention for early PPH  
3 management on the incidence of severe PPH (16). Designing this trial might have changed  
4 transfusion practices in PPH. However, no significant differences were found between the two  
5 trial arms regarding the rates of severe PPH and of blood transfusion. Thus, transfusion  
6 practices were probably not influenced by the Pithagore6 trial.

7

1 **Conclusion**

2

3           Contrasting with transfusion guidelines, omission of RBC transfusion for PPH was  
4 found in a large proportion of women with low haemoglobin level. This poor compliance with  
5 guidelines may be explained by poor integration of transfusion guidelines into everyday  
6 practice, fear of transfusion complications, French transfusion tradition, or factors related to  
7 healthcare organisation. The impact on maternal outcomes of this transfusion strategy remains  
8 to be determined. Transfusion practices varied according to delivery mode and cause of PPH,  
9 with operative vaginal delivery, coagulation disorders, and abnormal placenta insertion being  
10 characterised by higher blood loss and more transfusions. Knowledge of transfusion practices  
11 may improve the quality of care by helping clinicians to identify obstetrical situations at risk  
12 for transfusion.

13



1 **Acknowledgements**

2

3 We thank the AXA Research Funds for providing financial assistance as a doctoral grant. The  
4 authors want to thank staff from the participating maternity units. We are also grateful to the  
5 Pithagore6 group and to Dr Antoinette Wolfe MD for helping to prepare the manuscript.

6

1 **Funding statement**

2

3 The Pithagore6 project was funded by the French Ministry of Health under its Clinical  
4 Research Hospital Program (contract n°27-35).

5 This study was supported by a doctoral grant from AXA Research Funds.

6

## 1 **References**

2

3 1. Ford JB, Roberts CL, Simpson JM, Vaughan J, Cameron CA. Increased postpartum  
4 hemorrhage rates in Australia. *Int J Gynaecol Obstet.* 2007;98:237-43.

5 2. Joseph KS, Rouleau J, Kramer MS, Young DC, Liston RM, Baskett TF. Investigation  
6 of an increase in postpartum haemorrhage in Canada. *BJOG.* 2007;114:751-9.

7 3. Callaghan WM, Kuklina EV, Berg CJ. Trends in postpartum hemorrhage: United  
8 States, 1994-2006. *Am J Obstet Gynecol.* 2010;202:353 e1-6.

9 4. Lutomski J, Byrne B, Devane D, Greene R. Increasing trends in atonic postpartum  
10 haemorrhage in Ireland: an 11-year population-based cohort study. *BJOG* 2011;119:306-14.

11 5. Knight M, Callaghan WM, Berg C, Alexander S, Bouvier-Colle MH, Ford JB, et al.  
12 Trends in postpartum hemorrhage in high resource countries: a review and recommendations  
13 from the International Postpartum Hemorrhage Collaborative Group. *BMC Pregnancy*  
14 *Childbirth.* 2009;9:55.

15 6. Driessen M, Bouvier-Colle MH, Dupont C, Khoshnood B, Rudigoz RC, Deneux-  
16 Tharaux C. Postpartum hemorrhage resulting from uterine atony after vaginal delivery:  
17 factors associated with severity. *Obstet Gynecol.* 2011;117:21-31.

18 7. Bonnet MP, Deneux-Tharaux C, Bouvier-Colle MH. Critical care and transfusion  
19 management in maternal deaths from postpartum haemorrhage. *Eur J Obstet Gynecol Reprod*  
20 *Biol.* 2011;158:183-8.

21 8. Butwick AJ, Aleshi P, Fontaine M, Riley ET, Goodnough LT. Retrospective analysis  
22 of transfusion outcomes in pregnant patients at a tertiary obstetric center. *Int J Obstet Anesth.*  
23 2009;18:302-8.

24 9. Parker J, Thompson J, Stanworth S. A retrospective one-year single-centre survey of  
25 obstetric red cell transfusions. *Int J Obstet Anesth.* 2009;18:309-13.

- 1 10. Balki M, Dhumne S, Kasodekar S, Seaward G, Carvalho JC. Blood transfusion for  
2 primary postpartum hemorrhage: a tertiary care hospital review. *J Obstet Gynaecol Can.*  
3 2008;30:1002-7.
- 4 11. James AH, Paglia MJ, Gernsheimer T, Grotegut C, Thames B. Blood component  
5 therapy in postpartum hemorrhage. *Transfusion.* 2009;49:2430-3.
- 6 12. Kayem G, Kurinczuk J, Alfirevic Z, Spark P, Brocklehurst P, Knight M. Specific  
7 second-line therapies for postpartum haemorrhage: a national cohort study. *BJOG.*  
8 2011;118:856-64.
- 9 13. Zwart JJ, Dijk PD, van Roosmalen J. Peripartum hysterectomy and arterial  
10 embolization for major obstetric hemorrhage: a 2-year nationwide cohort study in the  
11 Netherlands. *Am J Obstet Gynecol.* 2010;202:150 e1-7.
- 12 14. Knight M. Peripartum hysterectomy in the UK: management and outcomes of the  
13 associated haemorrhage. *BJOG.* 2007;114:1380-7.
- 14 15. Holm C, Langhoff-Roos J, Petersen K, Norgaard A, Diness B. Severe postpartum  
15 haemorrhage and mode of delivery: a retrospective cohort study. *BJOG : an international*  
16 *journal of obstetrics and gynaecology.* 2012;119:596-604.
- 17 16. Deneux-Tharaux C, Dupont C, Colin C, Rabilloud M, Touzet S, Lansac J, et al.  
18 Multifaceted intervention to decrease the rate of severe postpartum haemorrhage: the  
19 PITHAGORE6 cluster-randomised controlled trial. *BJOG.* 2010;117:1278-87.
- 20 17. (afssaps). *Transfusion de globules rouges en situation d'urgence hémorragique,*  
21 *d'anesthésie et de réanimation-recommandations de bonne pratique.* 2002
- 22 18. Boulay G, Hamza J. [Anesthetic practices in patients with severe postpartum  
23 hemorrhage with persistent or worsening bleeding]. *J Gynecol Obstet Biol Reprod (Paris).*  
24 2004;33:4S80-4S8.

- 1 19. Sosa CG, Althabe F, Belizan JM, Buekens P. Risk factors for postpartum hemorrhage  
2 in vaginal deliveries in a Latin-American population. *Obstet Gynecol.* 2009;113:1313-9.
- 3 20. Kuklina EV, Whiteman MK, Hillis SD, Jamieson DJ, Meikle SF, Posner SF, et al. An  
4 enhanced method for identifying obstetric deliveries: implications for estimating maternal  
5 morbidity. *Maternal and child health journal.* 2008;12:469-77.
- 6 21. Zwart JJ, Yazdani ST, Harvey MS, de Vries RR, van Roosmalen J. Underreporting of  
7 major obstetric haemorrhage in the Netherlands. *Transfus med.* 2010;20:118-22.
- 8 22. So-Osman C, Cicilia J, Brand A, Schipperus M, Berning B, Scherjon S. Triggers and  
9 appropriateness of red blood cell transfusions in the postpartum patient--a retrospective audit.  
10 *Vox Sang.* 2009;98:65-9.
- 11 23. Lienhart A, Auroy Y, Pequignot F, Benhamou D, Warszawski J, Bovet M, et al.  
12 Survey of anesthesia-related mortality in France. *Anesthesiology.* 2006;105:1087-97.
- 13 24. Fries D, Krismer A, Klingler A, Streif W, Klima G, Wenzel V, et al. Effect of  
14 fibrinogen on reversal of dilutional coagulopathy: a porcine model. *British journal of*  
15 *anaesthesia.* 2005;95:172-7.
- 16 25. De Lorenzo C, Calatzis A, Welsch U, Heindl B. Fibrinogen concentrate reverses  
17 dilutional coagulopathy induced in vitro by saline but not by hydroxyethyl starch 6%.  
18 *Anesthesia and analgesia.* 2006;102:1194-200.
- 19 26. Bolton-Maggs PH, Perry DJ, Chalmers EA, Parapia LA, Wilde JT, Williams MD, et  
20 al. The rare coagulation disorders--review with guidelines for management from the United  
21 Kingdom Haemophilia Centre Doctors' Organisation. *Haemophilia : the official journal of the*  
22 *World Federation of Hemophilia.* 2004;10:593-628.
- 23 27. Haas T, Fries D, Velik-Salchner C, Oswald E, Innerhofer P. Fibrinogen in  
24 craniostomosis surgery. *Anesthesia and analgesia.* 2008;106:725-31.

- 1 28. Wikkelse AJ, Afshari A, Stensballe J, Langhoff-Roos J, Albrechtsen C, Ekelund K,  
2 et al. The FIB-PPH trial: fibrinogen concentrate as initial treatment for postpartum  
3 haemorrhage: study protocol for a randomised controlled trial. *Trials*. 2012;13:110.
- 4 29. Combs CA, Murphy EL, Laros RK, Jr. Factors associated with postpartum  
5 hemorrhage with vaginal birth. *Obstet Gynecol*. 1991;77:69-76.
- 6 30. Magann EF, Evans S, Hutchinson M, Collins R, Howard BC, Morrison JC.  
7 Postpartum hemorrhage after vaginal birth: an analysis of risk factors. *Southern medical*  
8 *journal*. 2005;98:419-22.
- 9 31. Stafford I, Dildy GA, Clark SL, Belfort MA. Visually estimated and calculated blood  
10 loss in vaginal and cesarean delivery. *Am J Obstet Gynecol*. 2008;199:519 e1-7.
- 11 32. Al-Zirqi I, Vangen S, Forsen L, Stray-Pedersen B. Prevalence and risk factors of  
12 severe obstetric haemorrhage. *BJOG*. 2008;115:1265-72.
- 13 33. Huissoud C, Carrabin N, Audibert F, Levrat A, Massignon D, Berland M, et al.  
14 Bedside assessment of fibrinogen level in postpartum haemorrhage by thrombelastometry  
15 *British journal of obstetrics and gynaecology*. 2009;101:755-61.
- 16 34. Scalea TM, Bochicchio KM, Lumpkins K, Hess JR, Dutton R, Pyle A, et al. Early  
17 aggressive use of fresh frozen plasma does not improve outcome in critically injured trauma  
18 patients. *Ann Surg*. 2008;248:578-84.
- 19 35. Saule I, Hawkins N. Transfusion practice in major obstetric haemorrhage : lessons  
20 from trauma. *Int J Obstet Anesth*. 2011;21:79-83.
- 21 36. Maegele M, Lefering R, Paffrath T, Simanski C, Wutzler S, Bouillon B. Changes in  
22 transfusion practice in multiple injury between 1993 and 2006: a retrospective analysis on  
23 5389 patients from the German Trauma Registry. *Transfus Med*. 2009;19:117-24.
- 24 37. Blondel B, Zeitlin J. [Perinatal health: situation in France and in the other members of  
25 the European Union]. *J Gynecol Obstet Biol Reprod (Paris)*. 2009;38:103-5.

- 1 38. Goffinet F, Mercier F, Teyssier V, Pierre F, Dreyfus M, Mignon A, et al. [Postpartum  
2 haemorrhage: recommendations for clinical practice by the CNGOF (December 2004)].  
3 *Gynecol Obstet Fertil.* 2005;33:268-74.
- 4 39. Practice Guidelines for blood component therapy: A report by the American Society of  
5 Anesthesiologists Task Force on Blood Component Therapy. *Anesthesiology.* 1996;84:732-  
6 47.
- 7 40. Murphy MF, Wallington TB, Kelsey P, Boulton F, Bruce M, Cohen H, et al.  
8 Guidelines for the clinical use of red cell transfusions. *British journal of haematology.*  
9 2001;113:24-31.
- 10 41. Bolliger D, Gorlinger K, Tanaka KA. Pathophysiology and treatment of coagulopathy  
11 in massive hemorrhage and hemodilution. *Anesthesiology.* 2010;113:1205-19.
- 12 42. Jairath V, Barkun AN. Improving outcomes from acute upper gastrointestinal  
13 bleeding. *Gut.* 2012;61:1246-9.
- 14 43. Frank SM, Savage WJ, Rothschild JA, Rivers RJ, Ness PM, Paul SL, et al. Variability  
15 in Blood and Blood Component Utilization as Assessed by an Anesthesia Information  
16 Management System. *Anesthesiology.* 2012;117:99-106.
- 17  
18

1 **Legends to Figures and Tables**

2

3 **Figure 1:** Study population

4 a: PPH defined only by a greater than 2 g/dL decline in the haemoglobin level

5 b: Clinical PPH: defined as a blood loss greater than 500mL or an excessive blood loss  
6 prompting manual removal of the placenta or examination of the uterine cavity (or both)

7 <sup>c</sup>: Late transfusion: transfusion starting more than 12 hours following PPH diagnosis

8 <sup>d</sup>: Early transfusion: transfusion starting within the 12 first hours after PPH diagnosis

9 Hb: haemoglobin

10

11 **Table 1:** Haemoglobin measurements and red-blood-cell transfusion during the whole  
12 postpartum hospital stay in women with postpartum haemorrhage

13 PPH, postpartum haemorrhage; Hb, haemoglobin; RBC, red blood cells; SD, standard  
14 deviation; IQR, interquartile range

15 <sup>a</sup>: lowest haemoglobin level measured during the 3 first postpartum days, whether the women  
16 were transfused or not before

17

18 **Table 2:** Among women with clinical postpartum haemorrhage, comparison of women given  
19 early transfusion<sup>a</sup> and of other women

20 Data on transfusion timing was lacking for 64 women with clinical postpartum haemorrhage,  
21 who were not included in the comparison.

22 Data are number of women (%) unless otherwise specified.

23 Data were missing for less than 5% of transfused women, except for body mass index  
24 (12.9%)



1 <sup>a</sup>: Women with transfusion started within 12 first hours following the diagnosis of clinical  
2 postpartum haemorrhage

3 <sup>b</sup>: Other women with clinical PPH (not transfused or with transfusion started more than 12  
4 hours after PPH diagnosis).

5 Hb: Haemoglobin, PPH: postpartum haemorrhage, IQR: interquartile range; SD: standard  
6 deviation

7

8 **Table 3:** Transfusion characteristics according to mode of delivery in women with clinical  
9 postpartum haemorrhage and early transfusion<sup>a</sup>

10 Data are number of women (%) unless otherwise specified.

11 <sup>a</sup>: Women with transfusion started within 12 first hours following the diagnosis of clinical  
12 postpartum haemorrhage

13 <sup>b</sup>: Test for comparison across the four groups

14 RBC: red blood cells; FFP: fresh frozen plasma; IQR: interquartile range; SD: standard  
15 deviation; NA: not applicable

16

17 **Table 4:** Blood loss severity in women with clinical postpartum haemorrhage and early  
18 transfusion<sup>1</sup>

19 Data are number of women (%).

20 <sup>1</sup>: Women with transfusion started within 12 first hours following the diagnosis of clinical  
21 postpartum haemorrhage

22 <sup>2</sup>: Test for comparison across the four groups

23 SD: standard deviation; DIC: disseminated intravascular coagulation; ICU: intensive care unit

24

## Tables

**Table 1:** Haemoglobin measurements and red-blood-cell transfusion during the whole hospital stay in women with postpartum haemorrhage

	<b>Clinical PPH N=6660</b>	<b>Clinical PPH and Hb&lt;7.0 g/dL N=858</b>	<b>Clinical PPH and Hb&lt;6.0 g/dL N=289</b>
<b>Postpartum Hb measurements n (%)</b>	5776 (86.7%)	858 (100)	289 (100)
<b>RBC transfusion n (%)</b>	647 (9.7%)	423 (49.3%)	219 (75.8%)
<b>Nadir of haemoglobin in case of RBC transfusion (g/dL) (mean (SD))</b>	6.6 ( $\pm$ 1.4)	5.8 ( $\pm$ 0.8)	5.2 ( $\pm$ 0.7)
<b>Number of RBC units transfused (median (IQR))</b>	3 (2-5)	3 (2-5)	3 (2-6)

PPH, postpartum haemorrhage; Hb, haemoglobin; RBC, red blood cells; SD, standard deviation; IQR, interquartile range

<sup>a</sup>: lowest haemoglobin level measured during the 3 first postpartum days, whether the women were transfused or not before

**Table 2:** Among women with clinical postpartum haemorrhage, comparison of women given early transfusion<sup>a</sup> and of other women

<b>Population characteristics</b>	<b>PPH with early RBC transfusion<sup>a</sup> (N=426)</b>	<b>Other clinical PPH<sup>b</sup> (n=6170)</b>	<b><i>p</i> value</b>
<b>Women and pregnancies</b>			
Maternal age (years)			
<25	65 (15.3)	970 (15.7)	
25-35	257 (60.3)	4062 (65.8)	0.009
>35	104 (24.4)	1137 (18.4)	
Body mass index (Kg/m <sup>2</sup> )			
≤18	22 (5.2)	284 (4.6)	
19-25	255 (59.9)	3837 (62.2)	0.29
26-30	55 (12.9)	848 (13.8)	
>30	25 (5.9)	415 (6.7)	
Primiparous	173 (40.6)	3130 (50.7)	<0.001
Prior PPH	29 (6.8)	287 (4.7)	0.04
Prior caesarean delivery	70 (16.4)	554 (9.0)	<0.001
Multiple pregnancy	33 (7.8)	216 (3.5)	<0.001
Mean prenatal Hb level (g/dL) (SD)	11.5 (±1.4)	12.0 (±1.2)	<0.001
<b>Labour and delivery</b>			
Gestational age <37 weeks	59 (13.8)	394(6.4)	0.0001
Mode of delivery			<0.001
Vaginal delivery	231 (54.2)	5345 (86.6)	

Spontaneous vaginal delivery	170 (73.6)	4147 (77.6)	
Operative vaginal delivery	61 (26.4)	1198 (22.4)	
Caesarean delivery	195 (23.1)	824 (13.4)	
Caesarean delivery before labour	109 (55.9)	439 (53.3)	
Caesarean delivery during labour	86 (44.1)	385 (46.7)	
Epidural or spinal analgesia/anaesthesia	336 (78.9)	4984 (80.8)	0.51
Mean birth weight (g) (SD)	3236 ( $\pm$ 704)	3377 ( $\pm$ 568)	<0.001
Median time from delivery to PPH diagnosis (IQR)	12 min (2-45)	15 min (9-30)	0.08

Data on transfusion timing was lacking for 64 cases of clinical postpartum haemorrhage, who were not included in the comparison.

Data are number of women (%) unless otherwise specified.

Data were missing for less than 5% of transfused women, except for body mass index (12.9%)

<sup>a</sup>: Women with transfusion started within 12 first hours following the diagnosis of clinical postpartum haemorrhage

<sup>b</sup>: Other women with clinical PPH (not transfused or with transfusion started more than 12 hours after PPH diagnosis).

Hb: Haemoglobin, PPH: postpartum haemorrhage, IQR: interquartile range; SD: standard deviation

**Table 3:** Transfusion characteristics according to mode of delivery in women with clinical postpartum haemorrhage and early transfusion<sup>a</sup>

	<b>Total (N=426)</b>	<b>Spontaneous vaginal delivery N=170 (40.0%)</b>	<b>Operative vaginal delivery N=61 (14.3%)</b>	<b>Caesarean delivery before labour N=109 (25.5%)</b>	<b>Caesarean delivery during labour N=86 (20.1%)</b>	<b><i>p</i> value<sup>b</sup></b>
<b>RBC only</b>	168 (39.4)	65 (38.2)	17 (27.9)	46 (42.2)	40 (46.5)	0.13
<b>FFP</b>	248 (58.1)	102 (60.0)	44 (72.1)	59 (54.1)	43 (50.0)	0.04
<b>Fibrinogen</b>	83 (19.5)	31 (18.2)	12 (19.7)	23 (21.1)	17 (19.8)	0.95
<b>Platelets</b>	52 (12.2)	18 (10.6)	13 (21.3)	15 (13.8)	6 (7.0)	0.06
<b>RBC+FFP+Platelets+Fibrinogen</b>	32 (7.5)	14 (8.2)	8 (13.1)	7 (6.4)	3 (3.5)	0.17
<b>Median transfused quantity (IQR)</b>						
<b>RBC (units)</b>	3 (2-6)	3 (2-5)	4 (3-9)	3 (2-6)	4 (2-5)	0.01
<b>FFP (units)</b>	4 (2-6)	3 (2-4)	4 (2-6)	4 (3-6)	3 (2-4)	0.004
<b>Fibrinogen (g)</b>	3 (3-4.5)	3 (1.5-4.5)	3 (3-7.5)	4 (3-5.5)	3 (2-4.5)	0.37
<b>Platelets (units)</b>	1 (1-2)	1 (1-2)	1 (1-2)	1 (1-2)	2 (1-2)	0.39
<b>≥10 RBC units</b>	46 (10.8)	10 (5.9)	15 (24.6)	16 (14.7)	5 (5.8)	<0.001

<b>FFP/RBC</b>						
<b>Median (IQR)</b>	0.8 (0.5-1)	0.7 (0.6-1)	0.8 (0.5-1)	0.8 (0.6-1)	0.6 (0.5-1)	0.38
<b>FFP/RBC<math>\geq</math>0.5</b>	209 (84.3)	85 (83.3)	39 (88.6)	52 (88.1)	33 (76.7)	0.36
<b>Median time from PPH diagnosis to RBC administration, hours (IQR)</b>	2 h 18 min (1h18min-3h 54min)	2 h 30 min (1h24min-4h18min)	2 h 12 min (1h18min-3h 48min)	2 h 00 (48min-3h36 min)	2 h 12 min (1h06min-3h48min)	0.12
<b>Use of pro-haemostatic agents</b>	17 (4.0)	6 (3.5)	7 (11.5)	2 (1.8)	2 (2.3)	NA

Data are number of women (%) unless otherwise specified.

<sup>a</sup>: Women with transfusion started within 12 first hours following the diagnosis of clinical postpartum haemorrhage

<sup>b</sup>: Test for comparison across the four groups

RBC: red blood cells; FFP: fresh frozen plasma; IQR: interquartile range; SD: standard deviation; NA: not applicable

**Table 4:** Blood loss severity in women with clinical postpartum haemorrhage and early transfusion<sup>a</sup>

	<b>Total</b>	<b>Spontaneous vaginal delivery</b>	<b>Operative vaginal delivery</b>	<b>Caesarean delivery before labour</b>	<b>Caesarean delivery during labour</b>	<i>p</i> value <sup>b</sup>
	<b>N=426</b>	<b>N=170 (40.0%)</b>	<b>N=61 (14.3%)</b>	<b>N=109 (25.5%)</b>	<b>N=86 (20.1%)</b>	
<b>Mean maximal Hb drop (g/dL) (SD)</b>	4.7 (1.9)	4.6 (1.8)	5.6 (2.0)	4.1 (1.9)	4.8 (1.8)	<0.001
<b>Secondary DIC</b>	110 (25.8)	42 (24.7)	19 (31.2)	22 (20.2)	27 (31.4)	0.23
<b>Embolisation</b>	106 (24.9)	49 (28.8)	19 (31.2)	22 (20.2)	16 (18.6)	0.12
<b>Conservative surgery</b>	58 (13.6)	12 (7.1)	12 (19.7)	23 (21.1)	11 (12.8)	0.004
<b>Hysterectomy</b>	64 (15.0)	23 (13.5)	13 (21.3)	23 (21.1)	5 (15.0)	0.01
<b>ICU admission</b>	180 (42.3)	64 (37.7)	33 (54.1)	45 (41.3)	38 (44.2)	0.16

Data are number of women (%).

<sup>a</sup>: Women with transfusion started within 12 first hours following the diagnosis of clinical postpartum haemorrhage

<sup>b</sup>: Test for comparison across the four groups

Hb: Haemoglobin; SD: standard deviation; DIC: disseminated intravascular coagulation; ICU: intensive care unit

