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Effect of a collector bag for measurement of postpartum blood loss after vaginal delivery: a cluster randomised trial in thirteen European countries

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Abstract

Background- Postpartum haemorrhage (PPH) remains a leading cause of maternal morbidity and mortality worldwide. Delay in diagnosis and care for PPH has been reported. The inaccuracy of visual estimation of postpartum blood loss has been demonstrated.

Objectives- To evaluate the effectiveness of the systematic use of a transparent plastic collector bag for measurement of postpartum blood loss after vaginal delivery in reducing the incidence of severe PPH

Design- A cluster randomised trial

Setting- Thirteen European countries

Participants- 78 maternity units and 25381 women who had a vaginal delivery

Interventions- Maternity units were randomly assigned to systematically use a collector bag (intervention group), or to continue to visually assess postpartum blood loss after vaginal delivery (control group)

Main outcome measures- The primary outcome was the incidence of severe PPH in vaginal deliveries, defined as a composite of one or more of the following events: blood transfusion, intravenous plasma expansion, arterial embolisation, surgical procedure, admission to intensive care unit, treatment with recombinant factor VII, or death.

Results- The incidence of severe PPH was 189 out of 11037 of vaginal deliveries (1.71%) in the intervention group compared to 295 out of 14344 in the control group (2.06%). The difference was not statistically significant either in individual level analysis (adjusted odds ratio 0.82; 95% CI 0.26 to 2.53) or in cluster level analysis (difference in weighted mean rate adjusted for baseline rate 0.16%; 95 % CI -0.69% to 1.02%).

Conclusion- The use of a collector bag after vaginal delivery did not reduce the rate of severe PPH as compared to visual estimation of postpartum blood loss.
1  **Trial registration**: International Standard Randomised Controlled Trial Number (ISRCTN)

2  66197422.
**Introduction**

Worldwide, postpartum haemorrhage (PPH) remains one of the leading causes of maternal mortality and the main component of severe morbidity, jeopardizing the woman’s fertility, exposing her to risks of transfusion and intensive care, and incurring costs. From reports in developed countries, about one percent of deliveries are associated with severe PPH. Decreasing the prevalence of severe PPH remains challenging. This appears all the more important given the recent increase in the incidence of PPH reported in several developed countries. Individual risk factors have been described but they poorly predict the occurrence of PPH. Interest has focused on care-processes as they are potentially amenable to change. Studies of maternal deaths show that most deaths due to PPH involve delayed and substandard care in the diagnosis and management of haemorrhage. Similar findings were drawn from a population-based study of severe non-lethal PPH. Delay in diagnosis and treatment of PPH may result from an underestimation of blood loss at delivery. Assessment of post-partum blood loss, particularly following vaginal birth, is recognised as difficult. Many studies demonstrate that visual estimates of peripartum blood loss are frequently inaccurate, showing an overestimation of blood loss at low volumes and an underestimation at larger volumes, the magnitude of underestimation typically increasing with the volume of haemorrhage.

The hypothesis of this study was that if blood loss is monitored and objectively measured by collection in a transparent plastic bag, rather than being visually assessed, care-giver response will be triggered more rapidly when excessive blood loss occurs. Specifically when bleeding is excessive but before haemorrhage has become catastrophic, appropriate management will take place without delay, so reducing the incidence of severe PPH. A preliminary study shows that a plastic collector bag constitutes a simple instrument to diagnose haemorrhage in the delivery room. However, the impact of its use on PPH-related health outcomes has never
been tested. Despite lacking evidence, the bag is routinely used in a significant proportion of maternity units in Belgium, France, Italy, and Portugal (Euphrates survey\textsuperscript{23}, unpublished data).

The objective of this trial was to evaluate the effectiveness of the systematic use of a transparent plastic collector bag for measurement of postpartum blood loss after vaginal delivery in reducing the incidence of severe PPH.

**Methods**

**Trial design**

A cluster-randomised design with maternity unit was the unit of randomization. Given the logistics of clinical practice on the delivery suite, contamination appeared to be inevitable in an individual-patient randomised trial setting.

**Setting**

The sites selected for the trial comprised 78 maternity units in 13 European countries (see Table1).

**Participants**

**Maternity units**

Maternity units were eligible if they had more than 200 vaginal deliveries annually (excluding water births), and no previous policy of routine use of collector bags. In addition, to ensure that the standard of care for management of the third stage of labour was similar across all participating units, they had to comply with the EUPHRATES consensus statement on the prevention and management of PPH\textsuperscript{24}; a minimum standard, not a detailed guideline.

**Women**

In all maternity units of participating countries (except Denmark), all women undergoing a vaginal delivery during the study period were included. In Denmark, enrolment into the study
in each maternity unit was midwife-dependant; if a midwife agreed to participate, all his/her vaginal deliveries were included.

**Randomization**

The random allocation was produced centrally by the National Perinatal Epidemiology Unit in Oxford, UK. A stratified design was used to ensure that the two arms of the trial were as similar as possible at baseline with respect to the stratification factors (i) country and (ii) size of maternity unit (median split within country). Maternity units were randomly allocated to either systematically use a collector bag after vaginal delivery (intervention arm), or not use the bag (control group).

**Intervention**

The trial was implemented between January 2006 and May 2007, depending on the country. Prior to participation, each centre was visited by the national coordinator. At the visit, staff were reminded of the EUPHRATES consensus statement on the prevention and management of PPH and familiarised with the processes and the data collection instrument. In the intervention group, a second visit from the national coordinator took place after randomisation, during which, use of the collector bag was explained to birth attendants with standard written instructions and a training video aid. The bag was to be placed under the pelvis of the mother as soon as the baby was born and before delivery of the placenta. It was transparent and graduated, allowing continuous monitoring of blood loss. It did not require sterilization and could be used in dorsal, lateral or lithotomy positions. Women delivering standing or crouching could be offered the opportunity to lie down for the third stage, allowing the bag to be placed under their pelvis. The bag was to be left under the woman’s buttocks until the birth attendant was no longer concerned about blood loss e.g. when the
sanitary towel was applied to the vulva. Bags were purchased centrally and provided to each
cluster in the intervention arm.

In the control group, no collector bag was used, postpartum blood loss being visually assessed.
During the study period, use of collector devices was monitored to assess compliance with
allocation.

Outcomes

The primary outcome for the trial was the incidence of severe PPH following vaginal
deliveries, defined as a composite of all women who experienced one or more of the
following: blood transfusion, intravenous plasma expansion, arterial embolisation, surgical
procedure, admission to intensive care unit, treatment with recombinant factor VII and death.
Secondary outcomes were each of the components of the primary outcome, manual removal
of the placenta and administration of prostaglandins after delivery.

Data collection

Each participating centre was asked to collect data from all women undergoing a vaginal
delivery for a period of 4 months.

Data were collected during two time intervals: a 1-month period pre-randomisation (baseline
period), and a 3-month period beginning immediately following randomisation in the control
group (trial period). In the intervention group, the 3-month period of data collection followed
a 2-week training period during which the unit started using the collector bag on women
undergoing vaginal delivery.

Data were collected using a form filled in by the birth attendants for each vaginal delivery,
and included information on the woman’s age, induction of labour, mode of delivery, number
of babies and birth weight, prophylactic uterotonics, and outcome data. Additionally, a second
form was used for deliveries where severe PPH occurred, collecting detailed information regarding delivery and PPH management. This form was used to cross-check criteria for the primary outcome.

**Sample size**

Sample size calculation took into account the cluster-randomised design; the intracluster correlation coefficient was estimated to be 0.01. Assuming an event rate for the primary outcome of 2.5% in the control group, in order to detect a decrease in the event rate to 1.5% (a 40% relative risk reduction) with 80% power, a 2-sided significance level of 5% and an average cluster size of 300 women, 82 clusters (41 in each arm of the trial) were required.

**Statistical analysis**

Participants/maternity units were analysed in the groups to which they were assigned regardless of the management received by individual women or deviation from the protocol. Baseline characteristics of maternity units and individual women were summarized with counts (percentages) for categorical variables, mean (standard deviation [SD]) for normally distributed continuous variables, or median (interquartile [IQR]) for other continuous variables. Comparative statistical analysis was performed at both individual and cluster level and took into account the effect of clustering. All statistical tests were two-sided (5% significance level) and not adjusted for multiple comparisons. Statistical analyses were performed using SPSS version 17 (SPSS) and Stata v10.0 software (Stata Corporation, College Station, Texas, USA).

*Individual woman level analysis* - primary and secondary outcomes were compared between the two study groups both unadjusted and adjusted for the effect of clustering. In order to determine the magnitude and direction of any differences in outcomes between the two
groups, crude odds ratios and 95% confidence intervals were calculated. Furthermore, logistic regression was used to adjust for clustering and key prognostic factors. The cluster randomised design imparts a data structure that facilitates the calculation of a valid intracluster correlation coefficient, \( \rho \).

Cluster level analysis was only performed on the primary outcome. Some hospitals contributed fewer events than others, and some recruited fewer women. We allowed these hospitals to have less effect on the treatment estimate by weighting the analysis based on the precision, i.e. calculating the weighted mean difference for the treatment comparison. A weighted linear regression model was used to test the effect of the intervention on the rate of severe PPH during the trial period, adjusting for the baseline rate, expressed as the weighted mean difference (plus 95% confidence interval).

**Ethical aspects**

Ethics approval was obtained in each country from relevant local or national research ethics committees. Consent to participate was taken from the maternity units. Because the procedure being tested was not invasive or different from current clinical practice, and because outcome data were routinely collected at maternity units and anonymously transmitted, no individual consent was sought.

**Role of the funding source**

The project was funded by the European Union (EU) under Framework 5 (contract QLG4-CT-2001-01352). EU had no role in the design, management, data collection, analyses, or interpretation of the data. EU had no role in the writing of the manuscript or in the decision to submit for publication.
Results

Figure 1 shows the flow of maternity units and women through the study. Of the 84 maternity units meeting the inclusion criteria, two maternity units declined to participate before allocation. Forty one maternity units were randomised to the intervention group and 41 to the control group. Two maternity units in each group opted out before receiving notification of allocation because they lacked the necessary resources. Thirty-nine maternity units in each group completed the trial. Table 1 shows the number of participating maternity units and women included in each country.

One maternity unit did not collect baseline data in the intervention group. Deviating from the protocol, the majority of maternity units (31 of 39) continued collecting data during the 2-week training period in the intervention arm. In these units, trial data collection started after the first month of baseline data collection. Four units in the control group collected trial data for more than 3 months (up to 5 months). Only the 3-month period of data collection specified in the protocol was considered for all units. In some Austrian hospitals, the number of women included was low, given the total expected number of deliveries. The national coordinator confirmed that the missing data were all caesarean deliveries, and that in some hospitals the caesarean rate was very high. Nevertheless, sensitivity analyses were performed, and showed that excluding these hospitals or even the entire Austrian data set did not influence the results.

Characteristics of maternity units and women

Baseline data were collected for 4937 in the intervention group and 4758 vaginal deliveries in the control group and characteristics of maternity units and women (Table 2) were broadly similar in the two groups for all factors, except for manual removal of the placenta and prophylactic uterotonics, which were more common among women in the intervention group.
Primary outcome

Individual level analysis

A total of 25381 women were included in the analysis (11037 in the intervention group and 14344 in the control group). The greater number of women in the control group was due to a larger median cluster size (241 and 284 in the intervention and control groups, respectively).

The incidence of severe PPH was 189 out of 11037 of vaginal deliveries (1.71%) in the intervention group compared to 295 out of 14344 in the control group (2.06%). The difference was not statistically significant (Table 3). The crude odds ratio for the effect of the intervention was 0.83 (95% CI, 0.69 to 1.00). The odds ratio adjusted for clustering was 0.83 (95% CI, 0.27 to 2.60); after further adjustment for age, prophylactic uterotonics in the third stage, mode of delivery and birth weight, the odds ratio was 0.82 (95% CI, 0.26 to 2.53).

Sensitivity analyses were conducted to test the robustness of this result excluding units deviating from the protocol, and also by country, and by baseline rate of severe PPH (median split by country); these analyses provided similar results.

Cluster level analysis

The weighted mean severe PPH rate was 1.71% (SD 2.51) in the intervention group and 2.06% (SD 3.52) in the control group. The intracluster correlation coefficient for severe PPH was 0.023. There was no significant difference in the rate of severe PPH between the two groups (weighted mean difference -0.34%, (-2.56% to 1.87%); p=0.75). Adjusting for the baseline rate of severe PPH resulted in a slight change in this result (adjusted weighted mean difference 0.16%, (-0.69% to 1.02%); p=0.70). Rates of severe PPH in the baseline and trial periods for each maternity unit were heterogeneous across units in different countries (Figure 2).

Figure 3 shows the difference in baseline and trial rates of severe PPH for each unit in the intervention group, according to the compliance of bag usage. There was no relationship
between the difference in severe PPH rates (baseline and trial) and the actual proportion of
bag use. The analysis of the intervention effect on the primary outcome, including in the
intervention arm only maternity units where the bag was used in at least 50% of vaginal
deliveries, showed no significant difference between the two groups (individual level analysis
adjusting for cluster and individual characteristics; adjusted OR 0.59, 95% CI (0.23-1.53)).

**Secondary outcomes (individual level analysis)**

Analyses were performed to test the effect of the intervention on the main components of the
primary outcome (Table 3). The proportion of blood transfusion, surgical procedure or
embolisation and of manual removal of placenta, did not substantially differ between the
intervention and control groups, whether after adjusting for cluster or after further adjusting
for other prognostic factors. There were no maternal deaths.

The proportions of receipt of intravenous plasma expanders and of prostaglandins use were
different between intervention and control groups, but the differences were not significant
after adjusting for clustering effect.

**Discussion**

**Strengths and limitations of study**

In this cluster randomised trial conducted on 25381 vaginal deliveries in 78 maternity units of
13 European countries, the systematic use of a collector bag after vaginal delivery did not
modify the rate of severe forms of postpartum haemorrhage. There was no evidence of
heterogeneity, the results not differing according to country or size of hospital.

This trial provides new results on an unexplored although controversial aspect of care in the third
stage of labour. Although objective measurement has been shown to increase the accuracy of
postpartum blood loss assessment compared to visual estimation\textsuperscript{15-21}, the routine use of a collector
bag is not associated with a significant decrease in severe PPH. This result constitutes an important
contribution to the on-going debate on strategies to improve the care of women with PPH and
decrease the incidence of severe cases.
Additionally, the cluster-randomised design, the large number of clusters and their diversity
provide good external validity to this trial.
There were small deviations from the protocol for data collection, but sensitivity analyses showed
that none of these changed the internal validity of the trial.
There was large heterogeneity of baseline rates for the severe event between units (0 to 13.4 %). In
theory, such a variation should be an asset, and reflect a broad range of levels of risk in the
participating maternity units. However, because these differences were strongly related to the
country, there remains some concern regarding the criteria in use for the management of PPH in
different parts of Europe. Again sensitivity analysis showed that this aspect did not alter the
results.
There was some heterogeneity in baseline data between the intervention and control groups.
Heterogeneity in PPH-related practices and PPH rates has been reported across maternity
units in Europe, both between and within countries\textsuperscript{4, 23}. Although randomization is expected
to balance these differences between the two arms, the number of units randomized, although
large for a cluster RCT, makes residual imbalance possible although probably very slight.
However, analyses were adjusted for the main determinants of PPH (individual level analysis),
and baseline rate of severe PPH (cluster-level analysis); in addition, sensitivity analysis
indicated that the absence of significant impact of the intervention was similar whether the
maternity units had high or low baseline rate of severe PPH. In consequence, any perceived or
real imbalance in these characteristics should have little or no impact on the findings.

\textit{Hypotheses for the results}
Different mechanisms may explain the absence of difference in the rates of severe PPH between maternity units which used the bag and those where blood loss was visually assessed. This may be due to a lack of compliance to the intervention. However, the persistent absence of difference between the 2 groups when the analysis was restricted to the units where the bag was used in a high proportion of deliveries suggests this is unlikely.

One potential reason for the apparent ineffectiveness of the intervention might be that the bags were actually not used correctly; in particular, there might be concern that the bags were covered most of the time and thus could not be viewed. However, because detailed oral and written instructions were provided and the training video clearly showed the care giver watching the bag and the graduations, such misuse is unlikely to explain the observed lack of effect.

Participation in the study may indicate a particular interest in the management of PPH so that existing management had little room for improvement. However, the variety of baseline rates of severe PPH in these units makes such a selection process unlikely.

It may be hypothesized that the intervention has a double effect, in two opposite directions: increasing the rate of ascertainment through increased vigilance and decreasing the prevalence rate through timely management of excessive bleeding. If these two components were of the same order of magnitude, the global effect would be no effect. However, if this explanation was realistic, one would expect different size of effects with different baseline rates and/or different degrees of compliance. None of this occurred, making it unlikely that a benefit of the intervention in terms of decreased severe outcome was balanced by an equivalent increase in ascertainment. In fact the intervention appeared to increase PPH rates, reflecting possibly, that the intervention was more effective on improving ascertainment than on changing practice.

A concomitant effect in the control group may also have contributed to the absence of difference between the two arms. Contamination of the intervention to control units is
unlikely since participating units were not in contact, and no use of bags was reported in any
control unit. Participation in a research study, independently of any specific intervention, has
been reported to change behaviors of participants (Hawthorne effect\textsuperscript{26}). The hypothesis that
the management of PPH would have improved in the control arm is, however, not supported
by the absence of change in the rate of severe PPH between the baseline and trial periods in
this group.

The most plausible explanation of the negative result of this trial is that having a more
accurate assessment of postpartum blood loss is not, by itself, sufficient to change behaviors
of care givers and improve PPH management. Lack of identification of women with excessive
postpartum bleeding is a considerable problem, potentially leading to higher levels of medical
intervention if the bleeding progresses to severe haemorrhage. We designed a strategy to
increase care-givers awareness. The fact that this has not translated into a change in clinical
outcomes probably reflects the complexity of management decisions, which are influenced by
multiple factors such as organization of the delivery ward, and how care givers perceive and
cope with emergencies.

\textit{Comparison with other studies}

We did not find any other published study assessing the effectiveness of the collector bag.
However we have identified other large multicentre randomised trials in the field of maternal
and child health where a diagnostic or screening test was evaluated without any associated
instructions about the management of abnormal results\textsuperscript{27-29}. None of these trials showed
benefit with the introduction of the test. In addition Althabe et al have shown that simple
information is not sufficient to impact birth attendants readiness to change\textsuperscript{30}. These various
reports suggest that the effect of enhanced diagnostic methods should include an
accompanying protocol of management, and maybe a specific behavioral intervention, which
in effect becomes a “complex intervention”.
Conclusions and policy implications

The practical implication of these results for high income countries, is that those units which are using a collector bag (at a cost between 1 and 11 € per bag in Europe) need to reconsider their practice, and maybe reallocate the resources to other aspects of care. Units which are not routinely using the bag should keep the same policy. For resource poor countries positive results of the use of the “kanga collector” have been reported. This needs to be tested in a randomised design. In the current context of reported on-going increase in the prevalence of PPH, further research is needed to develop and test effective strategies to decrease the prevalence of severe PPH through improvement of management. These will probably be multifaceted interventions, and in this context, the collector bag may warrant further investigation.
What this paper adds

What is already known on this subject

Delay in diagnosis and initial care for postpartum hemorrhage (PPH) has been reported, and may result from an underestimation of postpartum blood loss, due to the inaccuracy of visual assessment. A collector bag has been proposed as a useful tool to objectively measure postpartum blood loss. However, the impact of its use has never been tested. Despite lacking evidence, the bag is routinely used in a significant proportion of maternity units in Europe.

What this study adds

Our study suggests that, for western countries, the routine use of a collector bag to objectively assess postpartum blood loss after vaginal delivery, without specific guideline regarding threshold and action, does not reduce the incidence of severe PPH.
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Figure 1

Eligible maternity units/clusters (N=84)

Random allocation stratified on cluster size within country (N=82)

Allocated to control (Maternity units=41)
- Received notification of allocation (n=39)
- Did not receive notification of allocation (n=2)
  Did not have the necessary resources and opted out before receiving notification of allocation

Allocated to intervention (Maternity units=41)
- Received notification of allocation (n=39)
- Did not receive notification of allocation (n=2)
  Did not have the necessary resources and opted out before receiving notification of allocation

Analysis

Baseline assessment
- Maternity units (n=39)
- Women (n=4,937)
- Median cluster size (85)
- Cluster size inter-quartile range (51, 167)

Baseline assessment
- Maternity units (n=39)
- Women (n=4,758)
- Median cluster size (93)
- Cluster size inter-quartile range (44, 162)

Baseline assessment
- Maternity units (n=39)
- Women (n=14,344)
- Median cluster size (284)
- Cluster size inter-quartile range (113, 499)

Baseline assessment
- Maternity units (n=39)
- Women (n=11,037)
- Median cluster size (241)
- Cluster size inter-quartile range (148, 408)

Lost to follow up (n=0)

Lost to follow up (n=0)

Analysed
- Maternity units (n=39)
- Women (n=11,037)
- Median cluster size (241)
- Cluster size inter-quartile range (148, 408)

Analysed
- Maternity units (n=39)
- Women (n=4,758)
- Median cluster size (93)
- Cluster size inter-quartile range (44, 162)
Table 1- Number of maternity units and women in baseline and trial periods by allocation and by country*

<table>
<thead>
<tr>
<th>Country</th>
<th>Intervention</th>
<th>Control</th>
<th>Maternity units</th>
<th>Women</th>
<th>Total</th>
<th>% total</th>
<th>Int</th>
<th>Control</th>
<th>Total</th>
<th>Int</th>
<th>Control</th>
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</thead>
<tbody>
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<td>Austria</td>
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<td>3</td>
<td>1067</td>
<td>3.0</td>
<td>371</td>
<td>219</td>
<td>152</td>
<td>696</td>
<td>359</td>
<td>337</td>
<td></td>
</tr>
<tr>
<td>Belgium</td>
<td>8</td>
<td>8</td>
<td>6013</td>
<td>17.1</td>
<td>1552</td>
<td>728</td>
<td>824</td>
<td>4461</td>
<td>1867</td>
<td>2594</td>
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<tr>
<td>Denmark</td>
<td>3</td>
<td>3</td>
<td>1657</td>
<td>4.7</td>
<td>507</td>
<td>272</td>
<td>235</td>
<td>1150</td>
<td>562</td>
<td>588</td>
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<tr>
<td>Finland</td>
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<td>4805</td>
<td>13.7</td>
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<td>691</td>
<td>3458</td>
<td>1551</td>
<td>1907</td>
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<tr>
<td>France</td>
<td>3</td>
<td>3</td>
<td>3702</td>
<td>10.6</td>
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<td>544</td>
<td>428</td>
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<td>1351</td>
<td>1379</td>
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<tr>
<td>Hungary</td>
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<td>2230</td>
<td>6.4</td>
<td>562</td>
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<td>1668</td>
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<td>Ireland</td>
<td>2</td>
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<td>3971</td>
<td>11.3</td>
<td>950</td>
<td>300</td>
<td>650</td>
<td>3021</td>
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<td>2075</td>
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<td>926</td>
<td>2.6</td>
<td>196</td>
<td>138</td>
<td>58</td>
<td>730</td>
<td>491</td>
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<td>1</td>
<td>1084</td>
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<td>301</td>
<td>130</td>
<td>171</td>
<td>783</td>
<td>322</td>
<td>461</td>
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</tr>
<tr>
<td>Norway</td>
<td>1</td>
<td>1</td>
<td>668</td>
<td>1.9</td>
<td>143</td>
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<td>71</td>
<td>525</td>
<td>241</td>
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</tr>
<tr>
<td>Portugal</td>
<td>2</td>
<td>3</td>
<td>3274</td>
<td>9.3</td>
<td>810</td>
<td>338</td>
<td>472</td>
<td>2464</td>
<td>901</td>
<td>1563</td>
<td></td>
</tr>
<tr>
<td>Spain</td>
<td>4</td>
<td>3</td>
<td>4351</td>
<td>12.4</td>
<td>1595</td>
<td>1097</td>
<td>498</td>
<td>2756</td>
<td>1239</td>
<td>1517</td>
<td></td>
</tr>
<tr>
<td>Switzerland</td>
<td>3</td>
<td>3</td>
<td>1328</td>
<td>3.8</td>
<td>389</td>
<td>175</td>
<td>214</td>
<td>939</td>
<td>423</td>
<td>516</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>39</strong></td>
<td><strong>39</strong></td>
<td><strong>35076</strong></td>
<td><strong>100.0</strong></td>
<td><strong>9695</strong></td>
<td><strong>4937</strong></td>
<td><strong>4758</strong></td>
<td><strong>25381</strong></td>
<td><strong>11037</strong></td>
<td><strong>14344</strong></td>
<td></td>
</tr>
</tbody>
</table>

* Baseline data were unavailable in one maternity unit in the intervention group
### Table 2- Baseline characteristics of maternity units and individual women by allocation*

<table>
<thead>
<tr>
<th>Mosality</th>
<th>Intervention</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=38†</td>
<td>N=39</td>
<td></td>
</tr>
<tr>
<td>Rate of caesarean delivery − (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>21.1</td>
<td>21.7</td>
</tr>
<tr>
<td>Interquartile range</td>
<td>17.4-26.6</td>
<td>14.6-26.0</td>
</tr>
<tr>
<td>&gt;1600 deliveries/yr − no. (%)</td>
<td>20 (52.6)</td>
<td>19 (48.7)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Women</th>
<th>N=4937</th>
<th>N=4758</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age − yr</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>29.6±5.4</td>
<td>29.7±5.5</td>
</tr>
<tr>
<td>Median</td>
<td>30.0</td>
<td>30.0</td>
</tr>
<tr>
<td>Interquartile range</td>
<td>26-33</td>
<td>26-33</td>
</tr>
<tr>
<td>Missing data − no.</td>
<td>31</td>
<td>23</td>
</tr>
<tr>
<td>Mode of delivery − no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spontaneous vaginal delivery</td>
<td>4104 (83.1)</td>
<td>4062 (85.4)</td>
</tr>
<tr>
<td>Operative vaginal delivery</td>
<td>833 (16.9)</td>
<td>696 (14.6)</td>
</tr>
<tr>
<td>Induction − no. (%)</td>
<td>1080 (21.9)</td>
<td>1043 (21.9)</td>
</tr>
<tr>
<td>Number of babies − no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>4833 (98.5)</td>
<td>4645 (98.6)</td>
</tr>
<tr>
<td>Multiple</td>
<td>76 (1.5)</td>
<td>68 (1.4)</td>
</tr>
<tr>
<td>Missing data − no.</td>
<td>28</td>
<td>45</td>
</tr>
<tr>
<td>Birth weight − grams</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>3315±566.4</td>
<td>3349±549.1</td>
</tr>
<tr>
<td>Median</td>
<td>3330</td>
<td>3370</td>
</tr>
<tr>
<td>Interquartile range</td>
<td>3020-3660</td>
<td>3050-3690</td>
</tr>
<tr>
<td>Missing data − no.</td>
<td>26</td>
<td>29</td>
</tr>
<tr>
<td>Prophylactic uterotonics in 3rd stage − no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Missing data − no.</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Prostaglandin used after birth − no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Missing data − no.</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Manual removal of the placenta − no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Missing data − no.</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Severe PPH − no. (%)</td>
<td>60 (1.22)</td>
<td>90 (1.89)</td>
</tr>
</tbody>
</table>

* Plus-minus values are mean ±SD. Severe PPH denotes severe Post-Partum Haemorrhage defined by one of the following: maternal death, transfusion, plasma expansion, surgery/embolisation, ICU, recombinant factor VII.

† Baseline data were unavailable in one maternity unit.
Table 3- Main outcomes*

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Control</th>
<th>ICC (ρ)</th>
<th>Crude odds ratio (95% CI)</th>
<th>Adjusted OR (95% CI)†</th>
<th>Adjusted OR (95% CI)‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=11037</td>
<td>N=14344</td>
<td>no. (%)</td>
<td>no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary outcome</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe PPH</td>
<td>189 (1.71)</td>
<td>295 (2.06)</td>
<td>0.023</td>
<td>0.83 (0.69-1.00)</td>
<td>0.83 (0.27-2.60)</td>
</tr>
<tr>
<td></td>
<td>P=0.05</td>
<td>P=0.8</td>
<td>P=0.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondary outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>86 (0.78)</td>
<td>135 (0.94)</td>
<td>0.011</td>
<td>0.83 (0.63-1.68)</td>
<td>0.83 (0.35-1.96)</td>
</tr>
<tr>
<td></td>
<td>P=0.2</td>
<td>P=0.8</td>
<td>P=0.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plasma expander</td>
<td>127 (1.15)</td>
<td>222 (1.55)</td>
<td>0.022</td>
<td>0.74 (0.59-0.92)</td>
<td>0.74 (0.20-2.72)</td>
</tr>
<tr>
<td></td>
<td>P=0.007</td>
<td>P=0.7</td>
<td>P=1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgical procedure or embolisation</td>
<td>50 (0.45)</td>
<td>76 (0.53)</td>
<td>0.012</td>
<td>0.85 (0.60-1.22)</td>
<td>0.85 (0.20-3.63)</td>
</tr>
<tr>
<td></td>
<td>P=0.9</td>
<td>P=0.9</td>
<td>P=0.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Manual removal of placental</td>
<td>326 (2.95)</td>
<td>366 (2.55)</td>
<td>0.016</td>
<td>1.16 (1.00-1.35)</td>
<td>1.16 (0.76-1.77)</td>
</tr>
<tr>
<td></td>
<td>P=0.05</td>
<td>P=0.5</td>
<td>P=0.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prostaglandins use</td>
<td>501 (4.54)</td>
<td>766 (5.34)</td>
<td>0.129</td>
<td>0.84 (0.75-0.95)</td>
<td>0.84 (0.40-1.77)</td>
</tr>
<tr>
<td></td>
<td>P=0.004</td>
<td>P=0.7</td>
<td>P=0.7</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Severe PPH denotes severe Post-Partum Haemorrhage defined by one of the following: maternal death, transfusion, plasma expansion, surgery/embolisation, ICU, recombinant factor VII. ICC denotes Intracluster Correlation Coefficient (ρ)
† Adjusted for clustering (maternity unit)
‡ Adjusted for clustering (maternity unit), age of mother, prophylactic uterotonics using in the third stage, mode of delivery and birth weight
Figure 2

[Graph showing the relationship between severe PPH rate in the trial period and severe PPH rate in the baseline period, with points indicating data from the intervention group and control group.]
Figure 3

Proportion of women with measured blood loss (%)

Difference in severe PPH rate between baseline and trial period (%)
Legends for figures

Figure 1: Trial flow diagram

Figure 2: Rate of severe post-partum haemorrhage during baseline and trial periods for each maternity unit (Each dot represents one maternity unit. The diagonal line means no change in the PPH rate from baseline to trial period)

Figure 3: Difference in rate of severe post-partum haemorrhage (baseline rate - intervention rate) according to compliance with intervention (% of women with measured blood loss) in the 38 units in the intervention group during the trial period
References

Authors’ statements

Competing interest statement
All authors declare that the answer to the questions on your competing interest form are all No and therefore have nothing to declare.

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Contribution statements
I declare that I participated in the design of the trial, the implementation of the trial in my country, the central monitoring of data collection, writing the statistical analysis plan, the cleaning and analysis of the data and the drafting and revision of the paper and that I have seen and approved the final version. I had full access to all the data in the study and had final responsibility for the decision to submit for publication. I have no conflicts of interest.

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Clare Winter