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TITLE PAGE

Non-clinical interventions to prevent postpartum haemorrhage and improve its management: a systematic review

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STANDARD ABSTRACT

Postpartum haemorrhages (PPHs) account for around 200 deaths per year in the developed regions of the world. However, the efficacy of pharmacological and clinical interventions to prevent or manage PPHs is well established.

Our objective was to determine the effectiveness of non-clinical interventions targeting healthcare professionals, organisations or facilities in preventing PPH or improving its management.

We conducted a systematic review using the PRISMA four-step model. The MEDLINE and Cochrane databases were searched up to March 2019. Inclusion criteria were interventional studies, published in English of French language, aiming to reduce PPH outcomes for women in hospitals, regardless of study design. The studies' methodological quality was assessed according to the Cochrane EPOC criteria.

We found 32 studies that met the inclusion criteria. None met all the methodological quality criteria. Six types of non-clinical interventions were identified: guideline dissemination, audit with feedback, simulation, training, clinical pathway and multifaceted interventions. Eleven studies reported a significant reduction in PPH rates and/or its complications, five studies reported a significant increase and 16 studies no significant results.

The heterogeneity of the studies prevents us from identifying an effective non-clinical intervention in reducing PPH rates.

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Abstract word count: 189.

INTRODUCTION

Haemorrhage is the leading cause of maternal mortality worldwide [1]. With one-fifth of all maternal deaths classified as postpartum haemorrhages (PPHs), it is the most common pregnancy-related complication, resulting in more than 80 000 deaths per year [1]. These deaths are concentrated in regions with low levels of economic development, which is the main factor determining the risk of maternal death; one explanation is that many women deliver at home and are often attended by unskilled healthcare providers [1,2]. However, developed regions are not spared, with around 200 deaths per year attributable to PPH in hospitals [1].

A hospital environment with skilled personnel facilitates PPH prevention and management [3]. Associations of healthcare professionals regularly publish and update clinical guidelines on the pharmacological and/or surgical prevention and management of PPH in hospitals [4–9]. The efficacy and safety of pharmacological interventions for the prevention and management of PPH have been established for some time [10,11]. Improving prevention should reduce the overall rates (minor or major) of PPH, while improved management should reduce the rate of major PPH and of these complications, especially mortality and serious morbidity. In UK and Republic of Ireland, improvements in care might have made a difference in the outcomes of almost 60% of the 18 women who died from PPH or amniotic fluid embolism during the 2013–15 period [12]. In France, all 23 maternal haemorrhage-related deaths between 2010 and 2012 were ”avoidable” (13/23) or “possibly avoidable” (10/23), with none considered inevitable by the national committee of independent experts [13]. The potential for reducing the number of deaths from haemorrhage is clear. The partial application of the guidelines suggests that an improvement in prevention and management of PPH is feasible [14–17].

Translating guidelines from research findings to clinical practice is a long-standing concern [18]. This translation can be done through non-clinical intervention programs but only one Cochrane review targeting non-clinical interventions on an obstetrical topic was published and it was focused on unnecessary caesarean section [19]. To the best of our knowledge, no systematic review of the

74 literature describes the characteristics of non-clinical interventions for the prevention and
75 management of PPH and their efficacy in a hospital environment. The objective of the present study
76 was therefore to determine the effectiveness of non-clinical interventions in preventing PPH and
77 improving its management.
78

MATERIAL AND METHODS

We conducted a systematic literature review in four steps in accordance with the recommendations of the PRISMA Statement (Figure 1) [20,21]. In the first step, records were identified in the MEDLINE (via PubMed) and Cochrane databases from their inception through March 2019, by linking terms describing non-clinical interventions and to those describing PPH outcomes (Appendix S1). Non-clinical interventions refer to "interventions applied independently of a clinical encounter between a particular provider and patient in the context of patient care" [22]. They target women (e.g. implementation of a preventive clinical pathway), healthcare professionals (e.g. implementation of clinical practice guidelines) or healthcare organisations (e.g. establishment of a task force…). The search was restricted to records in English or French. The initial search of with MeSH terms was completed with a search in all field terms to take into account the six-month gap required for indexing in MeSH. Authors' personal knowledge was also used to identify records The snowball method was used to find new articles [23]. In the second step, two reviewers (LG and CD) independently screened the titles and abstracts of all records for eligibility. In the event of disagreement between the reviewers, records were deemed eligible. We included studies reporting PPH outcomes, as a primary or secondary outcome, for facility-based births, regardless of population, intervention or group of comparison. We excluded studies with no statistical analysis of the intervention's effect, no control group, investigating home births or aiming to improve women's access to hospital facilities. Commentaries (i.e., letters to the editor or editorials), protocols and description of programmes with no implementation were also excluded. Both reviewers (LG and CD) read the eligible articles in full. In case of disagreement, they discussed the article until reaching a consensus, if necessary by discussion with two other authors (PO and ST). In a fourth and final step, both reviewers (LG and CD) independently analysed each of the included studies, using a standardised data collection form. The methodological quality criteria, the study design, the content of the intervention and its efficacy were systematically retrieved.

The methodological quality was summarised with the scale developed by the Cochrane Effective Practice and Organisation of Care (EPOC) Review Group [24]. PPH rates (as a primary or secondary outcome) were considered reliable when they were based on a systematic measurement (with collection bag or weighing) or an objective criterion (number of deaths, or number of transfusions as a process outcome).

The description of non-clinical interventions included the country where the study took place, the number of women included according to the mode of delivery (caesarean section – CS, or vaginal delivery – VD), its objective (prevention of PPH, management of PPH, or both), the type of intervention, implementation period, evaluation period, accumulated post-intervention period (defined as the sum of the implementation and the evaluation periods), and the proportion of professionals involved.

The economy of the country of study was classified as developed, in transition, or developing, according to the United Nations classification [25]. The severity of the PPH was categorised as minor (500-1000 ml) or major (>1000 ml), as recommended by the Royal College of Obstetricians and Gynaecologists (RCOG) to differentiate the effects of non-clinical interventions on prevention from those on PPH management [26].

RESULTS

Search strategy

The electronic search and personal knowledge yielded a total of 520 records after removal of duplicates. From these, review of the full text of these publications showed that 32 studies met the inclusion criteria (Figure 1). Records identified through the MEDLINE database are available at https://www.ncbi.nlm.nih.gov/sites/myncbi/1nU7sizTmqy5r/collections/58024547/public/.

Quality assessment of the studies

No study met all EPOC criteria. Four studies were cluster randomised trials (RCTs) and 28 before-after studies. Of the four RCTs, one had PPH rates as its primary outcome [27]. Of the 28 before-after studies, 4 had objective PPH rates measures as their primary outcome [28–31]. The most common bias of the RCTs was the risk of contamination between groups, which affected 3 of the 4 trials [32–34]; among the 28 before-after studies, the most frequent source of bias was the lack of consideration by 14 studies of the spontaneous improvement of the characteristics of study and control groups (Table 1) [28,29,35–42]. Three before-after study included a contemporary control group from the implementation time to the measurement of the outcome [31,43,44]. PPH criteria differed between studies: blood loss (n=18), process outcomes (n=12), or both (n=1); one study did not define the criterion [34]. The methods used to quantify blood loss were only visually estimates (n=5) or measurement (n=5), the latter by collecting blood in a calibrated bag or by weighing the blood and collecting materials (drapes, dressings, napkins, etc.) [39,45]. Eight studies did not specify the method used to quantify blood loss and for one study the measurement method had changed between the observation and intervention period (Table 2).

Description of non-clinical interventions

The studies were published from 2004 to 2018; 11 studies were conducted in Europe, 9 in the USA, 2 in Australia, 3 in Latin America, 5 in Africa and 2 in Asia. The number of patients included ranged

146 from 419 to 197 306 women. Seventeen studies took place in 1 maternity unit and 15 studies took
147 place in more (range: 2–105 maternity units). In all, 26 studies concerned PPH after all deliveries (VD
148 and CS), while 5 examined PPH only after VD, and 1 after CS only (Table 2).
149 Four studies aimed to improve the prevention of PPH, 11 to improve the management of PPH after
150 diagnosis and 17 both to prevent and manage it. Implementation periods ranged from one day to
151 eight years. Interventions were implemented before their evaluation in 15 studies, conducted
152 simultaneously with its evaluation in 14 more, and mixed (with a refresher course) in 3. Evaluation
153 periods ranged from two months to eight years post-intervention, with 1–21 time points for
154 measurement. The accumulated post-intervention time ranged from two months to eight years. Six
155 studies reported the proportion of clinicians trained relative to the total number of staff targeted; it
156 ranged from 14% to 100% [29,30,34,35,43,46]. Eleven studies stated the percentage of professionals
157 trained without specifying a denominator, and 13 did not mention the number of trained
158 professionals. Only Nelissen *et al*. reported the number of births assisted by trained staff (Table 3)
159 [46].
160 PPH was the only obstetric complication targeted by the intervention in 26 studies; among the
161 remaining 6, it was associated with the implementation of a guideline for the management of other
162 emergency situations [27,31,34,37,44,47]. The interventions tested were a pathway (early warning
163 trigger tool; n=1), dissemination of guidelines (n=2), audit feedback (n=3), simulation (in a simulation
164 centre n=6, on-site n=4), training (n=5) and multifaceted interventions (i.e., an intervention with
165 more than one component; the number of components in the 11 such studies reviewed here ranged
166 from 3 to 7). Details of the content of the interventions are presented in Appendix S2.
167
168 ***Efficacy according to study design and intervention type***
169 Eleven studies reported a significant reduction of PPH rates after implementation of the non-clinical
170 interventions. Five studies reported a significant increase in PPH rates as a result of the non-clinical
171 intervention intended to reduce it, and 16 studies did not significantly modify PPH rates. A significant

172 reduction in PPH rates was observed in 1 of the 4 RCTs and 10 of the 28 before-after studies. The
173 sample size required was estimated in six studies, including four that reported significant results
174 [27,30,31,46]. PPH rates fell significantly in 5 of the 9 studies conducted in developing economies
175 (Africa, Asia, and Latin America), not in the only study conducted in a transitioning economy
176 (Kazakhstan), and in 6 of the 22 in developed economies (Table 2). The same types of interventions
177 were implemented regardless of the country's level of development (Appendix S2). Of the 26 studies
178 including both VD and CS populations, 7 found a significant reduction in the PPH rates, as did 4 of the
179 5 studies including an exclusively VD population; the study of an exclusively CS population did not.
180 Among the eleven studies that reported minor PPH outcomes, four found a significant reduction in
181 PPH rates [27,45,46,48], while of the twenty two that reported major PPH outcomes, nine found
182 significant reductions (Table 2) [27,28,30,35,39,40,45,48,49]. Of the four studies targeting only PPH
183 prevention, two had focused on the rate of minor PPH and one of them showed a significant
184 reduction [27]. Of the 11 studies targeting only PPH management, 7 focused on the major PPH rate
185 and 2 found that it fell significantly [30,35]. Among the 17 studies that targeted prevention and
186 management, PPH rates declined in 2 of the 4 examining minor PPH rates, 3 of the 7 looking at major
187 PPH rates and 2 of the 5 assessing all PPH (Table 2 and 3).
188 Only one study tested the impact of a clinical pathway using an early warning trigger tool and didn't
189 report a significant reduction of PPH. Neither of the 2 studies that used simple guideline
190 dissemination as an intervention reported a significant drop in PPH rates. Two of five studies that
191 used training as intervention did significantly reduce these rates. Of ten studies that used simulation
192 training as intervention, four were associated with significantly lower PPH rates, as were all three
193 studies that used audit and feedback as an intervention. Among the 11 multifaceted interventions
194 reported, 2 reported a significant decline of PPH. No relation was found between efficacy and the
195 number of components or any specific component of multifaceted interventions. For example,
196 Althabe et al. reported a significant reduction of PPH rates in an intervention with seven
197 components, as did Dumont et al. with only two [27,32]. The period of intervention implementation

198 appeared to be longer in the 12 studies reporting a positive impact (median interquartile range [IQR]:
199 9 [2–29] months) than in the 15 that did not (4 [1–13] months); the accumulated post-intervention
200 time was also greater in the positive studies (median [IQR]: 27 [15–39] months *vs.* 14 [12–24]
201 months, respectively). Of the nineteen studies reporting the number of trainees, seven showed a
202 significant reduction in PPH rates [30,35,39,40,46,49,50].

203 **COMMENT**

204 This systematic review included only 32 published studies evaluating the efficacy of non-clinical
205 interventions aimed at preventing and/or managing PPH. Overall the methodological quality and/or
206 reporting was poor. Although nearly one third of these studies reported a significant benefit from
207 non-clinical interventions, an half reported no significant difference, and five a significant negative
208 impact. It should be noted, however, that no study that used simple guideline dissemination
209 reported significant results.

210 A relatively small number of published studies have evaluated the efficacy of non-clinical
211 interventions targeting PPH in a hospital environment. This finding is surprising given the number of
212 maternal deaths due to PPH and the fact that almost all deaths due to haemorrhage are believed to
213 be potentially preventable [13,51]. Furthermore, the methodological failings of these publications
214 indicates the need for further studies on this topic, with the exception of studies of simple guideline
215 dissemination, long known to be ineffective [52].

216 The Medical Research Council (MRC) has published recommendations about experimental designs
217 for evaluating complex interventions [53–55]. These recommendations are very broad and must be
218 adapted to the local context of each medical team. However, our literature review leads us to
219 emphasise the importance of two specific recommendations of the MRC guidance. First,
220 experimental designs are preferred because they make it possible to avoid confounding the secular
221 evolution of medical practices, that is, trends over time, which are likely to influence the rate of PPH
222 independently of the intervention (e. g., induction of labour, prophylactic use of oxytocin, etc.). This
223 was the principal bias in the studies we reviewed. Secondly, the evaluation of process outcomes may
224 provide information about the functioning of non-clinical interventions, but it does not replace PPH
225 outcomes, which remain the clinical objective. They were, however, the primary endpoint for fewer
226 than half the studies included here. Furthermore, the choice of outcome must be linked to the
227 objective of the intervention. The minor PPH rate is appropriate for evaluating interventions
228 intended to improve prevention while PPH complications, such as the major PPH rate, are

229 appropriate for assessing interventions aimed at improving PPH management. In this review, only
230 half the studies used the right rate (minor or major) of PPH to evaluate a prevention or a
231 management programme.
232 In addition to the choice of minor or major PPH rates as outcomes, it is important to define how to
233 measure it. The recent core outcome sets propose that blood loss be measured to evaluate PPH rates
234 but fail to define how [56,57]. In our experience, one important difficulty of measuring blood loss to
235 characterise PPH is that it requires a certain period of practice to be able to do so accurately. This
236 point may explain the increases in PPH rates over time in the studies by Skupski et al. and Einerson el
237 al. [58,59]. A more rapidly reliable method is the shock index, based on medical constants and first
238 described in 1976 but only recently applied to the postpartum period [60,61].
239 Another potentially interesting result is that the median period of intervention implementation of
240 the studies that found a significant decrease in PPH rates was higher than that of those that did not;
241 however further studies are required for conclusions to be drawn. It is currently impossible to isolate
242 this potential result from the secular evolution of medical practices. A more general point is that the
243 insufficient quality of reporting does not allow clinicians or health decision-makers to judge the
244 applicability of published studies to their local context. One explanation for this finding may be the
245 lack of specific recommendations for reporting non-clinical interventions, but the authors of future
246 studies could use the MRC guidance and Criteria for Reporting the Development and Evaluation of
247 Complex Interventions in healthcare: revised guideline (CReDECI 2) recommendations to improve
248 reporting quality [55,62,63]. The MRC and NIHR have jointly commissioned an update of the MRC
249 guidance to be published in 2019.
250 The strength of this study lies in its search algorithm, which used a broad range of terms, without
251 restriction to a particular period or economic development level. This is underlined by the very few
252 articles identified only through personal knowledge or snowballing. The literature review was,
253 however, limited by its restriction to published studies, in English or French, referenced in MEDLINE
254 or the Cochrane Database.

255

256 **CONCLUSION**

257 International research about non-clinical interventions for improving the prevention and
258 management of PPH suffers from a severe lack of studies on this major public health issue, especially
259 compared to the many clinical studies published. Investigators should be encouraged to conduct
260 non-clinical interventions and to report all these elements with great rigour. This would allow other
261 obstetric teams to benefit from these studies.

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The authors whose names are listed immediately below certify that they have NO affiliations with or involvement in any organisation or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter of these research article.

Details of ethics approval

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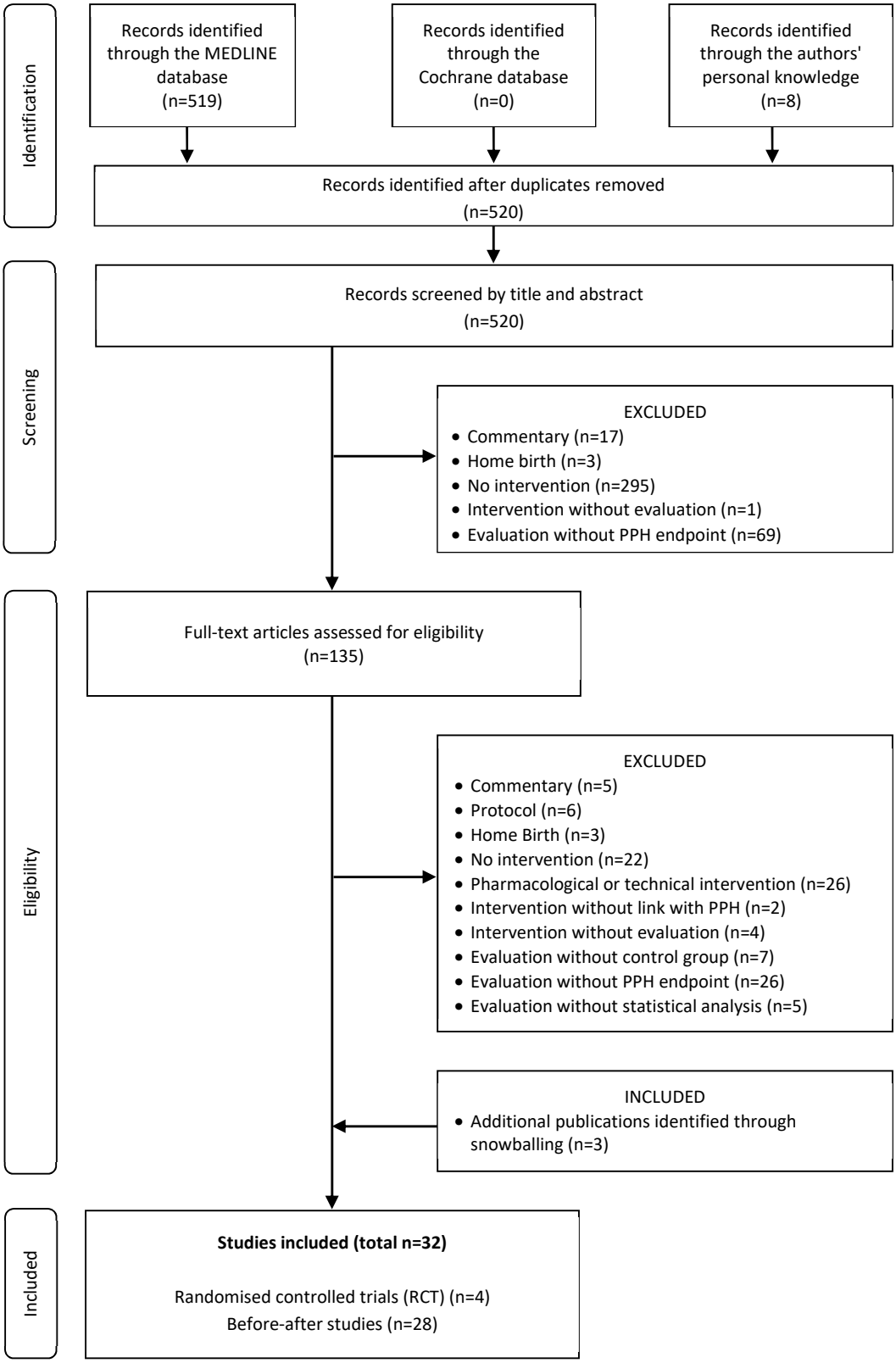

Figure 1 - Flow chart of the systematic review

Table 1 - Cochrane EPOC methodological quality criteria

Randomised Control Trials	Concealment of allocation	Follow-up of professionals (protection against exclusion bias)	Follow-up of patients or episodes of care	Blinded assessment or objective variable for primary outcome(s)	Baseline measurement	Reliable primary outcome measure(s)	Protection against contamination
Althabe et al, 2008 [27]	**DONE**	**DONE**	**DONE**	**NA**	**DONE**	**DONE**	**DONE**
Walker et al, 2016 [34]	**NC**	**ND**	**DONE**	**NA**	**DONE**	**DONE**	**ND**
Dumont et al, 2013 [32]	**DONE**	**DONE**	**DONE**	**NA**	**DONE**	**DONE**	**NC**
Deneux-Tharaux et al 2010 [33]	**DONE**	**DONE**	**DONE**	**DONE**	**ND**	**NC**	**ND**

Before-After Studies	Characteristics of study and control groups	Follow-up of professionals (protection against	Follow-up of patients	Blinded assessment or objective variable for primary outcome(s)	Baseline measurement	Reliable primary outcome measure(s)	Protection against contamination
Lee et al. 2014 [64]	**DONE**	**NC**	**DONE**	**NA**	**DONE**	**ND**	**DONE**
Da Graca et al. 2013 [65]	**DONE**	**NC**	**DONE**	**NC**	**DONE**	**ND**	**DONE**
Rizvi et al. 2004 [49]	**DONE**	**DONE**	**DONE**	**NC**	**DONE**	**ND**	**DONE**
Baldvinsdottir T et al. 2018 [66]	**ND**	**DONE**	**DONE**	**ND**	**DONE**	**ND**	**DONE**
Kumar A et al. 2018 [47]	**ND**	**DONE**	**DONE**	**ND**	**DONE**	**NC**	**DONE**
Egenberg S et al. Oct. 2017 [35]	**DONE**	**ND**	**DONE**	**NA**	**DONE**	**DONE**	**DONE**
Egenberg S et al. Sept. 2017 [30]	**ND**	**DONE**	**DONE**	**DONE**	**DONE**	**DONE**	**DONE**
Liabsuetrakul T et al. 2017 [43]	**DONE**	**NC**	**DONE**	**NC**	**DONE**	**ND**	**NC**
Fransen A et al. 2016 [31]	**DONE**	**DONE**	**DONE**	**DONE**	**DONE**	**DONE**	**DONE**
Shields LE et al. 2016 [44]	**ND**	**NA**	**DONE**	**NC**	**DONE**	**NC**	**DONE**
Ellard DR et al. 2016 [36]	**ND**	**NC**	**DONE**	**NC**	**DONE**	**NC**	**DONE**
Shoushtarian M et al. 2014 [37]	**ND**	**ND**	**DONE**	**NA**	**DONE**	**NC**	**DONE**
Skupski DW et al. 2006 [58]	**DONE**	**DONE**	**DONE**	**NC**	**DONE**	**ND**	**DONE**
Hamm RF et al. 2018 [67]	**DONE**	**DONE**	**DONE**	**NC**	**DONE**	**DONE**	**DONE**
Nelissen E et al. 2017 [46]	**DONE**	**NC**	**DONE**	**NC**	**DONE**	**ND**	**DONE**
Nadisauskiene RJ et al. 2016 [68]	**DONE**	**NC**	**DONE**	**NC**	**DONE**	**ND**	**DONE**
Einerson BD et al. 2015 [59]	**DONE**	**DO**	**DONE**	**NA**	**DONE**	**NC**	**DONE**
Egenberg S et al. 2015 [38]	**ND**	**NC**	**DONE**	**NA**	**DONE**	**ND**	**DONE**
Shields LE et al. 2015 [28]	**ND**	**NC**	**DONE**	**DONE**	**DONE**	**DONE**	**DONE**
Dupont C et al. 2014 [39]	**ND**	**DONE**	**DONE**	**NC**	**ND**	**DONE**	**DONE**
Lappen JR et al. 2013 [69]	**DONE**	**DONE**	**DONE**	**NC**	**DONE**	**NC**	**DONE**
Markova V et al. 2012 [29]	**ND**	**DONE**	**DONE**	**DONE**	**ND**	**DONE**	**DONE**
Sorensen BL et al. 2011 [45]	**DONE**	**NC**	**DONE**	**NC**	**DONE**	**DONE**	**DONE**
Dupont C et al. 2011 [40]	**ND**	**DONE**	**DONE**	**NC**	**ND**	**DONE**	**DONE**
Shields LE et al. 2011 [41]	**ND**	**NC**	**DONE**	**NC**	**DONE**	**ND**	**DONE**
Audureau E et al. 2009 [42]	**ND**	**DONE**	**DONE**	**NA**	**DONE**	**DONE**	**DONE**
Figueras A et al. 2008 [50]	**DONE**	**DONE**	**DONE**	**NA**	**DONE**	**NC**	**DONE**
Ducloy-Bouthors AS el al. 2008 [70]	**ND**	**NC**	**NC**	**NC**	**DONE**	**NC**	**DONE**

NC, not clear; ND, not done; NA, not applicable.

When the primary outcome of the study did not concern minor or major PPH rates directly, the methodological quality criterion regarding the objectivity of the primary outcome was considered not applicable.

Table 2 – Report of the efficacy according to intervention type and study design

Author. Year of publication. Country (Economic development level).	**Number of women (mode of delivery). Number of units; Year of intervention.**	**Intervention. Study design.**	**Definition of PPH as outcome. Method of estimation of blood loss.**	**PPH rates before *vs.* after intervention**	***P*-value**
Lee AI et al. 2014 **[64]**. USA (Dped).	901 (CS). 1 unit; 2008.	Guideline dissemination. Before-after study.	Blood loss >1000 ml. Visual estimation.	21% *vs.* 24%	NS
Da Graca J et al. 2013 **[65]**. USA (Dped).	1572 (VD and CS). 1 unit; 2011.	Guideline dissemination. Before-after study.	Blood loss >500 ml for VD and >1000 ml for CS. Visual estimation or weighing.	9.0% *vs.* 7.1%	NS
Althabe F et al. 2008 **[27]**. Argentina, Uruguay (Dping).	10 419 (VD). 19 units; 2003-2015.	Multifaceted intervention. RCT.	Minor PPH for blood loss ≥500 ml and major PPH for blood loss ≥1000 ml. Not detailed.	Minor PPH: • Control group: 18.6% *vs.* 6.9% • Intervention group: 9.8% *vs.* 8.1% Major PPH: • Control group: 3.0% *vs.* 0.8% • Intervention group: 1.5% *vs.* 0.6%	0.03 0.007
Rizvi F et al. 2004 **[49]**. Ireland (Dped).	6476 (VD and CS). 1 unit; 1999-2002.	Multifaceted intervention. Before-after study.	Blood loss >1000 ml. Visual estimation or weighing.	1.7% *vs.* 0.45%	0.01
Baldvinsdottir T et al. 2018 **[66]**. Sweden (Dped).	902 (VD). 1 unit, 2008.	In-centre simulation. Before-after study.	Blood loss ≥1000 ml. Visual estimation then weighing.	1632.5ml *vs.* 1738.6ml	0.03
Kumar A et al. 2018 **[47]**. Austria (Dped).	27749 (VD and CS). 3 units; 2011-2015.	Training. Before-after study.	Blood loss between 1000 and 1499ml Not detailed.	3.7% *vs.* 4.1%	NS

Egenberg S et al. Oct. 2017 **[35]**. Norway (Dped).	5446 (VD and CS). 1 unit; 2015.	On-site simulation. Before-after study.	Simple PPH for blood transfusion ≥ 1 unit; severe PPH for massive transfusion. Not detailed.	Simple PPH: 5% *vs.* 4% Severe PPH: 14% *vs.* 6%	NS 0.04
Egenberg S et al. Sept. 2017 **[30]**. Tanzania (Dping).	3308 (VD and CS). 1 unit; 2012-2014.	On-site simulation. Before-after study.	Blood transfusion for PPH management. Visual estimation.	3.2% *vs.* 1.7%	<0.01
Liabsuetrakul T et al. 2017 **[43]**. Thailand (Dping).	9459 (VD and CS). 6 units; 2011-2014.	Multifaceted intervention. Controlled before-after study.	PPH mentioned in clinical records. Visual estimation.	Control group: 1.4% *vs.* 1.7% Intervention group: 1.7% *vs.* 2.0%	NS
Fransen A et al. 2016 **[31]**. Netherlands (Dped).	56166 (VD and CS). 24 units; 2009-2011.	On-site simulation. Controlled before-after study.	Severe PPH management. Administration of >4 packed cells blood transfusion, or the performance of an embolization or hysterectomy.	0.14% *vs.* 0.28%	0.009
Shields LE et al. 2016 **[44]**. USA (Dped).	63252 (VD and CS). 29 units; 2012-2015.	Pathway. Controlled before-after study.	Blood loss >500 ml for VD and >1000 ml for CS. Not detailed.	2.9% *vs.* 2.7%	NS
Walker DM et al. 2016 **[34]**. Mexico (Dping).	50 589 (VD and CS). 24 units; 2010-2013.	In-centre simulation. Pair-matched RCT.	Not detailed. Not detailed.	Incidence rate ratio at 4, 8 and 12 months: 0.58/0.88/0.60	NS
Ellard DR et al. 2016 **[36]**. Tanzania (Dping).	49 834 (VD and CS) 16 units; 2011, 2013.	Training. Before-after study.	PPH mentioned in clinical records. Not detailed.	11.0% *vs.* 12.6%	NS
Shoushtarian M et al. 2014 **[37]**. Australia (Dped).	43 408 (VD and CS). 8 units; 2008-2011.	In-centre simulation. Before-after study.	Blood loss >1500 ml. Not detailed.	1.2% *vs.* 1.3%	NS

Skupski DW et al. 2006 **[58]**. USA (Dped).	18 723 (VD and CS) 1 unit; 2000-2005.	Multifaceted intervention. Before-after study.	Blood loss ≥1500 ml or PPH management. Not detailed.	0.2% *vs.* 0.4%	0.02
Hamm RF et al. 2018 **[67]**. USA (Dped).	1175 (VD and CS). 1 unit; 2013-2015.	Multifaceted intervention. Before-after study.	Blood loss ≥1000 ml. Visual estimation.	9.0% *vs.* 12.2%	NS
Nelissen E et al. 2017 **[46]**. Tanzania (Dping).	9446 (VD and CS). 1 unit; 2011-2013.	On-site simulation. Before-after study.	Blood loss ≥500 ml. Visual estimation.	2.1% *vs.* 1.3%	0.003
Nadisauskiene RJ et al. 2016 **[68]**. Kazakhstan (trans).	11 360 (VD and CS). 1 unit; 2012-2013.	Multifaceted intervention. Before-after study.	Simple PPH: blood loss ≥500 ml for VD or ≥1000 ml for CS; severe PPH: blood loss ≥1500 ml. Visual estimation.	Simple PPH: 1.17% *vs.* 1.02% Severe PPH: 0.24% *vs.* 0.22%	NS NS
Einerson BD et al. 2015 **[59]**. USA (Dped).	3105 (VD and CS). 1 unit; 2007-2011.	Multifaceted intervention. Before-after study.	Simple PPH: blood loss >500 ml for VD or >1000 ml for CS; severe PPH: blood loss >1500 ml. Not detailed.	Simple PPH: 5.3% *vs.* 6.0% Severe PPH: 21.5% *vs.* 26.6%	0.02 0.001
Egenberg S et al. 2015 **[38]**. Norway (Dped).	1080 (VD and CS) 1 unit; 2009, 2011.	In-centre simulation. Before-after study.	Blood loss >500 ml. Visual estimation.	11.2% *vs.* 11.2%	NS
Shields LE et al. 2015 **[28]**. USA (Dped).	32 059 (VD and CS). 29 units; 2011.	Audit and feedback. Before-after study.	Blood transfusion for PPH management. Visual estimation or weighing.	35.9‰ *vs.* 26.6‰	<0.01
Dupont C et al. 2014 **[39]**. France (Dped).	21 822 (VD). 1 unit; 2005-2012.	Audit and feedback. Before-after study.	Blood loss >1500 ml or intensive management. Measured with a collector bag.	1.2% *vs.* 0.6%	<0.001
Dumont A et al. 2013 **[32]**. Senegal & Mali (Dping).	197 306 (VD and CS) 46 units; 2008.	Multifaceted intervention. RCT.	Blood transfusion for PPH management. Not detailed.	Control group: 44.5% to 51.9% Intervention group: 43.4% *vs.* 45.7%	0.002
Lappen JR et al. 2013 **[69]**. USA (Dped).	419 (VD and CS) 1 unit; 2008-2009.	Multifaceted intervention. Before-after study.	Blood loss >500 ml for VD or >1000 ml for CS. Not detailed.	4.8% *vs.* 5.1%	NS

Markova V et al. 2012 **[29]**. Denmark (Dped).	10461 (VD and CS). 1 unit; 2003-2007.	On-site simulation. Before-after study.	Blood transfusion for PPH management. Not detailed.	Incidence rate ratio in 2003, 2005 and 2007: 1.5%/1.6%/1.2%	NS
Sorensen BL et al. 2011 **[45]**. Tanzania (Dping).	505 (VD). 1 unit; 2008.	Training. Before-after study.	Minor PPH: blood loss ≥500 ml; major PPH: blood loss ≥1000 ml. Weighing.	Minor PPH: 32.9% *vs.* 18.2% Major PPH: 9.2% *vs.* 4.3%	<0.05 <0.05
Dupont C et al. 2011 **[40]**. France (Dped).	18 804 (VD and CS). 2 units; 2005-2008.	Audit and feedback. Before-after study.	Intensive management. Visual estimation or weighing.	In hospital 1: 1.52% *vs.* 0.96% In hospital 2: 2.08% *vs.* 0.57%	0.048 <0.001
Shields LE et al. 2011 **[41]**. USA (Dped).	5813 (VD and CS) 1 unit; 2009.	In-centre simulation. Before-after study.	Simple PPH: blood loss >500 ml for VD or >1000 ml for CS; severe PPH: blood loss >1500 ml. Visual estimation or weighing.	Simple PPH successfully treated: 35% to 82% Severe PPH successfully treated: 11% to 10%	0.02 NS
Deneux-Tharaux C et al. 2010 **[33]**. France (Dped).	146 781 (VD and CS). 105 units; 2006.	Multifaceted intervention. RCT.	Intensive management. Visual estimation or measured.	1.64% *vs.* 1.65%	NS
Audureau E et al. 2009 **[42]**. France (Dped).	1219 (VD and CS). 19 units; 2002, 2005.	Multifaceted intervention. Before-after study.	Intensive management. Visual estimation or measured.	0.80% *vs.* 0.86%	NS
Figueras A et al. 2008 **[50]**. 5 countries in Latin America (Dping).	2247 (probably VD). 17 units; 2003-2005.	Training. Before-after study.	PPH mentioned in clinical records. Not detailed.	At 3 months: 12.7% *vs.* 6.9% At 12 months: 12.7% *vs.* 5.0%	<0.05 <0.05
Ducloy-Bouthors AS el al. 2008 **[70]**. France (Dped).	41992 (VD and CS). 5 units; 2004-2006.	Training. Before-after study.	Blood loss ≥500 ml. Not detailed.	0.88% vs. 1.25%	NS

Dped, Developed economies; Trans, Economies in transition; Dping, Developing economies; VD, vaginal delivery; CS, C-section; NS, not significant

Table 3 – Summary intervention description

First Author Year of publication	Intervention		Duration of the implementation	Duration of initial training and refresher course	Proportion of clinicians trained (number)	Accumulated post-intervention time	Relation between implementation and evaluation periods
Lee AI et al. 2014 [64].	P	Dissemination of guidelines	1 day	1 day Not Done (ND)	ND	2 months	Simultaneous
Da Graca J et al. 2013 [65].	P	Dissemination of guidelines	1 month	1 month ND	ND	6 months	Simultaneous
Althabe F et al. 2008 [27].	P	Multifaceted intervention	18 months	5 days and 1 day/hospital Monthly report of outcomes	ND	30 months	Simultaneous
Rizvi F et al. 2004 [49].	P	Multifaceted intervention	30 months	Not Clear (NC) ND	100%	36 months	Sequential
Baldvinsdottir T et al. 2018 [66].	M	In-centre simulation.	36 months	3 hours	100%	36 months	Simultaneous
Kumar A et al. 2018 [47].	M	Training	24 months	Half a day every month	84% (856/1021)	24 months	Simultaneous
Egenberg S et al. Oct. 2017 [35].	M	On-site simulation	2 months	Eight-hour training day repeated 1 year later	79% (82/104)	24 months	Mixed
Egenberg S et al. Sept. 2017 [30].	M	On-site simulation	2 weeks	Two weeks repeated 1 year later	84% (70/83)	13 months	Sequential
Liabsuetrakul T et al. 2017 [43].	M	Multifaceted intervention	2 months	One seminar session (unknown duration) ND	100% (105)	22 months	Simultaneous
Fransen A et al. 2016 [31].	M	In-centre simulation.	1 month	1 day (8 hours) ND	95% (447/471)	13 months	Sequential
Shields LE et al. 2016 [44].	M	Pathway	NA	NA NA	NA	13 months	Sequential
Walker DM et al. 2016 [34].	M	In-centre simulation	1 month	2 days ND	14% (450/3228)	13 months	Sequential
Ellard DR et al. 2016 [36].	M	Training	1 day	1 day ND	ND	12 months	Simultaneous
Shoushtarian M et al. 2014 [37].	M	In-centre simulation	12 months	1-day training course ND	51%	24 months	Sequential
Skupski DW et al. 2006 [58].	M	Multifaceted intervention	44 months	Weekly didactic sessions ND	100%	44 months	Simultaneous

Hamm RF et al. 2018 [67].	P and M	Multifaceted intervention	4 months	Unknown ND	ND	6 months	Sequential
Nelissen E et al. 2017 [46].	P and M	On-site simulation	1 month	Unknown ND	80% (8/10)	15 months	Sequential
Nadisauskiene RJ et al. 2016 [68].	P and M	Multifaceted intervention	4 months	Training for 2 months ND	ND	12 months	Sequential
Einerson BD et al. 2015 [59].	P and M	Multifaceted intervention	12 months	ND Periodic training for incoming staff only	100%	40 months	Simultaneous
Egenberg S et al. 2015[38].	P and M	In-centre simulation	12 months	Mandatory annual 6-h (birthing) simulator sessions ND	ND	24 months	Sequential
Shields LE et al. 2015 [28].	P and M	Audit and feedback	3 months	Initial protocol diffusion Monthly audit feedback	ND	10 months	Mixed
Dupont C et al. 2014 [39].	P and M	Audit and feedback	96 months	3 hours Every 3 months	100%	96 months	Simultaneous
Dumont A et al. 2013 [32].	P and M	Multifaceted intervention	24 months	6 days Quarterly visits by a trained external facilitator	ND	36 months	Sequential
Lappen JR et al. 2013 [69].	P and M	Multifaceted intervention	12 months	1 month ND	100%	18 months	Sequential
Markova V et al. 2012 [29].	P and M	On-site simulation	48 months	2.5-hour training session ND	100% (156)	48 months	Simultaneous
Sorensen BL et al. 2011 [45].	P and M	Training	2 days	2 days ND	ND	3 months	Simultaneous
Dupont C et al. 2011 [40].	P and M	Audit and feedback	48 months	3 hours Every 3 months	100%	48 months	Simultaneous
Shields LE et al. 2011 [41].	P and M	In-centre simulation	6 months	3 months ND	ND	18 months	Sequential
Deneux-Tharaux C et al. 2010 [33].	P and M	Multifaceted intervention	3 months	3 hours for presentation of guideline 3h for peer review, (3 months after initial intervention)	100%	14 months	Simultaneous
Audureau E et al. 2009 [42].	P and M	Multifaceted intervention	14 months	3 hours ND	100%	18 months	Sequential

Figueras A et al. 2008 [50].	P and M	Training	3 months	3 months ND	100%	15 months	Mixed
Ducloy-Bouthors AS el al. 2008 [70].	P and M	Training	ND	ND ND	ND	ND	Sequential

P, Prevention; M, Management; NA, Not applicable; ND, Not documented. Accumulated post-intervention time is defined as the sum of the implementation and the evaluation periods.