Effective Health Care Program

Management of Postpartum Hemorrhage

Executive Summary

Introduction

Postpartum hemorrhage (PPH) is commonly defined as blood loss exceeding 500 mL following vaginal birth and 1,000 mL following cesarean.[1] Definitions vary, however, and diagnosis of PPH is subjective and often based on inaccurate estimates of blood loss.[1-4] Moreover, average blood loss at birth frequently exceeds 500 or 1,000 mL,[4] and symptoms of hemorrhage or shock from blood loss may be hidden by the normal plasma volume increases that occur during pregnancy. PPH is often classified as primary/immediate/early, occurring within 24 hours of birth, or secondary/delayed/ late, occurring from more than 24 hours postbirth to up to 12 weeks postpartum. In addition, PPH may be described as third or fourth stage depending on whether it occurs before or after delivery of the placenta, respectively. Multiple studies have noted an increase in PPH in high-resource countries, including the United States, Canada, Australia, Ireland, and Norway, since the 1990s.[5-9]

PPH is a leading cause of maternal mortality and morbidity worldwide, and accounts for nearly one-quarter of all maternal pregnancy-related deaths.[10] Multiple studies have suggested that many deaths associated with PPH could be prevented with prompt recognition and more timely and aggressive treatment.[11-13]

Morbidity from PPH can be severe, with sequelae including organ failure, shock, edema, compartment syndrome, transfusion complications, thrombosis, acute respiratory distress syndrome, sepsis, anemia, intensive care, and prolonged hospitalization.[14-16]

Effective Health Care Program

The Effective Health Care Program was initiated in 2005 to provide valid evidence about the comparative effectiveness of different medical interventions. The object is to help consumers, health care providers, and others in making informed choices among treatment alternatives. Through its Comparative Effectiveness Reviews, the program supports systematic appraisals of existing scientific evidence regarding treatments for high-priority health conditions. It also promotes and generates new scientific evidence by identifying gaps in existing scientific evidence and supporting new research. The program puts special emphasis on translating findings into a variety of useful formats for different stakeholders, including consumers.

The full report and this summary are available at **www.effectivehealthcare. ahrq.gov/reports/final.cfm**.

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Effective Health Care

The most common etiology of PPH is uterine atony (impaired uterine contraction after birth), which occurs in about 80 percent of cases. Atony may be related to overdistention of the uterus, infection, placental abnormalities, or bladder distention.[17] Although the majority of women who develop PPH have no identifiable risk factors, clinical factors associated with uterine atony, such as multiple gestation, polyhydramnios, high parity, and prolonged labor, may lead to a higher index of suspicion.[14,15,17,18] Other causes of PPH include retained placenta or clots, lacerations, uterine rupture or inversion, and inherited or acquired coagulation abnormalities.[17,18]

Interventions To Manage PPH

Organizations and associations including the World Health Organization, International Confederation of Midwives, International Federation of Gynecologists and Obstetricians, American College of Obstetricians and Gynecologists, California Maternal Quality Care Collaborative, and Royal College of Obstetricians and Gynaecologists have released guidelines for PPH prevention and management.[10,15,17-21] Initial management includes identifying PPH, determining the cause, and implementing appropriate interventions based on the etiology.

 Interventions to treat PPH generally proceed from less to more invasive and include compression techniques, medications, procedures, and surgeries. PPH management may also involve adjunctive therapies, such as blood and fluid replacement and/or an antishock garment,[22,23] to treat the blood loss and other sequelae that result from PPH. PPH management varies significantly according to available resources.

Conservative management techniques, such as uterotonic medications, external uterine massage, and bimanual compression, are generally used as "first-line" treatments. Procedures used in PPH management include manual removal of the placenta, manual removal of clots, uterine balloon tamponade, and uterine artery embolization.[10,15,17,18] Laceration repair is indicated when PPH is a result of genital tract trauma.

Surgical options when other measures fail to control bleeding include curettage, uterine and other pelvic artery ligation, uterine compression sutures, and hysterectomy.[10,15,17,18] More invasive procedures (e.g., uterine balloon tamponade and uterine artery embolization) and surgical techniques are generally used after first-line conservative management has failed to control bleeding and can be considered second-line

interventions.[24] Table 1 in the full report includes brief descriptions of interventions used in PPH management.

After PPH has been controlled, followup management varies. It may include laboratory testing (e.g., hemoglobin and hematocrit), iron replacement therapy, and other interventions to assess and treat sequelae of PPH.

At a systems level, PPH has been the focus of perinatal care safety initiatives that attempt to improve patient outcomes by incorporating a variety of strategies, such as practice guidelines or protocols, simulation drills, and teamwork training.[25-29] These systems-level interventions may influence management of PPH.

Scope and Key Questions

This systematic review provides a comprehensive review of potential benefits of PPH management (medical and surgical), as well as harms associated with treatments in women with PPH. We assess intermediate outcomes, such as blood loss, hospital and intensive care unit (ICU) stay, and anemia, and longer term outcomes, including uterine preservation, fertility, breastfeeding, psychological impact and harms of treatment, and mortality related to treatment.

Key Questions

We synthesized evidence in the published literature to address the following Key Questions (KQs):

KQ1. What is the evidence for the effectiveness of interventions for management of postpartum hemorrhage?

a. What is the effectiveness of interventions intended to treat postpartum hemorrhage likely due to atony?

b. What is the effectiveness of interventions intended to treat postpartum hemorrhage likely due to retained placenta?

c. What is the effectiveness of interventions intended to treat postpartum hemorrhage likely due to genital tract trauma?

d. What is the effectiveness of interventions intended to treat postpartum hemorrhage likely due to uncommon causes (e.g., coagulopathies, uterine inversion, subinvolution, abnormal placentation)?

KQ2. What is the evidence for choosing one intervention over another and when to proceed to subsequent interventions for management of postpartum hemorrhage?

KQ3. What are the harms, including adverse events, associated with interventions for management of postpartum hemorrhage?

KQ4. What is the effectiveness of interventions to treat acute blood loss anemia after stabilization of postpartum hemorrhage?
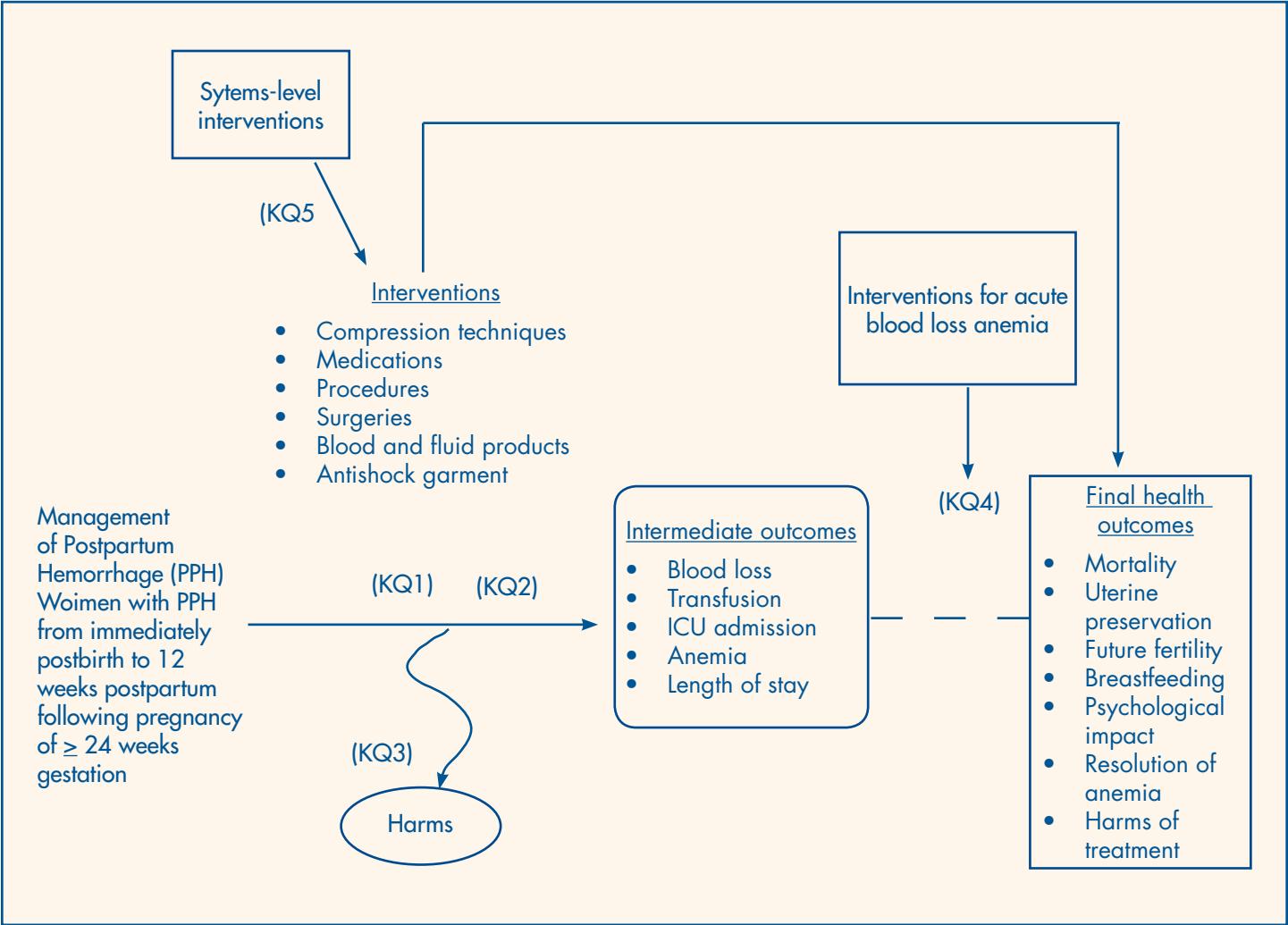
KQ5. What systems-level interventions are effective in improving management of postpartum hemorrhage?

Analytic Framework

The analytic framework illustrates the population, interventions, and outcomes that guided the literature search and synthesis (Figure A). The framework for management of PPH includes women with PPH from immediately postbirth to 12 weeks postpartum following pregnancy of at least 24 weeks' gestation. The figure depicts the KQs within the context of the population, intervention, comparator, outcomes, timing, and setting (PICOTS) parameters described in the review. In general, the figure illustrates how interventions such as compression techniques, medications, procedures, surgeries, blood and fluid products, antishock garments, or systems-level interventions may result in intermediate outcomes such as blood loss, transfusion, ICU admission, anemia, or length of stay and/or in final health outcomes such as mortality, uterine preservation, future fertility, breastfeeding, or psychological impact. Also, adverse events may occur at any point after the intervention is received.

Figure A. Analytic framework

ICU = intensive care unit; KQ = Key Question.

Methods

Literature Search Strategy

A librarian employed search strategies, provided in Appendix A of the full report, to retrieve research on interventions for PPH. We searched MEDLINE® via the PubMed® interface, the Cumulative Index of Nursing and Allied Health Literature (CINAHL®), and Embase (Excerpta Medica Database). We limited searches to the English language and to studies published from 1990 to the present in order to reflect current standards of care for PPH. Our last search was conducted in November 2014. We manually searched reference lists of included studies and of recent narrative and systematic reviews and meta-analyses.

Inclusion and Exclusion Criteria

We developed criteria for inclusion and exclusion (Table A) in consultation with a Technical Expert Panel. We limited studies to those published in English and conducted in Very High Human Development countries as ranked by the United Nations Development Programme Human Development Index (Table A). In the opinion of our clinical experts, processes of care and interventions available in these countries best reflect the system of health care in the United States. A considerable body of evidence addresses PPH management in developing countries.

However, the limited availability of skilled clinicians and treatment options in many of these countries results in different standards of care and clinical approaches from those in the United States.

PPH is a complex condition. Treatments are selected not only by PPH etiology and severity, but also by factors related to the setting of care, the availability of medications or other therapeutic options, the availability of personnel, and the standards of care in a given treatment center. Treatment availability and the feasibility of providing certain treatments differ across developed and developing nations, and even within any given nation. Because the context of care in most developing nations differs significantly from care in the United States, we instituted language and country limitations in order to identify studies that are most applicable to guiding care by clinicians in the United States, who are the intended audience for this report.

In order to provide contextual information about effectiveness and harms reported in studies conducted in developing nations, we provide summaries of recent reviews of interventions for PPH, which include studies conducted in any country, in the Discussion section (Findings in Relation to What Is Already Known) of the full report.

Table A. Inclusion criteria	
Category	**Criteria**
Study population	• KQs 1–3, 5: Women with PPH from immediately postbirth to 12 weeks postpartum following pregnancy >24 weeks' gestation • KQ4: Women with stabilized PPH and acute blood loss anemia • All modes of birth in any setting
Time period	1990 to present
Publication languages	English only
Country	Very High Human Development countries as indicated by the United Nations Development Programme Human Development Index. Countries as of April 2014 include Norway, Australia, United States, Netherlands, Germany, New Zealand, Ireland, Sweden, Switzerland, Japan, Canada, Republic of Korea, Hong Kong, Iceland, Denmark, Israel, Belgium, Austria, Singapore, France, Finland, Slovenia, Spain, Liechtenstein, Italy, Luxembourg, United Kingdom, Czech Republic, Greece, Brunei Darussalam, Cyprus, Malta, Andorra, Estonia, Slovakia, Qatar, Hungary, Barbados, Poland, Chile, Lithuania, United Arab Emirates, Portugal, Latvia, Argentina, Seychelles, and Croatia

Table A. Inclusion criteria (continued)	
Category	**Criteria**

Admissible evidence (study design and other criteria)	<u>Admissible designs</u>
	• KQs 1–2, 4: RCTs or prospective/retrospective cohort studies, population-based case series or registry studies with ≥50 cases of PPH treatment, case series of procedures (uterine balloon tamponade, uterine artery embolization) or surgical approaches with ≥50 women
	• KQ3: RCTs or prospective retrospective cohort studies, case series with ≥50 cases addressing interventions for PPH
	• KQ5: Pre-post studies related to large-scale health systems changes, RCTs, prospective/retrospective cohort studie
	<u>Other criteria</u>
	• Original research studies that provide sufficient detail regarding methods and results to enable use and adjustment of the data and results
	• Studies targeting women with PPH who meet the population criteria described above
	• Studies that address:
	  – Treatment modality aimed at treatment/management of PPH in a relevant population or treatment for acute blood loss anemia following stabilization of PPH
	  – Outcomes related to interventions; primary outcomes of interest include blood loss, transfusion, ICU admission, anemia, length of stay, mortality, uterine preservation, future fertility, breastfeeding, and psychological impact, as well as harms
	• Studies must include extractable data presented in text or tables (vs. solely in figures) on relevant outcomes
	• For KQ5, studies must explicitly assess effects of a systems-level intervention on PPH management as a primary or secondary aim; analytic models must indicate data analysis of the effect of the strategy as it relates to PPH treatment; results data include information about effects of strategy on management of PPH; discussion interprets the strategy as potentially having value/not having value for PPH management

ICU = intensive care unit; KQ = Key Question; PPH = postpartum hemorrhage; RCT = randomized controlled trial.

Study Selection

Two reviewers independently assessed each abstract. If one reviewer concluded that the article could be eligible based on the abstract, we retained it for review of the full text. Two reviewers independently assessed the full text of each included study, with any disagreements adjudicated by a senior reviewer.

Data Extraction and Synthesis

We extracted data from included studies into evidence tables that report study design, descriptions of the study population (for applicability), description of the interventions, and baseline and outcome data on constructs of interest. Data were initially extracted by one team member and reviewed for accuracy by a second. The final evidence tables are presented in Appendix D of the full report.

We completed evidence tables for all included studies, and data are presented in summary tables and analyzed qualitatively in the text. We did not conduct meta-analyses, given significant heterogeneity in the study populations, interventions, and outcomes.

Quality (Risk-of-Bias) Assessment of Individual Studies

We used tools appropriate for specific study designs to assess quality/risk of bias of individual studies: the Cochrane Risk of Bias tool for randomized trials;[30] the Newcastle-Ottawa Scale for Non-Randomized Studies;[31] the National Heart, Lung, and Blood Institute scale for pre-post studies;[32] a tool for case series adapted from RTI Item Bank questions;[33] and a four-item harms assessment instrument for cohort studies derived from the McMaster Quality Assessment Scale of Harms (McHarm) for Harms Outcomes[34] and the RTI Item Bank.[33] Appendix B of the full report includes questions used in each tool.

Two team members independently assessed each included study, with discrepancies resolved through discussion to reach consensus and/or adjudication by a senior reviewer. The results of these assessments were then translated to the Agency for Healthcare Research and Quality standard of "good," "fair," and "poor" quality designations, as described in the full report. Quality ratings for each study are in Appendix E of the full report.

Strength of the Body of Evidence

Two senior investigators graded the body of evidence for key intervention/outcome pairs using methods based on the "Methods Guide for Effectiveness and Comparative Effectiveness Reviews."[35] The team reviewed the final strength-of-evidence designation. The possible grades were:

- High: High confidence that the evidence reflects the true effect. Further research is unlikely to change estimates.

- Moderate: Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of effect and may change the estimate.

- Low: Low confidence that the evidence reflects the true effect. Further research is likely to change confidence in the estimate of effect and is also likely to change the estimate.

- Insufficient: Evidence is either unavailable or does not permit a conclusion.

Applicability

We assessed applicability by identifying potential PICOTS factors likely to affect the generalizability of results (i.e., applicability to the general population of women being treated for PPH). We considered factors related to the availability of interventions; severity of PPH; characteristics of the population, such as mode of birth, that may be associated with PPH; and setting of the intervention as particularly likely to affect applicability.

Results

Article Selection and Overview

We identified 3,266 nonduplicative titles or abstracts with potential relevance, with 920 proceeding to full-text review. We excluded 844 studies at full-text review and included 68 unique studies (76 publications) in the review. We present findings by intervention and outcome area where possible under each KQ. For KQ1, we integrated discussion of subquestions because there was not adequate

distinction in the literature to address different etiologies separately.

While a number of studies were classified as prospective or retrospective studies using our study classification algorithm (Appendix G of the full report), few cohort studies provided comparative analyses between the groups, and many were confounded by indication in that women who received interventions such as massive transfusion or hysterectomy likely had more severe cases of PPH. Additionally, initial management of PPH using first-line interventions such as uterotonics and uterine massage differed across studies and across women, as each study generally included a number of patients transferred from other hospitals. Thus, populations were heterogeneous in terms of severity and level of stabilization prior to second-line interventions. Given the lack of data from randomized or controlled studies of PPH management, we present data from cohort studies and case series, and note potential confounding.

The following sections summarize findings within the literature meeting our criteria. Overall, the evidence to answer questions about PPH management did not reach standards for high strength of evidence (Tables B–E). We briefly summarize strength-of-evidence findings in each section below and provide a full discussion of strength-of-evidence assessment in the Discussion section of this Executive Summary and in the full report.

KQ1. Effectiveness of Interventions for Management of PPH

Fifty-one unique studies examined the effectiveness of interventions for management of PPH. Some studies addressed multiple interventions. We classified these studies broadly as medical interventions, procedures, and surgical interventions, and more specifically by the type of intervention, including pharmacologic interventions (12 studies), transfusion as an intervention for management of acute PPH (4 studies), intrauterine balloon tamponade (5 studies), embolization (19 studies), uterine compression sutures (3 studies), uterine and other pelvic artery ligation (5 studies), embolization and hysterectomy (1 study), hysterectomy (8 studies), and combined approaches (4 studies). Studies that address transfusion as an intervention for anemia once PPH is stabilized are summarized under KQ4.

Pharmacologic Interventions

We identified few studies of pharmacologic interventions for PPH that met our review criteria (n = 12). Six small studies of fair and poor quality each addressed different drugs. One retrospective cohort study reported successful

control of bleeding following oxytocin and other uterotonics in 49 percent of women. One randomized controlled trial (RCT) of tranexamic acid versus no tranexamic acid reported significantly less blood loss, duration of bleeding, and need for transfusion in the tranexamic acid arm compared with control. A cohort study comparing misoprostol and methylergonovine reported no group differences in transfusion or need for other treatments or surgeries. Case series of sulprostone and carboprost tromethamine reported control of bleeding without additional procedures or surgeries in 83 and 88 percent of participants, respectively, and a cohort study assessing recombinant human soluble thrombomodulin reported greater D-dimer decreases in women with PPH and disseminated intravascular coagulopathy treated with thrombomodulin than in matched controls.

Six small studies of recombinant activated factor VIIa (rFVIIa) had mixed results. In one retrospective cohort study, women in the rFVIIa group required more blood products and had greater blood loss than women not receiving the treatment. In a case-control study, differences in change in prothrombin time were not significant between women treated with rFVIIa and those who were not. Used as a second-line intervention, rFVIIa controlled bleeding without the need for further procedures or surgeries in 27 to 31 percent of women in one cohort study, a rate that was similar to the rate for treatment with other second-line interventions in that study. In registry studies, bleeding was considered improved after one or multiple doses of rFVIIa in 64 to 80 percent of women after the final dose. No study included more than 177 women receiving rFVIIa.

Strength of evidence is insufficient for all outcomes of each of the agents studied (oxytocin and other uterotonics, misoprostol, tranexamic acid, carboprost tromethamine, thrombomodulin, and rFVIIa) for PPH management due to the study sizes and lack of studies addressing each agent.

Transfusion for Supportive Management of Ongoing PPH

Three studies of fair quality and one of poor quality addressed transfusion for supportive management of PPH. Two of the studies found that ICU admissions and death were higher with combined blood products versus single (whole blood or packed red blood cells) and massive transfusion versus nonmassive transfusion. These differences may reflect that women in the groups with poorer outcomes had more severe PPH. A third study found that estimated blood loss, blood products transfused, and mean length of stay did not differ between cryoprecipitate and fibrinogen concentrate groups, and

a fourth reported reduced use of blood products after the introduction of fibrinogen. Strength of evidence for outcomes related to transfusion is insufficient. While there were three fair-quality studies of transfusion, two of them were so confounded that we could not confidently ascertain their outcomes.

Procedures

Both of the procedures assessed in the studies we reviewed (uterine balloon tamponade, embolization) showed positive results for PPH management. The median success rate (defined as control of bleeding without additional procedures or surgeries) of intrauterine balloon tamponade as the initial second-line procedure (i.e., first procedure following conservative management) was 75 percent in three studies reporting data on success. In one study of a protocol change to add balloon tamponade as the initial procedure after medication failure, rates of some invasive procedures (beyond tamponade) decreased in women who had vaginal births. The median success rate for embolization as the initial second-line procedure among 15 studies providing such data was 89 percent (range, 58% to 98%). However, there was wide variation in the materials used for embolization, the arteries that were embolized, and the interventions that were used before and in conjunction with embolization. The availability of embolization, which is performed by an interventional radiologist, varies by hospital; therefore, this treatment modality is not available to all women with PPH. Strength of evidence for outcomes related to uterine balloon tamponade is insufficient, given the small number of studies and small sample sizes.

Strength of evidence is low for embolization controlling bleeding without additional procedures or surgeries.

Surgical Interventions

The effectiveness of surgical interventions varied. The success rate of uterine compression sutures was 60 and 70 percent in the two studies from which this could be ascertained. Ligation had a median success rate of 92 percent in three studies (range, 36% to 96%). Hysterectomy used as the first procedure after conservative management controlled bleeding without further surgeries or procedures in a median of 57 percent of women (range, 20% to 93%) in two studies. One study compared embolization and hysterectomy, and reported significantly more ICU admissions and a greater median length of stay in the hysterectomy group than the embolization group. Strength of evidence is insufficient for the success of uterine compression sutures and hysterectomy in controlling bleeding, given the few studies available.

Strength of evidence is low for ligation controlling bleeding without further procedures or surgeries.

Combined Approaches

Three studies examined a combination of medical and surgical interventions for secondary PPH. Interventions included conservative management (including uterotonics), transfusion, surgical evacuation, curettage, and hysterectomy. In the two studies that compared medical and surgical approaches, hospital readmission and repeat surgical evacuation occurred more frequently in women who initially received medical management versus surgical. One cohort study of women with primary PPH reported greater need for transfusion, ICU admission, and greater hospital length of stay in women undergoing procedures and/or surgery compared with women who were medically managed. Strength of evidence for studies of combination interventions and length of stay was insufficient, given the small sample sizes and inconsistency in interventions.

KQ2. Evidence for Choosing Interventions and Proceeding to Subsequent Interventions

We did not identify any studies addressing this question.

KQ3. Harms of Interventions for PPH

Harms varied considerably across the 50 studies reporting harms data. Harms were generally mild in the few studies of medications that met our review criteria. Four studies of rFVIIa reported on thrombotic events, but sample sizes were small and studies were of fair to poor quality. Few studies of uterine balloon tamponade reported adverse events, and studies of embolization reported on subsequent menstrual changes, infertility, and pregnancy complications, including spontaneous abortion. Few women, however, were followed long term, and rates of such complications ranged from 0 to 43 percent across studies. Two small studies assessing uterine compression sutures and preterm birth reported no differences in preterm births between cases and controls, and studies of ligation and hysterectomy reported primarily on operative injuries and reoperation.

Strength of evidence for harms of interventions was typically insufficient, given the diversity of harms reported in single studies. Strength of evidence was low for hematoma, infertility, and menstrual changes associated with embolization and low for a lack of association between embolization and spontaneous abortion. Strength of evidence was also low for the association between hysterectomy and operative organ damage and reoperation

due to the greater number of studies and more consistent reporting of adverse events.

KQ4. Effectiveness of Interventions for Acute Blood-Loss Anemia After Stabilization of PPH

Two small poor-quality RCTs addressed interventions for acute blood loss after PPH is stabilized. In a study comparing women treated with intravenous versus oral iron supplementation after PPH, there was no significant difference in hemoglobin level between groups at any time point. In a study that assessed differences in fatigue and quality of life between women treated with blood transfusion versus no transfusion, the difference in these outcomes between groups was minimal and possibly clinically equivalent. Strength of evidence is insufficient for all outcomes and harms in studies of interventions for anemia after PPH, given the few studies, small number of participants, and differences in intervention approaches.

KQ5. Effectiveness of Systems-Level Interventions

Across a range of systems-level interventions that range from a complex multiphase project with 11 distinct components to simple 3-component models for audit and feedback, findings are inconsistent about benefit. All sites, including those participating in the active sites of a null cluster randomized trial, were aware of a programmatic emphasis on improving response to and outcomes of PPH. Despite this built-in bias toward finding an effect—since estimated blood loss was rarely quantitatively measured and self-report of performance would be expected to be optimistic—results of a large trial and the higher quality studies do not demonstrate ability to reduce incidence or severity of PPH, or key maternal outcomes such as transfusion, hysterectomy, and ICU admission. Strength of evidence is moderate for a lack of benefit for systems-level interventions in reducing PPH incidence or severity, preventing hysterectomy, or affecting ICU admissions. Strength of evidence is moderate for no effect on the need for transfusion and insufficient for effects on mortality.

Discussion

Key Findings

We included 68 unique studies (76 publications) in this review, including 4 RCTs, 2 prospective and 14 retrospective cohort studies, 10 pre-post studies (studies that compare PPH management and/or outcomes before and after an intervention, such as introduction of a new protocol), 4 case-control studies, and 34 case series. Most

studies were conducted in Europe (n = 33), and 18 were conducted in the United States or Canada, 13 in Asia, 3 in Australia or New Zealand, and 1 in Argentina. No studies were of good quality for effectiveness outcomes. We considered 23 studies as fair quality for effectiveness outcomes and 38 as poor (including case series, which we considered poor quality by default). Seven studies provided only harms data. Among the 50 studies reporting harms, we considered 11 as good quality for harms reporting and the remainder as poor quality.

Six small studies of fair and poor quality addressed different pharmacologic agents. Three studies, each of different agents (oxytocin and other uterotonics, tranexamic acid, sulprostone, carboprost tromethamine), reported reduced bleeding or control of bleeding. One study comparing misoprostol and methylergonovine reported no group differences in outcomes, and one of recombinant human soluble thrombomodulin to treat disseminated intravascular coagulation reported greater decrease in D-dimer in the thrombomodulin arm. Six small studies of rFVIIa had mixed results related to need for transfusion and control of bleeding.

Medications commonly used for PPH in the United States are oxytocin, methylergonovine maleate, carboprost tromethamine, and misoprostol. One study that met our inclusion criteria addressed oxytocin; one study included methylergonovine maleate and misoprostol. Because evidence regarding first-line management, particularly pharmacologic management, is critical for decisionmaking by clinicians and guidelines developers, we summarize findings from other recent studies of agents and interventions conducted in any country in the Discussion section of the full report.

The success of uterine-sparing techniques, such as uterine balloon tamponade, embolization, uterine compression sutures, and uterine and other pelvic artery ligation, in controlling bleeding without the need for additional procedures or surgeries ranged from 36 to 98 percent. However, these data come from a limited number of studies with a small number of participants. Harms reporting was limited to 50 studies and was difficult to synthesize because diverse adverse events were reported inconsistently across studies. Only two studies addressed interventions for anemia after PPH is stabilized. Systems-level interventions (n = 9 studies) showed little benefit in reducing the incidence or severity of PPH or the need for transfusion or hysterectomy.

Strength of Evidence

We included case series in our assessment of strength of evidence for harms and success rates of procedures and surgeries, and we rated strength of evidence for outcomes we considered to be clinically significant, consistently defined, and plausibly linked to the intervention. Overall, the evidence to answer questions about PPH management did not reach standards for high strength of evidence (Tables B–E). Strength of evidence was insufficient for all interventions/outcomes except for the success of embolization and ligation in controlling bleeding without further procedures or surgeries, which had low strength of evidence.

Strength of Evidence for Interventions To Manage PPH

The strength of evidence for interventions is summarized below:

Pharmacologic interventions. Strength of evidence is insufficient for all outcomes of each agent studied (oxytocin and other uterotonics, misoprostol, tranexamic acid, carboprost tromethamine, thrombomodulin, and rFVIIa) for PPH management because of the study sizes and lack of studies addressing each agent.

Transfusion for supportive management of PPH. While three fair-quality studies addressed transfusion, two of them were so confounded that we could not confidently ascertain their outcomes; thus, strength of evidence for all outcomes in insufficient.

Uterine balloon tamponade. Strength of evidence for the success of uterine balloon tamponade in controlling bleeding is insufficient.

Uterine artery embolization. Strength of evidence for embolization controlling bleeding without additional procedures or surgeries is low because of a lack of comparative studies and small sample sizes in studies providing data to assess success of the intervention.

Uterine compression sutures. Strength of evidence is insufficient for the success of uterine compression sutures.

Uterine and other pelvic vessel ligation. Strength of evidence is low for ligation controlling bleeding without further surgeries or procedures.

Hysterectomy. Strength of evidence is insufficient for all outcomes of hysterectomy.

Combined interventions. Strength of evidence is insufficient for all outcomes.

As noted, we identified few studies of medications meeting our review criteria. However, a number of studies of misoprostol and oxytocin have been conducted in developing countries. Four recent systematic reviews of interventions for PPH, including two Cochrane reviews, assessed uterotonics, including misoprostol. We summarize these reviews fully in the Findings in Relation to What Is Already Known section in the full report and provide a brief summary here.

In one Cochrane review, oxytocin infusion was more effective and caused fewer side effects than misoprostol when used as first-line therapy for the treatment of primary PPH. When used after prophylactic uterotonics, misoprostol and oxytocin infusion had similar effects.

The review concluded that adding misoprostol for women receiving treatment with oxytocin did not appear to be beneficial. In another Cochrane review, differences in maternal mortality and morbidity, except for fever, did not differ significantly between misoprostol and control groups. The investigators concluded that misoprostol did not increase or decrease morbidity or mortality, with the exception of fever, and the lowest effective dose should be used. In another review of misoprostol versus placebo, misoprostol did not reduce PPH risk significantly compared with placebo. In the fourth review and meta-analysis, higher doses of misoprostol (600 vs. 400 micrograms) were no more effective at preventing blood loss.

Table B. Summary of evidence in studies addressing effectiveness of interventions (KQ1)

Category	Intervention	Key Outcome(s)	Strength of Evidence Grade	Findings
Pharmacologic Interventions	Oxytocin and other uterotonics	Control of bleeding	Insufficient	Control of bleeding in 45/91 women (49%) receiving oxytocin and other uterotonics in a single short-term study with high study limitations.
	Tranexamic acid vs. no tranexamic acid	Anemia, transfusion, blood loss, ICU stay	Insufficient	Less blood loss, need for transfusion, and progression to severe PPH in TXA group vs. control (p <.05) reported in a single small short-term cohort study with high study limitations.
	Misoprostol vs. methylergonovine maleate	Transfusion, uterine preservation	Insufficient for superiority of 1 agent over another in affecting any outcome	No group differences in need for transfusion or additional medical or surgical treatments in a single small short-term cohort study with high study limitations.
	Sulprostone	Success in controlling bleeding	Insufficient	In a single short-term study with high study limitations, bleeding was controlled in 83% of 1,370 women.
	Carboprost tromethamine	Success in controlling bleeding	Insufficient	In a single short-term study with high study limitations, bleeding was controlled by carboprost in 81% of 237 cases of PPH.

Table B. Summary of evidence in studies addressing effectiveness of interventions (KQ1) (continued)

Category	Intervention	Key Outcome(s)	Strength of Evidence Grade	Findings
Pharmacologic Interventions (continued)	Thrombomodulin vs. no thrombomodulin	Uterine preservation, bleeding, transfusion	Insufficient	Greater D-dimer decrease from baseline in intervention arm vs. control in a single small short-term cohort study with high study limitations.
	RFVIIa	Transfusion, anemia, uterine preservation, LOS	Insufficient	Need for transfusion was greater with rFVIIa in 1 small study with high study limitations and not different in another. Rates of hysterectomy, LOS were similar.
Other Medical Interventions	Transfusion for supportive management of ongoing PPH	ICU admission, LOS	Insufficient	Inconsistency in direction of effect (greater LOS and ICU admission in transfusion or whole blood groups in 2 studies; no group differences in another study); high study limitations.
Procedures	Uterine tamponade	Success in controlling bleeding	Insufficient	Tamponade without further procedure or surgery controlled bleeding in 75-86% of women in 3 studies, and tamponade plus additional intervention controlled bleeding in 86-98% in another, but studies were small with high study limitations.
	Embolization	Success in controlling bleeding	Low for positive effect in controlling bleeding	Median success rate of 89% as initial second-line intervention in 15 studies with high limitations; conservative management and severity of PPH varied across studies. A higher SOE is not possible due to the lack of comparisons in this literature and small sample sizes.
Surgeries	Uterine compression sutures	Success in controlling bleeding	Insufficient	In 2 small studies with medium limitations, bleeding controlled by suture following conservative management in 60-70% of women.
	Ligation	Success in controlling bleeding	Low for positive effect in controlling bleeding	92% success rate for controlling bleeding without further procedure or surgeries in 3 small studies of ligation alone with medium study limitations. Ligation with or without suture controlled bleeding in 91% in 1 case series.
	Hysterectomy	LOS, ICU admission	Insufficient	Insufficient SOE due to few comparative studies, high limitations.

Table B. Summary of evidence in studies addressing effectiveness of interventions (KQ1) (continued)

Category	Intervention	Key Outcome(s)	Strength of Evidence Grade	Findings
Other Interventions	Combined interventions	LOS in women with primary and secondary PPH	Insufficient	Greater LOS in women with primary PPH undergoing procedures/surgeries vs. medical management in 1 small study with high limitations. No differences in LOS between surgical and medical management groups in 2 small studies with high limitations addressing secondary PPH.

ICU = intensive care unit; KQ = Key Question; LOS = length of stay; PPH = postpartum hemorrhage; rFVIIa = recombinant activated factor VIIa; SOE = strength of evidence; TXA = tranexamic acid.

Strength of Evidence for Harms of Interventions

Generally strength of evidence was insufficient, given the diversity of harms reported in single studies. However, strength of evidence rose above insufficient for selected harms related to uterine compression sutures, embolization, and hysterectomy because of the greater number of studies and more consistent reporting of adverse events (Table C).

As noted, few studies of uterotonics met our inclusion criteria. However, harms reported in recent systematic reviews of uterotonics for PPH treatment included shivering and fever. (See Findings in Relation to What Is Already Known section in the full report for more information.) In one review, oral misoprostol was associated with a significant increase in vomiting and shivering compared with either oxytocin or rectal misoprostol. In another review, differences in maternal mortality and morbidity, except for fever, did not differ significantly between misoprostol and control groups. Risk of fever was increased in misoprostol groups and was highest in studies with a misoprostol dose of 600 micrograms or more. In another review of misoprostol versus placebo, shivering and fever were significantly more common in misoprostol arms. A fourth review noted more adverse effects related to misoprostol than placebo.

While evidence in the current review was insufficient to comment on the association between rFVIIa and thrombolic events, studies in other populations have suggested increased risk of arterial events. In one review of RCTs in nonhemophilia patients, the pooled relative risk of thrombolic events across studies of prophylactic and therapeutic uses of rFVIIa was 1.45 (95% confidence interval, 1.02 to 2.05). Another review of fertility outcomes following embolization, ligation, and sutures concluded that the techniques reviewed did not appear to compromise fertility, but the number and quality of studies were limited.

Table C. Summary of evidence in studies addressing harms of interventions (KQ3)

Intervention Category	Intervention	Key Outcome(s)	Strength of Evidence Grade	Findings
Pharmacologic Interventions	Tranexamic acid	All harms	Insufficient	In 1 small RCT with low study limitations, serious harms did not differ between groups and mild transient harms occurred more often in TXA group.
	Sulprostone	All harms	Insufficient	Insufficient SOE, as there was only 1 study considered poor quality for harms reporting.
	Methylergonovine maleate	Acute coronary syndrome and myocardial infarction	Low SOE for lack of association of methylergonovine maleate with acute coronary syndrome and myocardial infarction	No significant difference in the incidence of these conditions in the exposed and nonexposed groups in 1 large cohort study with low study limitations.
	Carboprost tromethamine	All harms	Insufficient	Insufficient SOE, as there was only 1 study considered poor quality for harms reporting.
	RFVIIa	Thromboembolic events	Insufficient	4 of 5 studies (unclear overlap in 2 studies) reported thromboembolic events (pulmonary embolus, deep vein thrombosis, myocardial infarction), but sample sizes were small and study limitations high.
Other Medical Interventions	Transfusion for supportive management of ongoing PPH	All harms	Insufficient	Inconsistency in harms reported in 7 studies with high study limitations.
Procedures	Uterine tamponade	All harms	Insufficient	Small studies with high limitations and few harms reported.
	Embolization	Infertility	Low SOE for negative effect of embolization on future fertility	Infertility rate among women who had embolization in these studies was greater than that of the overall population (range, 0 to 43%), but few women (n = 300) available for long-term followup; high study limitations and inconsistency in 5 studies.

Table C. Summary of evidence in studies addressing harms of interventions (KQ3) (continued)

Intervention Category	Intervention	Key Outcome(s)	Strength of Evidence Grade	Findings
Procedures (continued)	Embolization (continued)	Spontaneous abortion in subsequent pregnancy	Low SOE for lack of association between embolization and spontaneous abortion in subsequent pregnancy	Small number of women followed up; rates of miscarriage ranged from 5% to 21.4% in 7 studies with high study limitations. Rates were comparable to estimates in the general population.
		Menstrual changes	Low SOE for an association between embolization and subsequent menstrual changes	Rates of menstrual change, including heavier, lighter, or irregular menses and amenorrhea, ranged from 2% to 22% in 8 studies with high limitations.
		Hematoma	Low SOE for association between embolization and hematoma	Rates ranged from 1.7% to 6% in 7 studies with high limitations.
Surgeries	Uterine compression sutures	Preterm birth	Low SOE for no effect on subsequent preterm birth	In 2 studies with medium limitations, preterm births did not differ between women in case and control arms in subsequent pregnancies.
	Ligation	Surgical injury	Insufficient	High study limitations and imprecision in 2 studies. Injuries (inadvertent ligation of the ureters and secondary hysterectomy disunion with sepsis) related to ligation reported in both studies.
	Hysterectomy	Bladder and ureter lesions	Low SOE for association of hysterectomy and operative organ damage	Rates of bladder and ureter lesions ranged from 6% to 12% and 0.4% to 41%, respectively, in 6 small studies with high study limitations
		Reoperation	Low SOE for association between hysterectomy and reoperation	Rates of reoperation ranged from 1.8% to 29% in 5 small studies with high study limitations.

KQ = Key Question; PPH = postpartum hemorrhage; RCT = randomized controlled trial; rFVIIa = recombinant activated factor VIIa; SOE = strength of evidence; TXA = tranexamic acid.

Strength of Evidence for Interventions for Anemia

There is insufficient strength of evidence for all outcomes and harms in studies of interventions for anemia after PPH is stabilized, given the few studies, small number of participants, and differences in intervention approaches (Table D).

Table D. Summary of evidence in studies addressing interventions for anemia after PPH (KQ4)			
Intervention	**Key Outcome(s)**	**Strength of Evidence Grade**	**Findings**
Iron supplementation	Anemia	Insufficient	No differences in groups receiving oral vs. intravenous iron in 1 small RCT with high study limitations and indirect outcomes.
Transfusion for anemia	Fatigue	Insufficient	No significant group differences in 1 small RCT with high study limitations.
	Quality of life	Insufficient	No significant group differences in 1 small RCT with high study limitations.
Iron supplementation and transfusion for anemia	All harms (transfusion reactions, infections, endometritis, thromboembolic events)	Insufficient	Of 2 small RCTs, harms were not prespecified in 1 study. No serious adverse reactions were attributed to the study drugs in either RCT but reporting in 1 RCT is not clear.

KQ = Key Question; PPH = postpartum hemorrhage; RCT = randomized controlled trial.

Strength of Evidence for Systems-Level Interventions

Overall the strength of evidence for any systems-level intervention on any outcome is insufficient or moderate, as the observational data are biased and a single very large trial suggests that at least one clearly described and implemented program did not change risk of severe hemorrhage or meaningfully modify processes of care or overall maternal outcomes. Strength of evidence is moderate that these multicomponent interventions did not change specific outcomes, such as severity of PPH, transfusion, hysterectomy, and ICU admission (Table E).

Table E. Summary of evidence in studies addressing systems-level interventions for PPH (KQ5)

Intervention	Key Outcome(s)	Strength of Evidence Grade	Findings
Systems-Level Approaches	Incidence of PPH	Moderate SOE for lack of benefit in reducing PPH incidence	Sites were aware of objectives with regard to reducing PPH, and assessors of a somewhat subjective outcome were not masked in 1 large cluster RCT with medium study limitations.
	Severity of PPH	Moderate SOE for lack of benefit in reducing severity of PPH	Sites were aware of objectives with regard to reducing severity of PPH, and assessors of a somewhat subjective outcome were not masked. Severity was unchanged in 1 RCT, reduced in 2 pre-post studies, and had no difference in 3. Mean estimated blood loss >1,000mL declined in 1 study and increased in another.
	Transfusion	Moderate SOE for no effect on transfusion	Transfusion was unchanged in 1 RCT, increased in 1 pre-post study, and was unchanged in 2; 1 study found decreased use of total blood products related to decrease in risk of disseminated intravascular coagulation; another found decreased overall use of transfusion and blood products.
	Hysterectomy	Moderate SOE for lack of benefit in preventing hysterectomy	Hysterectomy was unchanged in 1 RCT with low study limitations. There was no significant change in 3 pre-post studies, in which hysterectomies increased in 2 and declined in the third. Risk significantly increased in 1 study and was similar between time periods in a third.
	ICU admission	Moderate SOE for lack of benefit	No change in 1 RCT and no change in 2 pre-post studies, all with low study limitations.
	Mortality	Insufficient SOE for benefit	Only 1 small pre-post study with medium study limitations reported on changes in mortality.

ICU = intensive care unit; KQ = Key Question; PPH = postpartum hemorrhage; RCT = randomized controlled trial; SOE = strength of evidence.

Applicability

Studies differed in terms of study population and outcome measures. Most studies did not make direct comparisons between treatments or characterize populations well in terms of severity of PPH and prior management strategies. This lack of direct comparison of treatment options hinders our ability to understand what treatments are most effective and in what order they should be used, both of which are paramount questions for clinicians. Overall, findings of studies in the review are generally applicable to the population of women who would be experiencing PPH in hospitals in high-resource nations. Most studies were conducted in Europe or the United States in tertiary care centers. Studies frequently included a number of women with PPH who were transferred from smaller or community hospitals, which can occur when women with PPH requiring additional treatment are stable enough to be moved to facilities with interventional radiology or other services. More women had PPH after cesarean birth than vaginal birth in the 50 studies reporting mode of birth (estimated 6,304 vaginal and 7,924 cesarean births among the 14,228 births for which mode was clearly reported). The most common cause of PPH was atony, which aligns with the most frequent cause of PPH in the larger community and literature. Studies of pharmacologic agents typically included women with mild to moderate PPH, while studies

of procedures or surgical approaches generally included women with more severe PPH that had not been controlled with first-line therapies such as uterotonics.

The uterotonics, blood products, and iron supplements studied are generally widely available; however, the accessibility of procedures such as embolization may be limited in smaller community hospitals. Similarly, community hospitals may lack personnel with experience with arterial ligation and compression sutures. Comparators across studies with more than one group were typically either no specific treatment (e.g., rFVIIa or no rFVIIa) or another treatment (e.g., embolization or ligation) and are likely confounded by patient and provider characteristics that may have affected the choice of intervention. For example, patients with more severe hemorrhage likely received more aggressive treatment, and providers could offer only the options available in their facilities. Outcomes addressed across studies were appropriate and clinically relevant; however, few studies reported longer term outcomes such as future fertility or patient-centered outcomes such as quality of life.

The populations included in the systems-level interventions, both in the United States and Europe, are similar in size and type (rural, academic, etc.) to current labor and delivery environments in the United States. Likewise the interventions designed and implemented in these studies were informed by processes of identifying evidence and crafting guidance that conform to typical quality improvement and outcomes-based research. The content of the interventions is feasible to implement across a full range of settings, and the approaches to measuring outcomes are applicable to practice. Overall the systems-level interventions assessed have good applicability to current practice in the United States.

Research Gaps

Future research needs around management of PPH are both clinical and methodologic. Priorities for future research include the following:

- Reaching consensus on definitions and criteria for PPH and first-line management strategies to promote consistency within the literature.

- Standardizing a definition of PPH, potentially with gradations of severity, to allow for meaningful comparison of outcomes.

- Conducting more rigorously controlled studies of all interventions for PPH management, especially medication studies, in light of the fact that these are considered first-line management and few studies in developed/high-resource nations addressed

agents commonly in use. While studies in the PPH population are likely to be retrospective, studies should clearly describe first-line management and timing of management to clarify the course of care. Studies must report a priori study size calculation to ensure that the number of subjects will be adequate to show a difference (if the study is designed for superiority). In addition, comparative studies must declare within the design and methods section whether the study is a superiority trial or a noninferiority trial.

- Conducting cluster RCTs of intervention bundles that address order of medications, order and timing of manual interventions such as uterine massage and bimanual compression, number of times to repeat medications prior to moving on to second-line interventions, hemodynamic monitoring, and supportive care such as transfusion.

- Clearly identifying the trajectory of care, including which interventions were used and the order and timing of interventions.

- Identifying markers that can inform the decision to move to an alternative intervention.

- Investigating the effectiveness of agents used to control bleeding in other clinical areas and of new medications to address PPH. It is likely that new agents would be compared with or added to existing agents and not compared with placebo.

- Conducting additional RCTs or controlled studies of treating anemia after PPH is stabilized.

- Conducting additional prospectively designed and reported studies that report data from large national databases. These studies can describe effects in larger population samples and may be valuable for identifying longer term harms—for example, effects on breastfeeding, psychological trauma, and future fertility.

- Replicating the intrauterine balloon tamponade study that found it was effective in reducing invasive interventions.

- Using and clearly reporting objective methods to diagnose PPH and evaluate management, including accurate measurement of blood loss. Visual estimation of blood loss is too imprecise to be used in research.

- Dedication to prospective objective measures, such as estimated blood loss, time course of intervention, and use of intervention components.

- Greater capture and multivariable adjustment, including metaregression, for known risk factors and confounders to allow better understanding of the attributable impact, if any, of the intervention.

- Attention to the possibility that effect modifiers hide efficacy in some groups, which means that studies will need to be powered and specify a priori stratified analyses by candidate effect modifiers, such as grand multiparity, route of birth, induction, prolonged oxytocin infusion, or infection in labor.

- Prespecifying harms, differentiating harms of interventions from sequelae of PPH wherever possible, and studying longer term effects of procedures and surgical interventions.

- Using multivariate modeling. The size of the study populations in systems-level interventions can clearly support multivariate modeling and could serve to drive better understanding of the general lack of effectiveness. In particular, such data are well-suited to use of risk-adjustment models, and adjusting for these underlying differences in study population characteristics would allow comparison not only across time periods but across studies.

- Attention to the possibility that systems-level interventions are working against a biologically determined risk of PPH, meaning that within a specific population with particular characteristics, there is an irreducible level of risk, and event rates cannot be driven below that "floor." If this floor were demonstrated with risk-adjustment methods, this finding would fundamentally change the focus of study design and care. A floor would suggest that we need very large pragmatic trials aimed not at reducing the occurrence of PPH but at diminishing associated morbidity, mortality, personal harm and distress, and costs. The systems-level intervention studies available now cannot fully inform this goal, but primary meta-analyses of the highest quality cohorts with risk adjustment could determine if the evidence seen in some of the included studies that suggest benefits are worth pursing on a larger scale, including a scale large enough to separate the influence of candidate components to determine their individual contributions to improvements in care.

Limitations of the Evidence Base

Studies included in this review are methodologically and clinically limited. There is not a universally agreed management strategy for PPH. Medications were typically used as the initial treatment; however, the specific drugs, dosages, and order varied. The selection of interventions, including which interventions were performed and in which order, was also inconsistent. Management was not well described in many studies, especially for women who transferred from other hospitals. Methods for estimating blood loss, when reported, varied and were limited. Overall, it was difficult to ascertain confidently the complete trajectory of care of women in many of the studies we reviewed, which compromises our ability to draw meaningful comparisons. As noted, few studies that met our criteria addressed commonly used uterotonics such as oxytocin; however, prior systematic reviews that have included studies in developing countries have reported similar effects on bleeding for misoprostol and oxytocin and benefits for misoprostol in reducing blood loss with side effects, including fever.

Procedures and surgical interventions also differed across studies. For example, materials used for embolization varied, as did the sites of embolization and ligation. There is no clear trigger for starting subsequent interventions, so success rates have limited reliability. It may be that women would have recovered after the first-line treatment if time allowed. In addition, there is the potential for cumulative effects of multiple interventions that cannot be measured. Outcomes other than control of bleeding can be difficult to assess. For example, transfusion could be an adverse outcome if treatment was not sufficient and timely to halt bleeding rapidly. Alternatively, early transfusion can be the appropriate intervention. Therefore, it is sometimes hard to know whether to classify transfusion as an adverse outcome. Measuring harms is similarly challenging. In some cases, it can be difficult to assess if harms are due to PPH or management interventions and how much each contributed, especially to deaths. There is a significant lack of truly comparative studies. Randomized studies would be ideal, yet are complex to conduct with a life-threatening condition such as PPH. Studies were typically conducted or data collected over long timeframes (median study duration, 5 years; range, 6 months to 29 years), and it is likely that interventions and patient characteristics would have changed over time, but few studies account for secular changes such as the introduction of new interventions.

In systems-level interventions, a natural tension exists between the desire to implement robust interventions and the challenges of understanding which components may have value. In the case of these interventions, it is particularly challenging because lower quality studies with looser measures of outcomes were more likely to

report intervention effects. The literature about systems-level interventions is limited by lack of analyses that seek to adjust for secular trends and changes in confounders, such as proportion of births by cesarean and trends in rising body-mass index. Likewise, lack of multivariable modeling may obscure the influence of elements of care, such as induction of labor, and comorbidities, such as chorioamnionitis, that could identify which predictors may be exerting substantial influence and inform new approaches to diminishing risk of PPH.

Implications for Clinical and Policy Decisionmaking

A limited body of evidence addresses interventions for managing PPH. Few studies addressed medications commonly used to treat PPH, precluding our ability to draw conclusions about their effectiveness. Success rates for uterine balloon tamponade or surgeries are typically above 60 percent (e.g., success of uterine balloon tamponade as the initial second-line therapy in one study was 86%; success rates for ligation as the first second-line intervention to control bleeding ranged from 36% to 96%). Studies of embolization suggested that it may be associated with a median rate of successful control of bleeding without the need for additional procedures or surgeries of 89 percent, with a wide range of success (58% to 98%) across studies. However, few studies clearly provided data on the success of these procedures and surgeries as the initial second-line approach, so rates are based on a small number of cases. Adverse events and longer term outcomes associated with procedures and surgical interventions are also not well understood. At this point, the evidence is insufficient to comment on the effectiveness and harms of most interventions for most outcomes.

Given the mixed and insufficient evidence, clinicians will likely need to continue to make individual decisions about the care of women with PPH based on each woman's clinical situation and the management options available in the setting. This body of evidence does not provide clear answers to the key clinical questions of what interventions to use and in what order.

Conclusions

A limited body of evidence addresses interventions for managing PPH. The most effective treatments and the order in which to use treatments remain unclear. Diagnosis of PPH is subjective, which makes it difficult to compare the severity of PPH and determine the comparability of participants within and across studies. The trajectory of care, rationale for choice of intervention, and component of care ultimately responsible for controlling bleeding

are also frequently unclear because of the need for rapid intervention in an emergency situation. Few studies included in this review addressed pharmacologic or medical management, including transfusion for supportive management of ongoing PPH, and the evidence reviewed is insufficient to comment on effects of such interventions. The success of uterine-sparing techniques, such as uterine balloon tamponade, embolization, uterine compression sutures, and uterine and other pelvic artery ligation, in controlling bleeding without the need for additional procedures or surgeries ranged from 36 to 98 percent. However, these data come from a limited number of studies with a small number of participants. Harms of interventions are diverse and not well understood. Some studies reported an association between rFVIIa and thromboembolic events, but sample sizes were small. Some studies with longer term followup reported adverse effects on future fertility and menstrual changes in women undergoing embolization. Need for reoperation was reported after hysterectomy. Evidence is insufficient to assess the effects of interventions for anemia after PPH is stabilized, and systems-level interventions showed little benefit in reducing the incidence or severity of PPH or the need for transfusion or hysterectomy. Further research is needed across all interventions for PPH management, especially pharmacologic interventions, which are the most frequently used first-line therapies.

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Full Report

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