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National and International Guidelines for Patient Blood Management in Obstetrics: A Qualitative Review

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Abstract

In developed countries, rates of postpartum hemorrhage (PPH) requiring transfusion have been increasing. As a result, anesthesiologists are being increasingly called upon to assist with the management of patients with severe PPH. First responders, including anesthesiologists, may adopt Patient Blood Management (PBM) recommendations of national societies or other agencies.

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However, it is unclear whether national and international obstetric societies' PPH guidelines account for contemporary PBM practices. We performed a qualitative review of PBM recommendations published by the following national obstetric societies and international groups: the American College of Obstetricians and Gynecologists; The Royal College of Obstetricians and Gynecologists, United Kingdom; The Royal Australian and New Zealand College of Obstetricians and Gynecologists; The Society of Obstetricians and Gynecologists of Canada; an interdisciplinary group of experts from Austria, Germany, and Switzerland; an international multidisciplinary consensus group; and the French College of Gynaecologists and Obstetricians. We also reviewed a PPH bundle, published by The National Partnership for Maternal Safety. On the basis of our review, we identified important differences in national and international societies' recommendations for transfusion and PBM. In the light of PBM advances in the nonobstetric setting, obstetric societies should determine the applicability of these recommendations in the obstetric setting. Partnerships among medical, obstetric, and anesthetic societies may also help standardize transfusion and PBM guidelines in obstetrics.

Rates of transfusion during childbirth have increased in resource-rich countries.¹ In the United States, the rate of severe postpartum hemorrhage (PPH) requiring transfusion increased from 30.4 to 96.4 per 10,000 delivery hospitalizations for the time periods between 1998 and 1999 to 2008 and 2009, respectively.² Thus, there is an onus for anesthesiologists to familiarize themselves with current recommendations in Patient Blood Management (PBM) in the setting of PPH.

As defined by the Institute of Medicine, clinical guidelines are "systemically developed statements to assist providers and patient decisions about appropriate health care for specific clinical circumstances."³ By providing a clear description and appraisal of scientific evidence, guidelines can enhance clinician and patient decision making. In recent years, there has been a surge in clinical practice guidelines, many giving inconsistent or opposing recommendations,⁴ which may negatively impact clinical care delivery.⁵ This is relevant to clinicians in the United States because government health care programs increasingly rely on guidelines to develop performance measures and quality metrics.⁶ In obstetrics, the presence of conflicting PBM guidelines may lead to important variations in clinical practice. For example, recommendations for fibrinogen supplementation differ across subspecialty societies. The European Society of Anaesthesiology recommends fibrinogen supplementation when fibrinogen levels are <200 mg/dL (in the setting of severe perioperative bleeding),⁷ whereas several obstetric societies recommend treatment for fibrinogen levels <100 mg/dL.^{8,9} Side-by-side comparison of PBM recommendations made by national obstetric societies would allow clinicians to assess the strengths and limitations of existing guidelines.

Guidelines for PPH management have been published by a number of obstetric societies, including the American College of Obstetricians and Gynecologists (ACOG); the Royal College of Obstetricians and Gynecologists (RCOG), United Kingdom; the Royal Australian and New Zealand College of Obstetricians and Gynecologists (RANZCOG); the Society of Obstetricians and Gynecologists of Canada (SOGC); and the French College of Gynaecologists and Obstetricians (CNGOF) in collaboration with the French Society of

Anesthesiology and Intensive Care. In a recent review, Dahlke et al¹⁰ compared each society's recommendations for PPH prevention and treatment, including uterotonic agents, interventional radiology procedures, and surgical interventions. However, in this review, PBM recommendations were not examined in detail.

In recent years, PBM has been developed as an evolving evidence-based approach with a number of key goals: (i) to identify, evaluate, and manage anemia; (ii) reduce iatrogenic blood loss; (iii) optimize hemostasis; and (iv) establish decision thresholds for transfusion.¹¹ All these aspects of PBM are applicable to PPH prevention and management. Other strategies that may be applicable to PPH management include fixed ratios of plasma-to-red blood cells,¹² massive transfusion and hemorrhage protocols,^{13,14} and pharmacological therapies such as prothrombotic and antifibrinolytic agents.¹⁵

The primary aims of this qualitative review were to assess PPH guidelines published by national obstetric societies, with a focus on recommendations for transfusion and PBM. Guidelines published by national anesthesiology, hematology, and transfusion societies were secondarily reviewed to assess transfusion and PBM recommendations applicable to obstetrics.

METHODS

We conducted our appraisal between April 1, 2015, and April 30, 2016. During this interval, we reviewed the most recent PPH guidelines published by the following national obstetric societies (RCOG,⁸ SOGC,¹⁶ ACOG,¹⁷ RANZCOG,⁹ and CNGOF¹⁸), an interdisciplinary group of experts from Austria, Germany, and Switzerland (D-A-CH),¹⁹ and an international expert panel convened to develop consensus recommendations for PPH management (hereafter referred to as expert panel).²⁰ The goal of D-A-CH was to develop a PPH algorithm by reviewing guidelines from national societies in Austria, Germany, Switzerland, and other international PPH algorithms. For each society, we searched Web sites to identify the most recently published guidelines. To confirm that we identified the most recent guidelines, we searched The National Guideline Clearinghouse (the Agency for Healthcare Research and Quality, US Government), MEDLINE, EMBASE, Ovid, Google Scholar, and Google. Last, we reviewed transfusion and PBM recommendations in the PPH bundle published by the National Partnership for Maternal Safety (NPMS) in 2015.*,²¹

Our review is intended to target anesthesia and obstetric providers from well-resourced countries. Therefore, we did not review PPH guidelines by the World Health Organization²² and the International Federation of Gynecology and Obstetrics,²³ which are more clinically relevant to providers in low-resource settings. Four authors (R.S., C.F.W., N.A., A.J.B.) reviewed each English language document independently using a data extraction form, and discrepancies were resolved by consensus. A.T. reviewed D-A-CH guidelines.

*Council on Patient Safety in Women's Health Care. Available at: <http://www.safehealthcareforeverywoman.org/default.php>. Accessed November 14, 2015.

For each set of guidelines, we evaluated the following background information: year of publication, information about the members of each guideline committee, definitions for PPH, and the information sources used by each society for developing their guidelines.

We reviewed specific aspects of each society's blood transfusion recommendations, including the indications for transfusion with red blood cells (RBCs), plasma, platelets (PLTs), and cryoprecipitate; and recommendations for fixed transfusion ratios and/or goal-directed transfusion therapy. We focused our review on the following key aspects of PBM: (i) transfusion therapy; (ii) pharmacological agents, such as recombinant factor VIIa (rFVIIa), tranexamic acid, fibrinogen concentrate; and (iii) other interventions, such as cell salvage. We also examined whether other approaches were recommended, such as autologous transfusion, coagulation monitoring using laboratory tests and point-of-care devices, such as thromboelastography (TEG) or rotational thromboelastometry (ROTEM).

We also evaluated whether obstetric-specific blood transfusion recommendations are described in PBM guidelines published since 2010 by nationally or internationally recognized anesthesia societies and blood bank organizations, including the AABB (formerly the American Association of Blood Banks),²⁴⁻²⁶ American Society of Anesthesiologists (ASA),²⁷ European Society of Anaesthesiology (ESA),⁷ British Committee for Standards in Haematology (BSCH),²⁸ National Blood Authority (NBA) of Australia,²⁹ and the Association of Anaesthetists of Great Britain and Ireland (AAGBI).³⁰

RESULTS

Background information for these PPH guidelines is presented in Table 1. We observed a wide range for the year of publication (2006 to 2016). For each society, an interdisciplinary committee developed the PPH guideline; yet, no specific criteria were described for selecting committee members. The ACOG did not provide details of their committee members' area of expertise. The other societies encompassed committee members from a number of disciplines, including obstetrics, gynecology, hematology, transfusion medicine, anesthesiology, family medicine, neonatology, nursing, and midwifery. Lay people were included on several committees, specifically a representative from the Jehovah's Witness Organization (RCOG) and a patient representative (RANZCOG). The RCOG, D-A-CH, CNGOF, and the expert panel provided details of each committee member's base institution and specialty.

The societies used different approaches to examine the literature. Five societies (ACOG, SOGC, RCOG, CNGOF, and the expert panel) provided details about the sources of information used to formulate their guidelines. In contrast, the RANZCOG, D-A-CH, and NPMS provided relatively limited information. The levels of evidence were graded differently by each society. The ACOG and the expert panel used the grading system method outlined by the US Preventative Services Task Force,[†] the SOGC used the Evaluation of Evidence criteria from the Canadian Task Force on Preventative Health Care,³¹ the RCOG

[†]Grade Definitions. U.S. Preventive Services Task Force, October 2014. Available at: <http://www.uspreventiveservicestaskforce.org/Page/Name/grade-definitions#grade-definitions-prior-to-may-2007>. Accessed on November 14, 2015.

used an internal grading system, the RANZCOG used a grading system endorsed by the Australian National Health and Medical Research Council,[‡] and the CNGOF used a framework defined by the French Health Authority.[§] Although the NPMS provided a resource listing for the bundle, no information was provided about how the quality of evidence was evaluated or how the strength of their recommendations was determined.

All societies used blood loss as a key determinant for classifying PPH (Table 1). Only the ACOG classified PPH according to mode of delivery: >500 mL for vaginal delivery versus >1000 mL for cesarean delivery.

Transfusion Recommendations

Key aspects of the national obstetric societies' transfusion recommendations are presented in Table 2. There were limited descriptions for blood ordering strategies by all societies. The RCOG and ACOG recommended preemptive ordering of blood products only for patients with suspected placenta accreta/percreta. The D-A-CH and RCOG recommended cross-matching and ordering blood as soon as PPH is recognized. Most societies based their indications for transfusion on the degree of blood loss. Target hematological indices were described by the RCOG, RANZCOG, CNGOF, and D-A-CH. For guiding resuscitation, the RANZCOG and D-A-CH described other physiologic indices, such as a pH >7.2. However, the frequency of laboratory testing was poorly described, with only the expert panel recommending testing of coagulation parameters every 45 to 60 minutes.

Broad consensus for plasma use was lacking. The RCOG and RANZCOG recommended fresh frozen plasma (FFP) in the setting of a prolonged prothrombin time (PT), or activated partial thromboplastin time (APTT). The D-A-CH stated that FFP should be considered for correcting a coagulation disorder. The CNGOF indicated that FFP can be administered without waiting for laboratory results, depending on hemorrhage severity. The majority of the societies did not describe fixed-ratio transfusion approaches, such as 1:1 of RBC:FFP. Only the RCOG suggested transfusing 4 units of FFP for every 6 units RBC.

Societies' recommendations for PLT transfusion were similar. In the setting of PPH, the RCOG, RANZCOG, CNGOF, and D-A-CH recommended PLT transfusion if the PLT count is $<50 \times 10^9/L$. Recommendations for fibrinogen supplementation (with cryoprecipitate or fibrinogen concentrate) were less consistent. Two societies (RCOG, and RANZCOG) recommended supplementation for a fibrinogen concentration <100 mg/dL. A higher threshold (200 mg/dL) was recommended by the expert panel and the CNGOF.

Three societies—the RANZCOG, NPMS, and the expert panel—made reference to a massive transfusion protocol (MTP). The RANZCOG guidelines contained an MTP algorithm, with criteria for activating the MTP (actual or anticipated transfusion of 4 units

[‡]National Health and Medical Research Council. NHMRC additional levels of evidence and grades for recommendations for developers of guidelines. Canberra; 2009. Available at: https://www.nhmrc.gov.au/_files_nhmrc/file/guidelines/developers/nhmrc_levels_grades_evidence_120423.pdf. Accessed on November 14, 2015.

[§]HAS. Les recommandations pour la pratique clinique. Base methodologique pour la realisation en France. Available at: http://www.has-sante.fr/por-tail/jcms/c_431294/les-recommandations-pour-la-pratique-clinique-base-methodologique-pour-leur-realisation-en-france. Accessed on April 30, 2016.

RBC in <4 hours). No society provided indications for discontinuing or deactivating an MTP.

Pharmacologic Agents

Recommendations for using pharmacologic agents are presented in Table 2. Among the societies, there was no consensus for administering rFVIIa. The RCOG, RANZCOG, D-A-CH, CNGOF, and the expert panel recommended rFVIIa for treating life-threatening or uncontrolled hemorrhage. Neither the ACOG nor the SOGC recommended rFVIIa. Both societies cite lack of evidence for efficacy; furthermore, ACOG expressed concern for potential thromboembolic events and cost implications.

Recommendations for using antifibrinolytic agents were also inconsistent. The RANZCOG, D-A-CH, and the expert panel recommended tranexamic acid. The CNGOF recommended that the use of tranexamic acid be at the clinician's discretion, despite stating that its use is not suitable for routine PPH management and that evidence is lacking to support its role. The RCOG recommended against using antifibrinolytics, stating that “there is a consensus view that fibrinolytics seldom, if ever, have a place in” (PPH management). No society recommended using TEG or ROTEM to detect hyperfibrinolysis before administering tranexamic acid. No other antifibrinolytics were discussed by the societies.

Other Interventions

We found few recommendations for other PBM strategies in the PPH guidelines, such as point-of-care testing and cell salvage. Only the D-A-CH and the expert panel included recommendations for point-of-care testing with TEG or ROTEM. Only ACOG and the RANZCOG made reference to cell salvage. The ACOG recommended autologous transfusion for women with rare antibodies. Although no society strongly endorsed colloids for volume replacement, the D-A-CH stated that colloids can falsely elevate fibrinogen levels.

Transfusion Recommendations From Other Societies

Table 3 summarizes the main recommendations from guidelines published since 2010 by anesthesiology societies (the ASA, the ESA, and the AAGBI) and transfusion societies (the AABB, the NBA, and BSCH). The aims of each society's guidelines differed (Table 3). Guidelines were geared to different patient populations: surgical patients (ESA and ASA), stable hospitalized patients (AABB), and patients with hemorrhage (BSCH). The NBA published several modules for PBM.^{||} In Table 3, we summarized the NBA recommendations specific to pregnancy and maternity (from module 5). The ESA, BSCH, NBA, and AAGBI guidelines included a specific section for obstetric hemorrhage. Because the AABB PLT guidelines did not include recommendations related to hemorrhage, they are excluded from our review.

Recommendations for transfusing RBC and plasma were inconsistent across the societies (Table 3). For example, both the ESA and the BCSH recommended fixed ratios of RBC:FFP,

^{||} Available at: <https://www.blood.gov.au/pbm-guidelines>. Accessed on April 30, 2016.

the BCSH recommended a FFP:RBC ratio of at least 1:2, and the AAGBI recommended fixed ratios only in the face of continued hemorrhage. In contrast, the ASA did not stipulate using fixed ratios. In their module on critical bleeding and massive transfusion,[¶] the NBA state that there is insufficient evidence to support or refute the use of specific ratios of RBCs to other blood components.

The use of laboratory indices for guiding PLT transfusion or fibrinogen supplementation was described by most of the societies. For fibrinogen supplementation, the ESA recommended fibrinogen concentrate over cryoprecipitate for treating hypofibrinogenemia.

Pharmacologic Agents

The AAGBI and NBA suggested tranexamic acid for managing women with severe PPH. The ESA and BSCH recommended tranexamic acid for adult trauma patients and in adult patients with nontraumatic major hemorrhage. However, the ASA was more reserved in their recommendations, highlighting the lack of safety data in obstetrics. The ASA, ESA, and NBA recommended that rFVIIa be considered as a rescue therapy, whereas the BCSH recommended against the use of rFVIIa. None of the AABB guidelines included adjuncts to transfusion management.

DISCUSSION

In general, guidelines published by the nonobstetric societies (ASA, ESA, AABB, and BSCH) contained more contemporary approaches to transfusion management and PBM compared with those published by obstetric societies. These approaches include a MTP, goal-directed therapy using point-of-care testing, and early treatment of hypofibrinogenemia.^{11,13,15,32,33} However, the evidence base that supports the use of these approaches in obstetrics is limited. It is likely that consensus of expert opinions fills gaps in areas lacking scientific evidence. To improve the quality of PBM guidelines in obstetrics, prospective clinical studies and cost-effectiveness studies are urgently needed for women with severe PPH.

Among the obstetric societies, reasons for the variation in the transfusion and PBM recommendations are uncertain. It is possible that different dates of publication, methods for guideline development and literature review, and different compositions of guideline review committees may account for some of this variation. Other factors include variation in the willingness of guideline committees to include evidence from the nonobstetric setting, and differences in expert opinion when evidence is lacking. Also, it is unclear whether societies took into account the cost-effectiveness of individual interventions, patient preferences and opinions, and the potential influence of outside agencies with special interests, such as pharmaceutical and device companies. These are important factors to consider when reviewing clinical practice guidelines.^{4,34} In particular, the involvement of patients and the public, including Jehovah's witnesses, in clinical practice guideline development has been endorsed by the Institute of Medicine.³⁵ Patient and public involvement is important for a number of reasons: to examine whether special interests are present; to determine whether

[¶]Available at: <https://www.blood.gov.au/pbm-module-1>. Accessed on April 30, 2016.

guidelines can be easily understood by patients; and to provide safeguards against conflict of interests that skew judgment of the guideline committee members.³⁵

In addition to scientific evidence and expert opinions, clinical practice guidelines should account for both the resource implications and the feasibility of the recommended interventions.³⁶ These have important implications for low-volume birth facilities in geographically remote locations that may have limited access to prothrombotic drugs or a sufficient blood bank inventory. It is unrealistic for national societies to account for all types and locations of birth facility, and as highlighted by the NMPS, an emergency hemorrhage action plan should be tailored according to the individual capabilities of each hospital. With data suggesting that hospital-level factors explain a large portion of the variability in transfusion rates in obstetrics,³⁷ more research is needed to determine the most clinically and cost-effective patient blood management approaches according to specific hospital characteristics.

Transfusion Criteria During Active Blood Loss

It is well-recognized that peripartum blood loss is inaccurately measured, with accuracy worsening at larger volumes of blood loss.^{38–41} Determining whether and how blood loss measurements influence clinical practice is challenging. In a high-quality systematic review of studies that evaluated methods of blood loss assessment, Hancock et al⁴² concluded that improved accuracy of blood loss measurement does not facilitate earlier recognition of PPH or prevent progression to more severe PPH. In contrast, data from an impact study from a large US health care system suggested that the introduction of a standardized approach to hemorrhage management, including immediate release of blood products from blood bank, may reduce the overall blood product use.⁴³ Despite the challenges faced in accurately quantifying blood loss, the magnitude and rate of blood loss will likely remain an inherent component of clinicians' transfusion decision-making.

Some of the societies recommended transfusion if unstable vital signs accompany blood loss. However, the strength of the associations between volume of blood loss with maternal heart rate and blood pressure is uncertain. In a systematic review, Pacagnella et al⁴⁴ observed that heart rate and blood pressure were associated with blood loss in 22 of 24 studies and 17 of 23 studies, respectively. However, values for area under the receiver-operating characteristics curve varied (heart rate = 0.56–0.79 and systolic blood pressure = 0.77–0.84, respectively). In trauma patients with shock, systolic blood pressure has been shown to correlate poorly with base deficit ($r = 0.28$).⁴⁵ Although marked heterogeneity may exist in patients' hemodynamic responses to early severe postpartum bleeding, clinicians will likely continue to account for vital signs when assessing clinical indications for transfusion. A survey of transfusion practice among ASA members provides some support for this assertion; 46% respondents indicated that the decision to transfuse is based on a number of factors: intraoperative hemodynamic status, medical condition of the patient, and age of the patient.⁴⁶ Technologies, including echocardiography and cardiac ultrasound, can provide more detailed information about patients' volume status and hemodynamic responses to resuscitation and transfusion. Fuller evaluation of these technologies is needed in the setting of PPH.^{47,48} Similarly, noninvasive hemoglobin monitors are commercially

available, but concerns about accuracy and precision may limit their clinical utility in the obstetric setting.⁴⁹

Preemptive Blood Ordering

Excluding patients with suspected abnormal placentation, obstetric societies' guidelines lacked information about preemptive or predelivery blood ordering. The California Maternal Quality Care Collaborative (CMQCC) published a bundle describing care practices for patients with obstetric hemorrhage, with an approach for risk-stratifying patients for PPH and pretransfusion testing.⁵⁰ The CMQCC assigned patients as low-, medium-, or high-risk category based on the presence/absence of selected risk factors. For each group, recommendations were as follows: no prenatal pretransfusion testing, type and screen testing, or type and cross-match for 2 units RBC, respectively. Two retrospective studies examined the accuracy of CMQCC risk stratification at single US obstetric centers. Wu et al⁵¹ reported transfusion rates of 2.1%, 4.5%, and 22.6% among low-, medium-, and high-risk women, respectively. In contrast, Dilla et al⁵² observed lower rates of transfusion in each group (0.8%, 2%, and 7.3%, respectively). Given that a wide variation in obstetric transfusion rates has previously been reported,³⁷ between-hospital differences in transfusion rates for each at-risk group are not unexpected. Nonetheless, the low transfusion rates reported in each low- and medium-risk group suggest that pretransfusion testing for these women may not be warranted.

In the nonobstetric setting, historical blood utilization data from anesthesia information systems have been used to determine preoperative blood orders for specific surgical procedures, referred to as the maximum surgical blood ordering schedule.^{53–55} To optimize blood ordering practices in obstetrics, investigations are needed of predelivery maximum blood ordering schedules coupled with blood component utilization relevant to the peripartum and postpartum periods.

Massive Transfusion Protocol

The majority of obstetric guidelines lacked detailed information about the availability of a MTP. Only 3 obstetric societies (RANZCOG, NPMS, and the expert panel) mentioned the use of a MTP, with limited information about the benefits of implementing a MTP. An institutional MTP can be vital for physicians managing severe and ongoing postpartum bleeding.^{56–58} A MTP provides a structured, systemwide process for the delivery of sufficient types and volumes of blood products, with short turnaround times from ordering to receipt of blood products. In addition, processes for MTP activation and deactivation are standardized. These attributes are important because the Confidential Enquiry into Maternal and Child Health (CEMACH: United Kingdom) have indicated that time delays in receiving blood products may contribute toward severe obstetric morbidity and mortality.⁵⁹ Furthermore, evidence suggests that rates of massive transfusion in obstetrics are increasing. In a study using administrative data from New York State, Mhyre et al⁶⁰ reported that the rate of massive transfusion during delivery hospitalizations increased from 6.2 per 10,000 deliveries between 1998 and 2002 to 7.3 per 10,000 deliveries between 2003 and 2007. Although no studies have compared maternal outcomes between those managed with a MTP versus nonprotocol-based transfusion strategies, there have been calls for hospitals to

implement a MTP as a key systemwide process for managing severe PPH.^{14,61} On the basis of a recent survey of directors of US academic obstetric anesthesia units, 93% units have a MTP in place.⁶² The median number of units of RBC, plasma, cryoprecipitate, and PLTs in the MTPs were 6, 4, 1, and 1, respectively.⁶² We are not aware of any studies that have examined the availability of a MTP in nonacademic units.

Fixed-Ratio Transfusion Approaches

Recommendations for using fixed ratios of plasma:RBC in obstetrics originate from the nonobstetric setting. In recent years, experts in obstetric hemostasis have questioned whether the use of fixed-ratio transfusions from nonobstetric settings is applicable to the management of PPH.^{15,20,32} These concerns were highlighted by the D-A-CH and the expert panel. However, no alternative approaches were discussed by these societies. In the trauma setting, the use of ratio-based transfusion with coagulation test-guided care has been advocated.⁶³ In the obstetric setting, there have been calls for comparative effectiveness studies to compare maternal outcomes for women managed with fixed ratios of plasma:RBC versus goal-directed approaches using laboratory and/or point-of-care measurement of coagulation parameters.⁶⁴

Decision to Transfuse in Patients With Acute Anemia After PPH

Several societies (RCOG, D-A-CH, ASA, and AABB) recommend RBC transfusion according to a threshold or nadir hemoglobin value. It is uncertain whether this guidance applies to the period of active blood loss or after arrest of bleeding. Among nonobstetric, nonbleeding (“stable”) anemic patients, liberal transfusion approaches do not reduce rates of mortality or morbidity compared with restrictive approaches.^{65,66} Furthermore, evidence suggests that adopting a restrictive transfusion approach either within single institutions or health care systems can decrease the number of RBCs transfused per patient and potentially improve patient outcomes (by reducing mortality rate and length of hospital stay).^{67–70} These results have not been confirmed in the obstetric setting. In a randomized, nonblinded study to assess the effect of RBC transfusion versus no intervention on the maternal quality of life among women with PPH and early postpartum anemia (Hb 4.8–7.9 g/dL 12- to 24-hours postpartum), Prick et al⁷¹ did not demonstrate non-inferiority with the non-RBC-based approach. However, on postpartum day 3, the authors noted that women in the no intervention group only had a 0.78 higher mean physical fatigue score compared with those receiving RBC (physical fatigue scores range from 4 to 20; higher scores indicating more fatigue). These data should not discount the need to consider treatment for postpartum anemia, especially as important maternal morbidities are associated with this condition, including depression,^{72–74} fatigue,⁷⁵ and impaired cognition.⁷⁶ These morbidities can negatively impact maternal-child bonding and the mother's ability to provide newborn care.⁷⁷ There is also an underappreciation of the high prevalence of postpartum anemia. In the United States, Bodnar et al⁷⁸ reported that 19% women in low-income groups had a hemoglobin <12 g/dL between 4 and 26 weeks postpartum. Iron replacement therapy has been recommended for the treatment of mild to moderate iron deficiency anemia.⁷⁹ With anemia detection, diagnosis, and treatment recognized a key facet of PBM,⁸⁰ obstetric societies may need to consider whether postpartum anemia screening should be incorporated into PBM guidelines.

Laboratory Indices and Point-of-Care Testing

Many societies included laboratory indices (PT, APTT, international normalized ratio [INR], fibrinogen) as transfusion triggers or “therapeutic goals.” However, the usefulness of PT, APTT, and INR as triggers for transfusion therapy has been called into question.^{32,81} There is a lack of high-quality evidence to substantiate whether a trigger of 1.5-fold prolongation of APTT/PT or INR is helpful for diagnosing coagulopathic bleeding or to indicate whether supportive therapy should be given.⁸¹ It is worth noting that the PT and APTT can often remain normal in the face of severe obstetric bleeding.^{32,82–84} Furthermore, the onset and severity of coagulopathy may vary according to the etiology of obstetric hemorrhage. In contrast, recent evidence suggests that, during the early stage of bleeding, a low fibrinogen level (<200 mg/dL) can be an important marker for severe PPH and the need for advanced surgical/medical intervention for PPH management.^{85–87} In general, obstetric societies’ recommendations did not account for new data on fibrinogen changes during PPH. The expert panel was the only obstetric group recommending supplementation if fibrinogen <200 mg/dL, whereas other obstetric societies recommended a lower threshold (100 mg/dL).

Several societies recommended using point-of-care devices (TEG, ROTEM) to assess the maternal coagulation profile. The application of these technologies in the obstetric setting has been promoted by experts in obstetric hemostasis.^{33,88} Benefits of these devices include quicker turnaround times compared with standard laboratory tests, and identification of specific coagulation defects, including functional fibrinogen deficiency and fibrinolysis. Point-of-care testing and laboratory tests of coagulation can be incorporated into an integrated, goal-directed approach for transfusion decision making.^{32,89} However, these tests are not available in most labor and delivery units. In addition to equipment costs, these devices require regular calibration, and TEG/ROTEM data interpretation requires education.

Pharmacological Treatment: Antifibrinolytics, rFVIIa, and Fibrinogen Concentrate

Three obstetric societies provided recommendations for antifibrinolytics, whereas 1 society (RCOG) recommended against its use. Several meta-analyses^{90,91} and a systematic review⁹² suggest that tranexamic acid, given either prophylactically or therapeutically, results only in modest, nonclinically significant reductions in blood loss (149 mL and 92 mL, respectively) compared with standard approaches. Of note, the majority of studies assessed the effect of tranexamic acid on patients undergoing elective cesarean delivery. The authors of these systematic reviews expressed concern about the methodological quality of investigations assessing tranexamic acid efficacy. The results of the World Maternal Antifibrinolytic Trial (WOMAN) study, an international study randomizing 20,000 women who experience PPH after vaginal or cesarean delivery to 1 to 2 g tranexamic acid versus placebo, may provide new data on whether tranexamic acid reduces severe hemorrhage-related morbidity or death.⁹³

Because of the dearth of high-quality evidence on rFVIIa, societies’ recommendations are predominantly based on expert opinion. This may explain the variation in recommendations for rFVIIa across obstetric societies. Anecdotal obstetric reports or registry data suggest that rFVIIa may be a viable therapeutic option for patients with severe refractory obstetric hemorrhage,^{94–97} but have also described severe thrombotic complications.

Data on the efficacy of fibrinogen concentrate are relatively limited. In a multicenter, randomized study, administration of fibrinogen concentrate in the early stage of PPH did not reduce RBC requirements compared with placebo.⁹⁸ However, only 2.2% patients had a fibrinogen level <200 mg/dL at the time of study enrollment. Data from ongoing studies will provide important information for determining whether fibrinogen concentrate improves outcomes for women with severe PPH.^{99,100}

We acknowledge that our review has limitations. We did not review PBM recommendations published by all obstetric, anesthetic, hematology societies, nor national agencies and consensus groups. For example, the Subcommittee on Women's Health Issues of the International Society of Thrombosis and Hemostasis recently published guidelines on the management of coagulopathy associated with PPH.¹⁰¹ We elected to exclude these guidelines because PBM guidelines for patients without coagulopathy were not discussed. Although a bundle of care is a structured approach for improving processes of care and patient outcomes,¹⁰² the content of a bundle and clinical practice guidelines comprise evidence-based practices. Therefore, we believe that the PBM recommendations in the NMPS bundle were worthy of comparison with those of national obstetric societies. We cannot determine the extent to which clinicians follow PBM and transfusion guidelines for PPH management. In the IOM report (Clinical Practice Guidelines We Can Trust),³⁵ it is possible that easy access to clinical practice guidelines may be out of reach for some clinicians. In addition, there may be large gaps between recommended care and delivered care. Clinical decision support systems, embedded in anesthesia or electronic medical record systems, may provide a vehicle for improving rates of clinician adherence to clinical practice guidelines.¹⁰³ Last, we acknowledge that we did not perform a quantitative assessment of guideline quality using validated instruments, such as The Appraisal of Guidelines for Research & Evaluation (AGREE II).¹⁰⁴ These tools can be used by policy makers and health care providers to help make decisions about which guidelines should be recommended for clinical use. Our goal was to present PBM and transfusion recommendations, sourced from obstetric and nonobstetric societies' guidelines, to allow side-by-side comparisons of content material.

CONCLUSIONS

In this review of current professional society guidelines, we observed inconsistencies in obstetric and nonobstetric societies' PBM and transfusion recommendations for PPH management. These inconsistencies may hinder how clinicians provide quality care to patients with severe PPH. We advise obstetric, anesthesiology, and transfusion societies to form interdisciplinary partnerships to achieve better consensus for these recommendations. Applying IOM standards may also improve how future PBM guidelines are developed.³⁵ These include standardizing (i) how evidence is evaluated (including relative benefit/harm and cost-effectiveness of individual interventions), and (ii) the strength of recommendations and how these recommendations are articulated. Evidence that is extrapolated from nonobstetric populations should be clearly identified, with the goal to develop a robust context-specific evidence base for obstetric hemorrhage. Last, societies should fully disclose conflicts of interest for guideline authors, obtain greater patient and public involvement,

perform external review, and more regularly update guidelines as new practice-changing evidence emerges.

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REFERENCES

1. Knight M, Callaghan WM, Berg C, et al. Trends in postpartum hemorrhage in high resource countries: a review and recommendations from the International Postpartum Hemorrhage Collaborative Group. *BMC Pregnancy Childbirth*. 2009; 9:55. [PubMed: 19943928]
2. Callaghan WM, Creanga AA, Kuklina EV. Severe maternal morbidity among delivery and postpartum hospitalizations in the United States. *Obstet Gynecol*. 2012; 120:1029–1036. [PubMed: 23090519]
3. Institute of Medicine Committee. *Clinical Practice Guidelines: Directions for a New Program*. National Academy Press; Washington, DC: 1990.
4. Woolf SH, Grol R, Hutchinson A, Eccles M, Grimshaw J. Clinical guidelines: potential benefits, limitations, and harms of clinical guidelines. *BMJ*. 1999; 318:527–530. [PubMed: 10024268]
5. Jackson R, Feder G. Guidelines for clinical guidelines. *BMJ*. 1998; 317:427–428. [PubMed: 9703522]
6. Schmidt C. Conflicting clinical guidelines. *J Natl Cancer Inst*. 2013; 105:2–3. [PubMed: 23257157]
7. Kozek-Langenecker SA, Afshari A, Albaladejo P, et al. Management of severe perioperative bleeding: guidelines from the European Society of Anaesthesiology. *Eur J Anaesthesiol*. 2013; 30:270–382. [PubMed: 23656742]
8. Royal College of Obstetricians and Gynaecologists. *Prevention and Management of Postpartum Haemorrhage (Green-top Guideline 52)*. RCOG; London: 2009.
9. Royal Australian and New Zealand College of Obstetricians and Gynaecologists. [April 15, 2016] Management of Postpartum Hemorrhage. Mar. 2011 Available at: <http://www.ranzcog.edu.au/college-statements-guidelines.html>.
10. Dahlke JD, Mendez-Figueroa H, Maggio L, et al. Prevention and management of postpartum hemorrhage: a comparison of 4 national guidelines. *Am J Obstet Gynecol*. 2015; 213:76, e1–10. [PubMed: 25731692]
11. Goodnough LT, Shander A. Patient blood management. *Anesthesiology*. 2012; 116:1367–1376. [PubMed: 22487863]
12. Holcomb JB, Tilley BC, Baraniuk S, et al. PROPPR Study Group. Transfusion of plasma, platelets, and red blood cells in a 1:1:1 vs a 1:1:2 ratio and mortality in patients with severe trauma: the PROPPR randomized clinical trial. *JAMA*. 2015; 313:471–482. [PubMed: 25647203]
13. Butwick AJ, Goodnough LT. Transfusion and coagulation management in major obstetric hemorrhage. *Curr Opin Anaesthesiol*. 2015; 28:275–284. [PubMed: 25812005]
14. Gutierrez MC, Goodnough LT, Druzin M, Butwick AJ. Postpartum hemorrhage treated with a massive transfusion protocol at a tertiary obstetric center: a retrospective study. *Int J Obstet Anesth*. 2012; 21:230–235. [PubMed: 22647592]
15. Ducloy-Bouthors AS, Susen S, Wong CA, Butwick A, Vallet B, Lockhart E. Medical advances in the treatment of postpartum hemorrhage. *Anesth Analg*. 2014; 119:1140–1147. [PubMed: 25329026]
16. Leduc D, Senikas V, Lalonde AB, et al. Clinical Practice Obstetrics Committee; Society of Obstetricians and Gynaecologists of Canada. Active management of the third stage of labour:

prevention and treatment of postpartum hemorrhage. *J Obstet Gynaecol Can.* 2009; 31:980–993. [PubMed: 19941729]

17. Postpartum hemorrhage. ACOG Practice Bulletin No. 76. American College of Obstetricians and Gynecologists. *Obstet Gynecol.* 2006; 108:1039–1047. [PubMed: 17012482]
18. Sentilhes L, Vayssire C, Deneux-Tharaux C, et al. Postpartum hemorrhage: guidelines for clinical practice from the French College of Gynaecologists and Obstetricians (CNGOF): in collaboration with the French Society of Anesthesiology and Intensive Care (SFAR). *Eur J Obstet Gynecol Reprod Biol.* 2016; 198:12–21. [PubMed: 26773243]
19. Schlembach D, Mrtl MG, Girard T, et al. [Management of postpartum hemorrhage (PPH): algorithm of the interdisciplinary D-A-CH consensus group PPH (Germany - Austria - Switzerland)]. *Anaesthesist.* 2014; 63:234–242. [PubMed: 24584885]
20. Abdul-Kadir R, McLintock C, Ducloy AS, et al. Evaluation and management of postpartum hemorrhage: consensus from an international expert panel. *Transfusion.* 2014; 54:1756–1768. [PubMed: 24617726]
21. Main EK, Goffman D, Scavone BM, et al. National Partnership for Maternal Safety; Council for Patient Safety in Women's Health Care. National Partnership for Maternal Safety: consensus bundle on obstetric hemorrhage. *Anesth Analg.* 2015; 121:142–148. [PubMed: 26091046]
22. Tunalp O, Souza JP, Glmezoglu M. World Health Organization. New WHO recommendations on prevention and treatment of postpartum hemorrhage. *Int J Gynaecol Obstet.* 2013; 123:254–256. [PubMed: 24054054]
23. Lalonde A. International Federation of Gynecology and Obstetrics. Prevention and treatment of postpartum hemorrhage in low-resource settings. *Int J Gynaecol Obstet.* 2012; 117:108–118. [PubMed: 22502595]
24. Carson JL, Grossman BJ, Kleinman S, et al. Clinical Transfusion Medicine Committee of the AABB. Red blood cell transfusion: a clinical practice guideline from the AABB*. *Ann Intern Med.* 2012; 157:49–58. [PubMed: 22751760]
25. Kaufman RM, Djulbegovic B, Gernsheimer T, et al. AABB. Platelet transfusion: a clinical practice guideline from the AABB. *Ann Intern Med.* 2015; 162:205–213. [PubMed: 25383671]
26. Roback JD, Caldwell S, Carson J, et al. American Association for the Study of Liver; American Academy of Pediatrics; United States Army; American Society of Anesthesiology; American Society of Hematology. Evidence-based practice guidelines for plasma transfusion. *Transfusion.* 2010; 50:1227–1239. [PubMed: 20345562]
27. Practice guidelines for perioperative blood management: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Blood Management*. *Anesthesiology.* 2015; 122:241–275. [PubMed: 25545654]
28. Hunt BJ, Allard S, Keeling D, Norfolk D, Stanworth SJ, Pendry K. British Committee for Standards in Haematology. A practical guideline for the haematological management of major haemorrhage. *Br J Haematol.* 2015; 170:788–803. [PubMed: 26147359]
29. National Blood Authority (NBA). Patient Blood Management Guidelines: Module 5—Obstetrics and Maternity. NBA; Canberra, Australia: 2015.
30. Klein AA, Arnold P, Bingham RM, et al. AAGBI guidelines: the use of blood components and their alternatives 2016. *Anaesthesia.* 2016; 71:829–842. [PubMed: 27062274]
31. New grades for recommendations from the Canadian Task Force on Preventive Health Care. *CMAJ.* 2003; 169:207–208. [PubMed: 12900479]
32. Collis RE, Collins PW. Haemostatic management of obstetric haemorrhage. *Anaesthesia.* 2015; 70(suppl 1):78–86. e27–e28. [PubMed: 25440400]
33. Solomon C, Collis RE, Collins PW. Haemostatic monitoring during postpartum haemorrhage and implications for management. *Br J Anaesth.* 2012; 109:851–863. [PubMed: 23075633]
34. Montori VM, Brito JP, Murad MH. The optimal practice of evidence-based medicine: incorporating patient preferences in practice guidelines. *JAMA.* 2013; 310:2503–2504. [PubMed: 24165826]
35. IOM (Institute of Medicine). Clinical Practice Guidelines We Can Trust. The National Academies Press; Washington, DC: 2011.

36. Shekelle PG, Woolf SH, Eccles M, Grimshaw J. Clinical guidelines: developing guidelines. *BMJ*. 1999; 318:593–596. [PubMed: 10037645]
37. Patterson JA, Roberts CL, Isbister JP, et al. What factors contribute to hospital variation in obstetric transfusion rates? *Vox Sang*. 2015; 108:37–45. [PubMed: 25092527]
38. Bose P, Regan F, Paterson-Brown S. Improving the accuracy of estimated blood loss at obstetric haemorrhage using clinical reconstructions. *BJOG*. 2006; 113:919–924. [PubMed: 16907938]
39. Stafford I, Dildy GA, Clark SL, Belfort MA. Visually estimated and calculated blood loss in vaginal and cesarean delivery. *Am J Obstet Gynecol*. 2008; 199:519.e1–519.e7. [PubMed: 18639209]
40. Toledo P, McCarthy RJ, Hewlett BJ, Fitzgerald PC, Wong CA. The accuracy of blood loss estimation after simulated vaginal delivery. *Anesth Analg*. 2007; 105:1736–1740. [PubMed: 18042876]
41. Lilley G, Burkett-St-Laurent D, Precious E, et al. Measurement of blood loss during postpartum haemorrhage. *Int J Obstet Anesth*. 2015; 24:8–14. [PubMed: 25433576]
42. Hancock A, Weeks AD, Lavender DT. Is accurate and reliable blood loss estimation the ‘crucial step’ in early detection of postpartum haemorrhage: an integrative review of the literature. *BMC Pregnancy Childbirth*. 2015; 15:230. [PubMed: 26415952]
43. Shields LE, Wiesner S, Fulton J, Pelletreau B. Comprehensive maternal hemorrhage protocols reduce the use of blood products and improve patient safety. *Am J Obstet Gynecol*. 2015; 212:272–280. [PubMed: 25025944]
44. Pacagnella RC, Souza JP, Durocher J, et al. A systematic review of the relationship between blood loss and clinical signs. *PLoS One*. 2013; 8:e57594. [PubMed: 23483915]
45. Parks JK, Elliott AC, Gentilello LM, Shafi S. Systemic hypotension is a late marker of shock after trauma: a validation study of Advanced Trauma Life Support principles in a large national sample. *Am J Surg*. 2006; 192:727–731. [PubMed: 17161083]
46. Nuttall GA, Stehling LC, Beighley CM, Faust RJ, American Society of Anesthesiologists Committee on Transfusion Medicine. Current transfusion practices of members of the American Society of Anesthesiologists: a survey. *Anesthesiology*. 2003; 99:1433–1443. [PubMed: 14639159]
47. Armstrong S, Fernando R, Columb M. Minimally- and noninvasive assessment of maternal cardiac output: go with the flow! *Int J Obstet Anesth*. 2011; 20:330–340. [PubMed: 21925868]
48. Gouveia V, Marcelino P, Reuter DA. The role of transesophageal echocardiography in the intraoperative period. *Curr Cardiol Rev*. 2011; 7:184–196. [PubMed: 22758616]
49. Rice MJ, Gravenstein N, Morey TE. Noninvasive hemoglobin monitoring: how accurate is enough? *Anesth Analg*. 2013; 117:902–907. [PubMed: 23842195]
50. Bingham, D.; Melsop, K.; Main, E. The California Maternal Quality Care Collaborative (CMQCC). Stanford University; Palo Alto, CA: 2010. CMQCC Obstetric Hemorrhage Toolkit Hospital Level Implementation Guide..
51. Wu E, Jolley JA, Hargrove BA, Caughey AB, Chung JH. Implementation of an obstetric hemorrhage risk assessment: validation and evaluation of its impact on pretransfusion testing and hemorrhage outcomes. *J Matern Fetal Neonatal Med*. 2015; 28:71–76. [PubMed: 24670202]
52. Dilla AJ, Waters JH, Yazer MH. Clinical validation of risk stratification criteria for peripartum hemorrhage. *Obstet Gynecol*. 2013; 122:120–126. [PubMed: 23743452]
53. Dexter F, Epstein RH. Applying systematic criteria for type and screen based on procedure's probability of erythrocyte transfusion. *Anesthesiology*. 2014; 120:241.
54. Frank SM, Rothschild JA, Masear CG, et al. Optimizing preoperative blood ordering with data acquired from an anesthesia information management system. *Anesthesiology*. 2013; 118:1286–1297. [PubMed: 23695091]
55. Rinehart JB, Lee TC, Kaneshiro K, Tran MH, Sun C, Kain ZN. Perioperative blood ordering optimization process using information from an anesthesia information management system. *Transfusion*. 2016; 56:938–945. [PubMed: 26876784]
56. Goodnough LT, Spain DA, Maggio P. Logistics of transfusion support for patients with massive hemorrhage. *Curr Opin Anaesthesiol*. 2013; 26:208–214. [PubMed: 23446185]

57. Boisen ML, Collins RA, Yazer MH, Waters JH. Pretransfusion testing and transfusion of uncrossmatched erythrocytes. *Anesthesiology*. 2015; 122:191–195. [PubMed: 25127209]
58. Goodnough LT, Daniels K, Wong AE, Viele M, Fontaine MF, Butwick AJ. How we treat: transfusion medicine support of obstetric services. *Transfusion*. 2011; 51:2540–2548. [PubMed: 21542850]
59. Lewis, G. The Seventh Report on Confidential Enquiries into Maternal Deaths in the United Kingdom. CEMACH; London: 2007. The Confidential Enquiry into Maternal and Child Health (CEMACH). Saving mothers' lives: reviewing maternal deaths to make motherhood safer—2003–2005..
60. Mhyre JM, Shilkrut A, Kuklina EV, et al. Massive blood trans-fusion during hospitalization for delivery in New York State, 1998-2007. *Obstet Gynecol*. 2013; 122:1288–1294. [PubMed: 24201690]
61. Clark SL, Hankins GD. Preventing maternal death: 10 clinical diamonds. *Obstet Gynecol*. 2012; 119:360–364. [PubMed: 22270288]
62. Kacmar RM, Mhyre JM, Scavone BM, Fuller AJ, Toledo P. The use of postpartum hemorrhage protocols in United States academic obstetric anesthesia units. *Anesth Analg*. 2014; 119:906–910. [PubMed: 25238236]
63. Janelle GM, Shore-Lesserson L, Smith CE, Levy JH, Shander A. What is the PROPPR transfusion strategy in trauma resuscitation? *Anesth Analg*. 2016; 122:1216–1219. [PubMed: 26991624]
64. van der Bom JG. Rotem in postpartum hemorrhage. *Blood*. 2014; 124:1700–1701. [PubMed: 25214195]
65. Holst LB, Petersen MW, Haase N, Perner A, Wetterslev J. Restrictive versus liberal transfusion strategy for red blood cell transfusion: systematic review of randomised trials with meta-analysis and trial sequential analysis. *BMJ*. 2015; 350:h1354. [PubMed: 25805204]
66. Spahn DR, Spahn GH, Stein P. Evidence base for restrictive transfusion triggers in high-risk patients. *Transfus Med Hemother*. 2015; 42:110–114. [PubMed: 26019706]
67. Goodnough LT, Maggio P, Hadhazy E, et al. Restrictive blood transfusion practices are associated with improved patient outcomes. *Transfusion*. 2014; 54:2753–2759. [PubMed: 24995770]
68. Oliver JC, Griffin RL, Hannon T, Marques MB. The success of our patient blood management program depended on an institution-wide change in transfusion practices. *Transfusion*. 2014; 54:2617–2624. [PubMed: 24410741]
69. Roubinian NH, Escobar GJ, Liu V, et al. NHLBI Recipient Epidemiology and Donor Evaluation Study (REDS-III). Trends in red blood cell transfusion and 30-day mortality among hospitalized patients. *Transfusion*. 2014; 54:2678–2686. [PubMed: 25135770]
70. Yerrabothala S, Desrosiers KP, Szczepiorkowski ZM, Dunbar NM. Significant reduction in red blood cell transfusions in a general hospital after successful implementation of a restrictive transfusion policy supported by prospective computerized order auditing. *Transfusion*. 2014; 54:2640–2645. [PubMed: 24673396]
71. Prick BW, Jansen AJ, Steegers EA, et al. Transfusion policy after severe postpartum haemorrhage: a randomised non-inferiority trial. *BJOG*. 2014; 121:1005–1014. [PubMed: 24405687]
72. Gaynes, BN.; Gavin, N.; Melzer-Brody, S., et al. Perinatal Depression: Prevalence, Screening Accuracy, and Screening Outcomes. Agency for Healthcare Research and Quality; Rockville, MD: 2005.
73. Corwin EJ, Murray-Kolb LE, Beard JL. Low hemoglobin level is a risk factor for postpartum depression. *J Nutr*. 2003; 133:4139–4142. [PubMed: 14652362]
74. Eckerdal P, Kollia N, Löfblad J, et al. Delineating the association between heavy postpartum haemorrhage and postpartum depression. *PLoS One*. 2016; 11:e0144274. [PubMed: 26807799]
75. Lee KA, Zaffke ME. Longitudinal changes in fatigue and energy during pregnancy and the postpartum period. *J Obstet Gynecol Neonatal Nurs*. 1999; 28:183–191.
76. Beard JL, Hendricks MK, Perez EM, et al. Maternal iron deficiency anemia affects postpartum emotions and cognition. *J Nutr*. 2005; 135:267–272. [PubMed: 15671224]
77. Murray-Kolb LE, Beard JL. Iron deficiency and child and maternal health. *Am J Clin Nutr*. 2009; 89:946S–950S. [PubMed: 19158210]

78. Bodnar LM, Siega-Riz AM, Miller WC, Cogswell ME, McDonald T. Who should be screened for postpartum anemia? An evaluation of current recommendations. *Am J Epidemiol.* 2002; 156:903–912. [PubMed: 12419762]
79. Milman N. Postpartum anemia II: prevention and treatment. *Ann Hematol.* 2012; 91:143–154. [PubMed: 22160256]
80. Muñoz M, Gómez-Ramírez S, Kozek-Langeneker S, et al. ‘Fit to fly’: overcoming barriers to preoperative haemoglobin optimization in surgical patients. *Br J Anaesth.* 2015; 115:15–24. [PubMed: 26089443]
81. Haas T, Fries D, Tanaka KA, Asmis L, Curry NS, Schöchl H. Usefulness of standard plasma coagulation tests in the management of perioperative coagulopathic bleeding: is there any evidence? *Br J Anaesth.* 2015; 114:217–224. [PubMed: 25204698]
82. Collins PW, Lilley G, Bruynseels D, et al. Fibrin-based clot formation as an early and rapid biomarker for progression of postpartum hemorrhage: a prospective study. *Blood.* 2014; 124:1727–1736. [PubMed: 25024304]
83. de Lloyd L, Bovington R, Kaye A, et al. Standard haemostatic tests following major obstetric haemorrhage. *Int J Obstet Anesth.* 2011; 20:135–141. [PubMed: 21439811]
84. Green L, Knight M, Seeney F, et al. The haematological features and transfusion management of women who required massive transfusion for major obstetric haemorrhage in the UK: a population based study. *Br J Haematol.* 2016; 172:616–624. [PubMed: 26683982]
85. Charbit B, Mandelbrot L, Samain E, et al. PPH Study Group. The decrease of fibrinogen is an early predictor of the severity of postpartum hemorrhage. *J Thromb Haemost.* 2007; 5:266–273. [PubMed: 17087729]
86. Cortet M, Deneux-Tharaux C, Dupont C, et al. Association between fibrinogen level and severity of postpartum haemorrhage: secondary analysis of a prospective trial. *Br J Anaesth.* 2012; 108:984–989. [PubMed: 22490316]
87. Gayat E, Resche-Rigon M, Morel O, et al. Predictive factors of advanced interventional procedures in a multicentre severe post-partum haemorrhage study. *Intensive Care Med.* 2011; 37:1816–1825. [PubMed: 21805157]
88. de Lange NM, Lancé MD, de Groot R, Beckers EA, Henskens YM, Scheepers HC. Obstetric hemorrhage and coagulation: an update. Thromboelastography, thromboelastometry, and conventional coagulation tests in the diagnosis and prediction of postpartum hemorrhage. *Obstet Gynecol Surv.* 2012; 67:426–435. [PubMed: 22926249]
89. Mallaiah S, Barclay P, Harrod I, Chevannes C, Bhalla A. Introduction of an algorithm for ROTEM-guided fibrinogen concentrate administration in major obstetric haemorrhage. *Anaesthesia.* 2015; 70:166–175. [PubMed: 25289791]
90. Alam A, Choi S. Prophylactic use of tranexamic acid for post-partum bleeding outcomes: a systematic review and meta-analysis of randomized controlled trials. *Transfus Med Rev.* 2015; 29:231–241. [PubMed: 26282735]
91. Ferrer P, Roberts I, Sydenham E, Blackhall K, Shakur H. Anti-fibrinolytic agents in post partum haemorrhage: a systematic review. *BMC Pregnancy Childbirth.* 2009; 9:29. [PubMed: 19604358]
92. Sentilhes L, Lasocki S, Ducloy-Bouthors AS, et al. Tranexamic acid for the prevention and treatment of postpartum haemorrhage. *Br J Anaesth.* 2015; 114:576–587. [PubMed: 25571934]
93. Shakur H, Elbourne D, Gülmezoglu M, et al. The WOMAN Trial (World Maternal Antifibrinolytic Trial): tranexamic acid for the treatment of postpartum haemorrhage: an international randomised, double blind placebo controlled trial. *Trials.* 2010; 11:40. [PubMed: 20398351]
94. Alfirevic Z, Elbourne D, Pavord S, et al. Use of recombinant activated factor VII in primary postpartum hemorrhage: the Northern European registry 2000–2004. *Obstet Gynecol.* 2007; 110:1270–1278. [PubMed: 18055720]
95. Franchini M, Lippi G, Franchi M. The use of recombinant activated factor VII in obstetric and gynaecological haemorrhage. *BJOG.* 2007; 114:8–15. [PubMed: 17233855]
96. Phillips LE, McLintock C, Pollock W, et al. Australian and New Zealand Haemostasis Registry. Recombinant activated factor VII in obstetric hemorrhage: experiences from the Australian and New Zealand Haemostasis Registry. *Anesth Analg.* 2009; 109:1908–1915. [PubMed: 19923520]

97. Sobieszczyk S, Breborowicz GH, Platcanov V, Tanchev S, Kessler CM. Recombinant factor VIIa in the management of postpartum bleeds: an audit of clinical use. *Acta Obstet Gynecol Scand*. 2006; 85:1239–1247. [PubMed: 17068684]
98. Wikkelsø AJ, Edwards HM, Afshari A, et al. FIB-PPH trial group. Pre-emptive treatment with fibrinogen concentrate for postpartum haemorrhage: randomized controlled trial. *Br J Anaesth*. 2015; 114:623–633. [PubMed: 25586727]
99. Aawar N, Alikhan R, Bruynseels D, et al. Fibrinogen concentrate versus placebo for treatment of postpartum haemorrhage: study protocol for a randomised controlled trial. *Trials*. 2015; 16:169. [PubMed: 25906770]
100. Ducloy-Bouthors AS, Mignon A, Huissoud C, Grouin JM, Mercier FJ. Fibrinogen concentrate as a treatment for post-partum haemorrhage-induced coagulopathy: a study protocol for a randomized multicentre controlled trial. The Fibrinogen in haemorrhage of DELivery (FIDEL) trial. *Anaesth Crit Care Pain Med*. 2016 [epub ahead of print].
101. Collins P, Abdul-Kadir R, Thachil J. Subcommittees on Women's Health Issues in Thrombosis and Haemostasis and on Disseminated Intravascular Coagulation. Management of coagulopathy associated with postpartum hemorrhage: guidance from the SSC of the ISTH. *J Thromb Haemost*. 2016; 14:205–210. [PubMed: 27028301]
102. Institute for Healthcare Improvement. [March 30, 2016] Evidence-based care bundles. Available at: <http://www.ihl.org/resources/Pages/ImprovementStories/WhatIsaBundle.aspx>
103. Wanderer JP, Ehrenfeld JM. Clinical decision support for perioperative information management systems. *Semin Cardiothorac Vasc Anesth*. 2013; 17:288–293. [PubMed: 23690340]
104. Brouwers MC, Kho ME, Browman GP, et al. AGREE Next Steps Consortium. AGREE II: advancing guideline development, reporting and evaluation in health care. *CMAJ*. 2010; 182:E839–E842. [PubMed: 20603348]

Table 1

Background Information for National and International Obstetric Societies' Postpartum Hemorrhage Guidelines

	ACOG—USA	SOGC—Canada	RCOG—UK	RANZCOG—Australia, New Zealand	D-A-CH—Germany, Austria, Switzerland	International Expert Panel ^a	National Partnership for Maternal Safety	CNGOF—France
Year of publication	2006 (reaffirmed in 2015)	2009	2009; minor revisions in 2011	2014; amended in 2015	2014 ^b	2014	2015	2016
Guideline committee	The ACOG committee on practice bulletins	The SOGC clinical practice obstetrics committee	The RCOG guidelines and audit committee. Peer review of guidelines by representatives from obstetrics, anesthesiology, hematology, blood service, Jehovah's Witness organization, and midwifery.	The RANZCOG Women's Health Committee including representatives from obstetrics, general practice, consumer groups, and midwifery.	A cross-border algorithm action team with representatives from obstetrics, anesthesiology, and critical care.	International experts in obstetrics, hematology, and anesthesiology	Council on Patient Safety in Women's Health Care. Guidelines committee comprises representatives from anesthesia, obstetric, blood bank, family practice, nurse, and midwifery societies	The CNGOF appointed a steering committee to define questions for experts. The committee experts reviewed the literature to answer questions raised. Experts comprised obstetricians, anesthesiologists, and midwives. Conflicts of interest were described
Definitions for PPH	EBL > 500 mL (VD). EBL > 1000 mL (CD)	The volume of EBL that causes hemodynamic instability	Minor PPH: EBL 500–1000 mL. Moderate PPH: EBL 1000–2000 mL. Severe PPH: EBL >2000 mL ^b OR Clinical signs of shock	EBL > 500 mL. Severe PPH: EBL 1000 mL OR Clinical signs of shock	EBL > 500 mL within 24 h after delivery. Severe PPH: EBL >1500–2000 mL or EBL > 150 mL/min or EBL >50% of the circulating volume within 3 h	Active bleeding >1000 mL within 24 h after birth that continues despite the use of initial measures including first-line uterotonic agents and uterine massage	Cumulative blood loss of 1000 mL or blood loss accompanied by signs and symptoms of hypovolemia within 24 h of delivery	EBL 500 mL. Severe PPH: EBL 1000 mL
Details of literature searches and other sources of information	Medline, Cochrane library, ACOG internal resources and documents. English language publications between 1901 and 2006. Expert	Medline, PubMed, Cochrane database of systematic reviews, ACP journal club, BMJ Clinical Evidence. Publications between 1995 and 2007	Cochrane library, Trip database, Medline, PubMed. Human studies and English language publications between 2002 and 2007. National Library for	Literature search; no specific details provided. Expert opinions also considered.	Existing national and international guidelines plus a review of the literature	PubMed	No specific details provided	Medline, Cochrane library, bibliographies of articles. Search restricted to English and French language articles up to mid-2014. Articles considered included original research, review articles, guidelines

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	ACOG—USA	SOGC—Canada	RCOG—UK	RANZCOG—Australia, New Zealand	D-A-CH—Germany, Austria, Switzerland	International Expert Panel ^a	National Partnership for Maternal Safety	CNGOF—France
	opinions also considered.		Health and National Guidelines Clearing House were also searched.					from other obstetric societies and agencies.
Were criteria used to assess the quality and strength of evidence?	Yes	Yes	Yes	No	No	Yes	No	Yes
Was a rating system used for the strength of recommendations?	Yes	Yes	Yes	Yes	No	Yes	No	Yes

Abbreviations: ACOG, American College of Obstetricians and Gynecologists; ACP, American College of Physicians; CD, cesarean delivery; CNGOF, French College of Gynaecologists and Obstetricians in collaboration with the French Society of Anesthesiology and Intensive Care); D-A-CH, Germany, Austria, and Switzerland; EBL, estimated blood loss; RANZCOG, Royal Australian and New Zealand College of Obstetricians and Gynaecologists; RCOG, Royal College of Obstetricians and Gynaecologists; SOGC, Society of Obstetricians and Gynaecologists of Canada; VD, vaginal delivery.

Members of an expert panel were convened in November 2011. Consensus recommendations were published in Transfusion 2014; 54: 1756–68. Financial support for the consensus meeting was provided by CSL Behring (Marburg, Germany). Experts received funding support and honoraria from CSL Behring to attend the consensus meeting. No other conflicts of interest of funding sources were declared.

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Table 2

commendations in National and International Obstetric Societies' Postpartum Hemorrhage Guidelines

ACOG—USA	SOGC—Canada	RCOG—UK	RANZCOG—Australia, New Zealand	D-A-CH—Germany, Austria, Switzerland	International Expert Panel ^a	National Partnership for Maternal Safety	CNGOF—France
the extent of blood loss is significant and going, especially if vital signs are unstable	Not discussed	Blood loss >1000 mL and continuing to bleed or clinical shock	Blood should be considered early to restore oxygen-carrying capacity	Transfuse according to clinical picture. Blood loss is often underestimated	To maintain circulating blood volume and tissue oxygenation if initial treatment unsuccessful with ongoing blood loss >1000 mL	Not discussed	Indications for specific blood components were described for PPH management after vaginal delivery
Replacement for oxygen-carrying capacity not for volume placement	Not discussed	Therapeutic goal = Hb >8 g/dL. If fully crossmatched blood is unavailable, in an emergency, use O-negative RhD-negative blood. If the ABO and rhesus group is known, use ABO and D group compatible uncrossmatched blood	Request 4 units RBC or other locally agreed volume. Consider group specific or O-negative RhD-negative blood early	No specific recommendations for RBC transfusion. Therapeutic goal = Hb level between 8 and 10 g/dL	Not discussed	Transfusion protocols are recommended that allow emergency release of blood products. Emergency release products can include O-negative RBCs or type specific RBC	RBC transfusion based principally on clinical signs of PPH severity, without necessarily waiting for laboratory test results. Maintain Hb level >8 g/dL
Not discussed	Not discussed	Therapeutic goal = PT < 1.5× mean control, PTT < 1.5× mean control. Transfuse 4 units FFP for every 6 units of RBC or if PT/APTT > 1.5× normal. For “relentless” bleeding, give up to 1 L FFP empirically.	Therapeutic goal = PT/APTT < 1.5× normal and INR 1.5. Transfuse FFP 15 mL/kg if INR > 1.5	FFP >20–30 mL/kg is recommended to correct a coagulation disorder	Not discussed	AB plasma can be provided as an emergency release product. Although no specific advice is given, the bundle makes reference to fixed-ratio transfusion regimens and the use of coagulation/P OC testing	If severe PPH or coagulopathy, FFP can be given without awaiting laboratory results
Not discussed	Not discussed	Therapeutic goal PLT count >75 × 10 ⁹ /L. Transfuse platelets if PLT count < 50 × 10 ⁹ /L	Therapeutic goal = PLT count > 50 × 10 ⁹ /L. Transfuse 1 adult “dose” PLT if PLT count <50 × 10 ⁹ /L	Therapeutic goal = PLT count > 50 × 10 ⁹ /L. No specific recommendations for PLT transfusion	Not discussed (for patients without inherited PLT function disorders)	Not discussed	Order PLTs early to maintain PLT count >50 × 10 ⁹ /L
Not discussed	Not discussed	Transfuse cryoprecipitate if fibrinogen <1 g/L. For “relentless”	Therapeutic goal = fibrinogen > 1 g/L. Transfuse 3–4 g cryoprecipitate if	Not discussed	Can be considered for fibrinogen supplementation.	Monitor fibrinogen levels and	Therapeutic goal = fibrinogen level 2 g/L. No clear

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COG—USA	SOGC—Canada	RCOG—UK	RANZCOG—Australia, New Zealand	D-A-CH—Germany, Austria, Switzerland	International Expert Panel ^a	National Partnership for Maternal Safety	CNGOF—France
Not discussed	Not discussed	bleeding, give up to 10 units (2 packs) cryoprecipitate empirically	fibrinogen <1 g/L. Consider early as DIC often present	Not discussed	Maintain fibrinogen concentration >2.0 g/L	replace with cryoprecipitate	recommendation for fibrinogen concentrate or cryoprecipitate is described
Not discussed	Not discussed	Not discussed	An MTP is described ^c	Not discussed	An MTP is recommended for the correction of coagulopathy for ongoing, uncontrolled PPH >2000 mL	Yes; each unit to establish its own MTP	Not discussed
Not discussed	Not discussed	Antifibrinolytics not recommended	Tranexamic acid 1 g over 10 min then 1 g over 8 h if massive transfusion protocol activated	If TEG or ROTEM is unavailable and severe PPH (see Table 1); give 2 g of tranexamic acid with fibrinogen concentrate (2–4 g)	In the early treatment of severe PPH, administer tranexamic acid before fibrinogen supplementation (1 g, then repeat 1 g after 30 min followed by a 1 g/h infusion).	Not discussed	Tranexamic acid may be useful although clinical value is unproven. Use at clinician discretion. Recommended for PPH secondary to refractory uterine atony (1 g dose, repeated if ineffective after first dose). Not recommended to prevent PPH during CD
Not discussed	Not discussed	Only recommend, after consulting an hematologist, for patients with life-threatening hemorrhage. Fibrinogen level should be >1 g/L and PLT count should be >20 × 10 ⁹ /L before RVIIa is given	Consider if uncontrolled hemorrhage in a salvageable patient, failed surgical or radiological measures to control bleeding AND adequate blood component replacement AND pH >7.2, temperature >34°C	As a last resort (90 µg/kg bolus, if hemorrhage persists repeat after 20 min), only if pH >7.2, fibrinogen level >1.5 g/L, temperature >35°C, PLT >50 × 10 ⁹ /L, and hyperfibrinolysis has been excluded	For life-threatening PPH, consider as an adjunct to other surgical treatments (90 µg/kg bolus, repeat if no clinical response within 15–30 min). Adequate levels of PLT and fibrinogen are essential. Check and correct PLT and fibrinogen levels before RVIIa is given	Not discussed	No evidence to support recommending RVIIa for PPH prevention or treatment. Consider only for uncontrolled hemorrhage after failure of conventional treatment and correction of PLT levels and other hemostatic indices
Not discussed	Not discussed	Current evidence supports the use of cell salvage in obstetrics	Consider cell salvage where appropriate	Not discussed	Not discussed	Not discussed	Not discussed
Not discussed	Not discussed	Special blood filters should not be used as they slow infusions. A maximum of 3.5 L warmed crystalloid or 1–2 L colloid may be given while waiting for blood to arrive	Consider patient's previous hemoglobin and blood volume when assessing severity of hemorrhage. Other therapeutic goals include: base excess <–6; lactate <4 mmol/L; pH >7.2; calcium >1.1 mmol/L. Tolerate	Point-of-care testing for coagulation, such as TEG, suggested for coagulation analysis. Other therapeutic goals include: systolic BP >80 mm Hg; pH >7.2; temperature >35°C; calcium >0.8 mmol/L	Perform coagulation screen (including PLT, PT, APTT, and fibrinogen level) when persistent (ongoing) PPH is declared. Assess coagulation status every 45–60 min until	Establish a PPH response team including blood bank	Prevent severe antenatal anemia with iron supplements. Laboratory monitoring of

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COG—USA	SOGC—Canada	RCOG—UK	RANZCOG—Australia, New Zealand	D-A-CH—Germany, Austria, Switzerland	International Expert Panel ^a	National Partnership for Maternal Safety	CNGOF—France
may be useful in the postpartum period			permissive hypotension (BP 80–100 mm Hg systolic) until active bleeding controlled		bleeding controlled and coagulation defects corrected. If available, point-of-care testing can also be performed		coagulation recommended. All maternity units should be associated with a blood bank, and practitioners should be familiar with local logistics to procure blood products. Blood should be available within 30 min

of Obstetricians and Gynecologists; APTT, activated partial thromboplastin time; BP blood pressure; CD, cesarean delivery; CNGOF, French College of Obstetrics and Gynecology; FFP, fresh frozen plasma; Hb, hemoglobin; D-A-CH, Germany, Austria, and Switzerland; POC, point of care; PPH, postpartum hemorrhage; PT, prothrombin time; RANZCOG, Royal College of Obstetricians and Gynaecologists; RBC, packed red blood cells; RCOG, Royal College of Obstetricians and Gynaecologists; ROTEM, rotational thromboelastography.

Consensus recommendations were published in Transfusion 2014; 54: 1756–68. Financial support for the consensus meeting was provided by the National Blood Authority from CSL Behring to attend the consensus meeting. No other conflicts of interest of funding sources were declared.

from the Royal College of Obstetricians and Gynecologists was sourced from the Patient Blood Management Guidelines: published by the National Blood Authority, Australia. 2011. URL: <http://www.blood.gov.au/system/files/documents/pbm-module-1.pdf> (Accessed

Table 3
National Anesthesia and Transfusion Societies' Recommendations for Transfusion

	AABB—USA	ASA—USA	ESA—Europe ^a	BCSH—UK	NBA—Australia	AAGBI—UK
Year	RBC guidelines: 2012; plasma guidelines: 2010; platelet guidelines: 2014	2015	2013	2015	2015	2016
Aims	RBC guidelines: "to focus on Hb concentration thresholds and other clinical variables that might trigger RBC transfusion." Plasma guidelines: To help direct appropriate transfusion of plasma	Improve the perioperative management of blood transfusion and adjunct therapies and to reduce the risk of adverse outcomes associated with transfusions, bleeding, or anemia	To identify patients for whom the perioperative bleeding risk is increased; to correct preoperative anemia and patients' tolerance to bleeding; [to deliver] targeted procoagulant interventions to reduce bleeding, morbidity, mortality, and costs	To provide recommendations for the hematological management of major hemorrhage in any clinical situation	To improve clinical outcomes by avoiding unnecessary exposure to blood components. "Three pillars" are described: optimization of blood volume and red cell mass, minimization of blood loss, and optimization of anemia tolerance	To formalize guidance on the clinical indications and risks of transfusion, blood conservation, and the transfusion process
Did the guidelines have a section with specific recommendations for pregnant women?	No	Obstetric patients referenced in platelet and cryoprecipitate recommendations	Yes	Yes	Yes. Patient Blood Management Guidelines: Module 5 —Obstetrics and Maternity. (Other modules reviewed critical bleeding/ massive transfusion, perioperative, medical, and critical care settings)	Yes
RBC	A restrictive transfusion strategy was recommended (Hb trigger between 7-8 g/dL) for hospitalized patients. Restrictive strategy in hospitalized patients with preexisting cardiovascular disease: consider transfusion for symptomatic patients or a Hb level <8 g/dL. Transfusion decisions should be influenced by	Consider a restrictive RBC transfusion strategy. Justification for treating Hb levels between 6 and 10 g/dL should take into account rate/magnitude of blood loss, intravascular volume status, signs of organ ischemia, and adequacy of cardiopulmonary reserve. Reassess RBC requirements after each unit if possible	A target Hb level between 7-9 g/dL is recommended during active bleeding; ESA recommends PPH management by a multidisciplinary team, predelivery risk assessment, and early recognition of severe PPH	Rate of RBC administration guided by rate of blood loss and hemodynamic compromise. The aim is to maintain an Hb level that supports adequate oxygen delivery to tissues. Hospitals should ensure that emergency group O RBC or group-specific RBC are available for life-threatening hemorrhage. Until group known use O RhD-negative units in females <50 y	Use of RBC is life-saving for patients requiring massive transfusion. MTP use for critical bleeding may reduce the risk of morbidity/mortality. For nonbleeding patients, consider single unit RBC transfusion, followed by clinical reassessment. RBC transfusion for a Hb <7 g/dL may be associated with reduced mortality but may not be required for well-compensated patients or where	Transfuse RBC for major hemorrhage (group O Rh-negative RBC should be available and transfused for life-threatening hemorrhage for women of childbearing potential). An Hb threshold = 7 g/dL is a guide for RBC transfusion

	AABB—USA	ASA—USA	ESA—Europe ^a	BCSH—UK	NBA—Australia	AAGBI—UK
Plasma	symptoms, as well as Hb level Plasma should be given to trauma patients requiring massive transfusion. Could not recommend for or against FFP:RBC transfusion ratio of 1:3 or more in trauma patients during massive transfusion. Could not recommend for or against plasma transfusion to patients undergoing surgery in the absence of massive transfusion	Correction of excessive microvascular bleeding if INR >2. For correction of excessive microvascular bleeding in massively transfused patients with >1 blood volume or when PT/INR/APTT cannot be measured in a timely fashion. Urgent reversal of warfarin therapy. Correction of known coagulation factor deficiencies	For life-threatening hemorrhage, a fixed product ratio or individualized procoagulant intervention and factor substitution were recommended	Transfuse FFP in at least a 1:2 ratio with RBC, before transitioning to goal-directed transfusion using laboratory tests. Once bleeding is controlled, consider FFP (15–20 mL/kg) if PT or APTT >1.5× normal. If laboratory results are not available, transfuse FFP in at least a 1:2 ratio with RBC, before blood product use guided by laboratory results	For major obstetric hemorrhage, suggest transfusion of 1.5 mL/kg FFP	PPH associated with atony or trauma is unlikely to be associated with hemostatic impairment unless diagnosis is delayed. If laboratory coagulation status unknown, withhold FFP until 4 units RBC have been administered, then use a 1:1 ratio RBC:FFP until results of hemostatic tests are known. Point-of-care testing, with measurement of fibrinogen levels, is recommended
PLTs	No recommendations for PLT transfusion for patients experiencing perioperative blood loss	PLT count <50 × 10 ⁹ /L in the presence of excessive bleeding. Rarely indicated if the platelet count >100 × 10 ⁹ /L	See plasma recommendation. PLT count <100 × 10 ⁹ /L at the onset of labor, particularly combined with plasma fibrinogen concentration <2.9 g/L indicates an increased risk of PPH.	Therapeutic goal = PLT count > 50 × 10 ⁹ /L. Transfuse if PLT count <100 × 10 ⁹ /L and ongoing bleeding	For major obstetric hemorrhage, suggest transfusion of 1 adult therapeutic dose of PLTs. A PLT count >50 × 10 ⁹ /L is acceptable for VD or CD	If patient is actively bleeding, transfuse to a therapeutic goal = PLT count >75 × 10 ⁹ /L. In the obstetric setting, PLT transfusion is rarely required and should only be given once the PLT count is known
Fibrinogen replacement therapies	Not discussed	Cryoprecipitate is indicated when laboratory evidence indicates fibrinolysis, or when the fibrinogen concentration <80–100 mg/dL in the presence of excessive bleeding. The ASA note that cryoprecipitate may be indicated at higher fibrinogen concentrations in actively bleeding obstetric patients. Consider	For perioperative bleeding, consider fibrinogen supplementation if the fibrinogen concentration <1.5–2.0 g/L or functional fibrinogen deficit detected by thromboelastography or rotational thromboelastometry. A higher fibrinogen trigger value may be needed for treating hypofibrinogenemia in obstetric patients.	Therapeutic goal = plasma fibrinogen concentration >1.5 g/L. For obstetric hemorrhage, early fibrinogen supplementation if levels <2 g/dL and ongoing bleeding	For major obstetric hemorrhage, suggest 3–4 g cryoprecipitate. Consider fibrinogen concentrate when available and acceptable to women	Plasma fibrinogen levels <3 g/L are associated with progression to major obstetric hemorrhage. Fibrinogen should be replaced with either cryoprecipitate or fibrinogen concentrate

	AABB—USA	ASA—USA	ESA—Europe ^a	BCSH—UK	NBA—Australia	AAGBI—UK
MTP	In the context of plasma transfusion only. No recommendations are given for MTP components	Cryoprecipitate as an adjunct in massively transfused patients when fibrinogen concentrations cannot be measured in a timely fashion Recommended for massively bleeding patients. No recommendations are given for MTP components	Cryoprecipitate indicated if there is a lack of available fibrinogen concentrate for the treatment of bleeding and hypofibrinogenemia	Described as part of a major hemorrhage protocol (non-specific to obstetric hemorrhage)	Activate MTP early. The MTP should be modified for the obstetric patient because fibrinogen level of 2 g/L indicates critical physiological derangement and is associated with severe PPH	Most major hemorrhage packs contained 4 U RBC and 4 U FFP ± PLTs. If hemorrhage is life-threatening, transfuse group O Rh-negative RBC to women of childbearing potential. Group-specific RBC should be rapidly prepared by the laboratory after receiving a blood sample
Pharmacological agents ^b	Not discussed	Consider antifibrinolytics (tranexamic acid, ε-aminocaproic acid) if fibrinolysis is suspected or documented. The ASA note that the safety of antifibrinolytics has not been established in hypercoagulable patients, including pregnant patients. Consider desmopressin for patients with excessive bleeding and platelet dysfunction. PCC may be used in patients with excessive bleeding and increased INR. Fibrinogen concentrate may be used for excessive bleeding	Tranexamic acid is recommended; no dosing regimen is described. Consider prophylactic tranexamic acid before cesarean delivery. Tranexamic acid is also recommended for antepartum bleeding. Use DDAVP under specific fibrinogen concentrate dose of 25–50 mg/kg	Tranexamic acid 1 g over 10 min followed by 1 g over 8 h (trauma recommendation). The use of tranexamic acid was recommended for major obstetric hemorrhage	For patients with significant blood loss, consider tranexamic acid within 3 h of hemorrhage onset. Consider prothrombin complex concentrate when available and acceptable to women	Tranexamic acid 1 g for severe PPH (>500 mL VD, >1000 mL CD)
Recombinant FVIIa	Not discussed	Consider when traditional options for treating coagulopathic	Consider as a last-line therapy after the platelet count and fibrinogen level have been optimized	Not recommended	Consider for life-threatening hemorrhage only if conventional measures have failed.	Late use in the exsanguinating patient is almost always associated

	AABB—USA	ASA—USA	ESA—Europe ^a	BCSH—UK	NBA—Australia	AAGBI—UK
Cell salvage	Not discussed	Reinfuse recovered red blood cells as a blood-sparing intervention in the intraoperative period, when appropriate	Cell salvage is well tolerated (during cesarean delivery), provided that precautions are placed against rhesus isoimmunization	Access to 24-h cell salvage support should be available in cardiac, obstetric, trauma, and vascular centers	Pay strict attention to blood loss control, and physiological, metabolic, and coagulation parameters. Suggested initial dose = 90 µg/kg	with no benefit, a high risk of mortality, and thrombotic complications. Except under hematological direction, not recommended for clinical use Recommended with leukocyte filter, if abnormal bleeding occurs during CD
Other pregnancy-specific recommendations	Not discussed	Anemia threshold = 11.0 g/dL for pregnant women. Cryoprecipitate may be indicated at a higher fibrinogen concentration in actively bleeding obstetric patients	Thromboelastometry can identify obstetric coagulopathy and hyperfibrinolysis and guide hemostatic therapy. APTT and PT values are of limited predictive value for PPH	Not discussed	Iron therapy for iron deficiency anemia is recommended. During major obstetric hemorrhage, measure temperature, acid-base, ionized calcium, Hb, PLT, PT/INR, APTT, and fibrinogen level. For patients with abnormal coagulation tests who are not bleeding, the routine use of FFP or cryoprecipitate is not recommended. Optimize patients with preexisting hematological conditions before delivery	POC testing preferred over laboratory testing due to speed

Abbreviations: AABB, formerly, the American Association of Blood Banks; AAGBI, Association of Anaesthetists of Great Britain and Ireland; APTT, activated partial thromboplastin time; ASA, American Society of Anesthesiologists; BCSH, British Committee for Standards in Haematology; CD, cesarean delivery; ESA, European Society of Anaesthesiology; FFP, fresh frozen plasma; Hb, hemoglobin; INR, international normalized ratio; MTP, massive transfusion protocol; NBA, National Blood Authority (of Australia); PCC, prothrombin complex concentrate; PLT, platelet; POC, point of care; PPH, postpartum hemorrhage; PT, prothrombin time; RBC, packed red blood cells; VD, vaginal delivery.

^aOnly the transfusion recommendations specific to obstetrics are described in this table.

Not including recombinant factor VII.
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