**POSTPARTUM HAEMORRHAGE: LATEST DEVELOPMENTS IN ITS PREDICTION, DRUG TREATMENT AND MONITORING**

**Dr Thuan Phan,** PhD Student at the University of Liverpool, Consultant in Obstetrics and Gynaecology, Tu Du Hospital, Ho Chi Minh City, Vietnam

**Prof Andrew D Weeks,** Professor of International Maternal Health at the University of Liverpool, and Consultant Obstetrician at Liverpool Women’s Hospital, Liverpool, UK

**Address for correspondence:**

**Dr Thuan Phan**

Department of Women’s and Children’s Health

University of Liverpool

Liverpool Women’s Hospital

Crown Street

LIVERPOOL L8 7SS

p.thuan@liverpool.ac.uk

**Conflicts of Interest Statement**

We have no conflicts of interest to disclose.

**ABSTRACT**

With increasing rates of postpartum haemorrhage (PPH) globally, there have been multiple recent developments to ensure that birthing women are safe. This focussed literature review will focus on 3 aspects: PPH prediction, blood loss measurement, uterotonic use and the thromboelastogram.

The unpredictable nature of postpartum haemorrhage is a significant hurdle. Evidence-based tools, such as guidelines and prediction tools, have shown promise in improving prediction and management strategies. However, the lack of consensus and agreement on risk factors poses obstacles to developing accurate models. Existing tools like the obstetric haemorrhage toolkit and maternal safety bundles show promise but face limitations. Ongoing research in the USA explores the development of individual-level PPH risk index, providing personalised care to pregnant women.

Accurate blood loss quantification such as gravimetric or volumetric measurements is essential for prompt PPH diagnosis and appropriate interventions but challenging in busy clinical settings. This review article will discuss ways of achieving this.

Finally, recent advancements in prophylaxis and treatment using medication (uterotonics and tranexamic acid) and in monitoring using thromboelastograms emphasise the need for effective prediction and management strategies. This critical review underscores the need for further research to enhance prediction tools, refine management protocols, and address the existing challenges to improve maternal outcomes.

**Keywords:** Postpartum haemorrhage, PPH, maternal morbidity, thromboelastogram, Treatment bundles

**BACKGROUND**

Postpartum haemorrhage (PPH) continues to be the leading factor of maternal mortality and morbidity in the world. Although death from PPH is considered a preventable event, PPH is still responsible for around 8% and 20% of maternal deaths in developed and developing countries respectively (Say et al. 2014). A primary PPH is typically understood as a blood loss of 500mls or more within 24 hours of birth (WHO 2012). The blood loss threshold used by clinicians to trigger interventions, however, may be higher or lower, depending on a woman’s situation. Healthy pregnant women can endure a higher blood loss, whereas blood loss of less than 500mls may cause severe adverse consequences in women with anaemia or chronic disease (Faysal et al. 2023; Glonnegger et al. 2023). Individualisation of care is therefore important not only to understand a woman’s underlying chance of having a PPH, but the effect that it might have on her.

Evidence-based tools such as interdisciplinary guidelines, care bundles, checklists and protocols have contributed to improving maternal outcomes and reducing maternal mortality (Arora et al. 2016). In a major US programme, the severity of PPH and the use of blood products significantly declined as a result of the introduction of these tools (Shields et al. 2015). In the UK, the OBS Cymru protocol, with its routine gravimetric blood loss assessment and structured volume-related actions, has improved outcomes across Wales and is now being adopted by many English maternity units (Bell et al. 2021; Bell et al. 2020). Additionally, the use of these protocols alongside clinical tools such as shock index and early warning scores have a good ability to predict unfavourable outcomes in women with PPH (Henriquez et al. 2018).

Recent evidence shows that the incidence of PPH is increasing, particularly in developed nations and high-resource settings (Huang et al. 2023; Knight et al. 2009; Pettersen et al. 2023). Although the reason for this is unclear, the rise in underlying risk factors of obesity, pre-eclampsia and caesarean section are all thought to be important (Ford et al. 2015; Weeks 2015). Additionally, although numerous risk factors have been determined, PPH remains unpredictable, and even the lowest risk women may suddenly suffer this obstetric emergency (Huang et al. 2023). This means that all pregnant women are considered at risk for PPH, imposing a heavy burden on the prevention and treatment of PPH.

**IS PPH REALLY ‘UNPREDICTABLE’?**

It is commonly stated that ‘PPH is unpredictable’ and so midwives and obstetricians always need to be prepared. Whilst this is true to a certain extent true, it is also clear that the risk of PPH is far higher in a woman with three previous caesarean sections (CS) and placenta praevia than it is in a low-risk home birthing parous woman in spontaneous labour (Huang et al. 2023; Thams et al. 2023). Thus, whilst the chance of PPH can never be removed, it can be useful to identify higher-risk women so as to plan their care.

It is also important to note that PPH is only a symptom and consists of several underlying pathologies. The risk of each pathology is affected to a different degree by various risk factors (Green et al. 2016). So, in the example above, the woman with placenta praevia is at risk of surgical blood loss. In contrast, the home birthing parous woman is very low risk of surgical blood loss, trauma or atonic uterus, but still has a risk of retained placenta which could unexpectedly result in severe postnatal bleeding (Olsen and Clausen 2023). For a nulliparous woman with induced labour having a CS at 9cm for dystocia unresponsive to many hours of oxytocin augmentation, the risk is of atonic uterus (Alexander et al. 2023). So not all risk factors point towards the same type of PPH.

The risk factors are currently categorised into three groups, including maternal, fetal and pregnancy-related factors (Sade et al. 2022). Through a meta-analysis, Ende et al. summarised the evidence and quantified risk factors for atonic PPH. They identified 47 potential factors and 15 likely factors, but there were still 32 factors showing conflicting or unclear evidence (Ende et al. 2021). This provides a major obstacle to PPH prediction: a lack of agreement and consensus on risk factors for PPH. Additionally, these factors may be affected by demography and epidemiology, and the evidence supporting or denying each factor might fluctuate (Sade et al. 2022). Therefore, PPH prediction tools are never going to provide a complete solution to PPH care, especially given the fact that clinical staff still need to be prepared for PPH in all women at births.

Despite these reservations, the obstetric haemorrhage tool kit developed by California Maternal Quality Care Collaborative (CMQCC) is considered the first PPH predictable tool to assist obstetricians, midwives and healthcare organisations with prompt recognition and response to the bleeding (Bingham et al. 2010; Main et al. 2017). In 2017, the Association of Women’s Health, Obstetric and Neonatal Nurses (AWHONN) also designed a PPH risk assessment table to guide clinical decision-making (AWHONN 2017). Shortly thereafter, in 2019 the Safe Motherhood Initiative in the USA released Maternal Safety Bundles for Obstetric Haemorrhage (MSBOH) (ACOG 2019a). Developed by expert consensus, these three tools provide the probability of PPH depending on the presence and absence of its risk factors. (Table 1) Although there have been limitations, recent studies demonstrated that the use of these tools has contributed to improved maternal outcomes when compared to traditional risk assessments of individual clinicians (Dilla et al. 2013; Kawakita et al. 2019; Ruppel et al. 2020).

To develop this concept further, there are ongoing attempts to develop an individual-level PPH risk index instead of just stratifying the risk from low to high. These are being explored through the use of new statistical models, machine learning and artificial intelligence (Rajkomar et al. 2019). Several models have been developed and studied for PPH prediction, but none have yet been validated and implemented (Neary et al. 2021).

Although identifying PPH risk factors has received much attention, there are still many women who experience a PPH without any risk factors (Huang et al. 2023). Thus, every single woman needs to be considered at risk for PPH after giving birth, and at every delivery, maternal care staff must be ready and prepared to manage this condition (Abdul-Kadir et al. 2014; Evensen et al. 2017).

**DECIDING WHEN TO TREAT A PPH**

An accurate assessment of blood loss in the third stage is important for two distinct reasons. The first is to make the initial diagnosis of PPH, and the second is to determine how severe it is and when to escalate treatment (Natrella et al. 2018; Powell et al. 2022). Previous research has often incorrectly considered the two together and assumed that accurate quantification of blood loss volume will solve both problems. However, most clinicians do not use blood loss volume to initiate PPH care, relying instead on intuition, ‘hunch’ and a woman’s underlying condition (Hancock et al. 2015). Thus, a woman having a second stage CS after a long labour may easily have 800mls blood loss during an uncomplicated CS and not have received any specific PPH treatment. In contrast, a woman with underlying anaemia and twins who starts to trickle immediately after vaginal birth might very reasonably be given uterotonics to induce contraction or tonicity of the uterus after the loss of only 100mls, just because of a recognition of the underlying risk and the wish to initiate treatment early. In PPH simulations using manikins, UK clinicians started uterotonics as soon as they considered the blood loss abnormal, with none awaiting any specific blood loss volume (Hancock et al. 2015). One, however, failed to recognise the mannikin’s slow trickle of blood and ‘discharged the women back to the ward’ without further intervention, demonstrating very nicely that the initiation of PPH treatment is far more complex than simple quantification.

Within limits, the exact timing of treatment **initiation** can be individualised to the woman’s underlying risk and cause of PPH. The most critical element is that it is not missed – either through a neglected slow trickle, or the slow filling of the uterus or vagina with blood. To prevent these, immediate postnatal monitoring of vaginal loss, uterine fundal height and maternal blood pressure and pulse are all critical, and it is important to not neglect them simply because the vaginal loss appears to have stopped. Quantification of vaginal blood loss at all births is also recommended not only to ensure that a PPH of 500mls is not missed, but also so as to triangulate with any postnatal symptoms. In Table 2, we propose a protocol aimed at assisting maternity care personnel in standardising the assessment, diagnosis, and PPH treatment. This protocol also encourages individualisation of care for women with potential PPH risks.

**Table 1:** Comparison between PPH predictable tools used in the USA

|  |  |  |  |
| --- | --- | --- | --- |
|  | **California Maternal Quality Care Collaborative (CMQCC)** | **Association of Women’s Health, Obstetric and Neonatal Nurses (AWHONN)** | **ACOG - Maternal Safety Bundle****for Obstetric Hemorrhage (MSBOH)** |
| ***Admission and labour risk factors*** | ***Additional birth and ongoing postpartum risk factors*** | ***Admission and labour risk factors*** | ***Intrapartum risk factors*** |
| **LOW RISK** | * No previous uterine incision
* Singleton pregnancy
* ≤ 4 vaginal births
* No known bleeding disorders
* No history of PPH
 |  | * No previous uterine incision
* Singleton pregnancy
* ≤ 4 previous vaginal births
* No known bleeding disorders
* No history of PPH
 |  |  |
| **MEDIUM RISK** | * Prior caesarean(s) or uterine surgery
* Multiple gestation
* > 4 vaginal births
* Chorioamnionitis
* History of previous PPH
* Large uterine fibroid
* Platelets 50-100,000
* Haematocrit < 30% (Hgb < 10)
* Polyhydramnios
* Gestational age <37 or >41 weeks
* Preeclampsia
* Prolonged labour/Induction (>24 hours)
 | * Caesarean during this admission – especially if urgent/emergent/2nd stage
* Operative vaginal birth
* Genital tract trauma including 3rd and 4th degree lacerations
* Quantitative cumulative blood loss 500-1000mls with a vaginal birth
 | * Induction of labour (with oxytocin) or Cervical ripening
* Multiple gestation
* >4 previous vaginal births
* Prior caesarean birth or prior uterine incision
* Large uterine fibroids
* History of one previous PPH
* Family history in first degree relatives who experienced PPH
* Chorioamnionitis
* Fetal demise
* Polyhydramnios
 | * Prior caesarean, uterine surgery, or multiple laparotomies
* Multiple gestation
* >4 prior births
* Large myomas
* EFW >4000 g
* Obesity (BMI >40)
* Haematocrit <30%
 | * Chorioamnionitis
* Prolonged oxytocin >24 hours
* Prolonged 2nd stage
* Magnesium sulphate
 |
| **HIGH RISK** | * 2 or more medium risk factors
* Placenta previa, low lying placenta
* Suspected/known placenta accreta spectrum
* Abruption or active bleeding (greater than show)
* Known coagulopathy
* History of >1 prior PPH
* HELLP Syndrome
* Platelets <50,000
* Haematocrit <24% (Hgb <8)
* Fetal demise
 | * Active bleeding soaking >1 pad per hour or passing a ≥6 cm clot
* Retained placenta
* Non-lower transverse uterine incision for caesarean
* Quantitative cumulative blood loss ≥1000mls or treated for haemorrhage
* Received general anaesthesia
* Uterine rupture
 | * 2 or More medium risk factors
* Active bleeding more than “bloody show”
* Suspected placenta accreta or percreta
* Placenta previa, low lying placenta
* Known coagulopathy
* History of more than one previous PPH
* Haematocrit <30
* Platelets <100,000/mm3
 | * 2 or more medium risk factors
* Placenta previa/low lying
* Suspected accreta/percreta
* Platelet count <70,000
* Active bleeding
* Known coagulopathy
 | * 2 or more medium risk factors
* New active bleeding
 |
| **INTERVENTION:*** **LOW RISK:** Routine obstetric care, Type and Hold (blood type identified and specimen on hold in blood bank).
* **MEDIUM RISK:** Notify care team, Blood ‘Type and Screen’ (no blood on hold for a particular patient but available in the blood bank).
* **HIGH RISK:** Notify care team, Mobilise resources, Blood ‘Type and Cross’ (cross-matched blood on hold in blood bank).
 |

Accurate measurement of blood loss volume is mainly important in order to manage an ongoing PPH and **escalate** multi-disciplinary care in a timely manner (Forbes et al. 2023; Kumaraswami and Butwick 2022). Visual estimation and cumulative, quantitative measurement are two common methods to assess the blood loss in clinical practice (Lilley et al. 2015; Natrella et al. 2018; Powell et al. 2022). Visual estimation is quick, simple, and free, and allows midwives and doctors to recognise and respond to the ongoing bleeding (Natrella et al. 2018). However, the estimates are commonly very inaccurate, especially at the extremes of blood loss with a tendency to ‘normalise’ values (Bamberg et al. 2016). While underestimation occurs in situations with higher blood loss, overestimation takes place in cases with lower amount of blood loss (Davis et al. 2019).

To improve the **accuracy of assessment**, quantitative blood loss has been suggested as an objective approach (Powell et al. 2022). This can be carried out using either the gravimetric method (based on weighing of swabs) or volumetric method (blood loss collection in waterproof drapes or suction bottles). Each can only start after discarding the amniotic fluid expelled with the baby. Although routine measurement of cumulative blood loss can seem complex and laborious to implement in a busy maternity department (Federspiel et al. 2022), quantitative measurement should replace visual estimation of blood loss in all women whenever possible so as to start timely intervention and prevent ‘missing’ cases of PPH (ACOG 2019b; Hire et al. 2020). This is now recommended by all leading authorities around the world such as WHO, RCOG, ACOG, SOGC and FIGO (ACOG 2017; Escobar et al. 2022; RCOG 2017; Robinson et al. 2022; WHO 2012).

It is common for appropriate PPH treatment to be delayed due to the underestimation of blood loss, and this is a common cause of maternal morbidities and mortalities (Turkoglu and Friedman 2023). Recent studies show an association between timely intervention and outcomes (Ameh and Althabe 2022; Turkoglu and Friedman 2023; Weeks 2015). Delay in PPH recognition and treatment results in an increased rate of hypotension, blood transfusion and severe PPH (Federspiel et al. 2022; Knight 2019). Conversely, overestimation of blood loss might bring overtreatment, increasing the burden on medical resources and iatrogenic harm (Bláha and Bartošová 2022).

**Table 2:** Suggested protocol for the assessment, diagnosis and initiation of PPH treatment

|  |
| --- |
| **Assessment of blood loss** |
| Change soiled drapes immediately after birth so as to remove amniotic fluid |
| Measure all subsequent loss until no loss for 15 minutes  – collect blood and weigh all soiled swabs  |
| Monitor for hidden blood loss by palpating the top of the uterus (check height, tone and centrality), blood pressure and pulse for 6 hours postnatally  |
| Document urine void within 6 hours |
| **Diagnosis of PPH and initiation of treatment** |
| Can be individualised (up to 500mls) according to the woman’s situation and underlying risks |
| Once loss reaches 500mls, PPH treatment must be initiated unless already started or blood loss stopped. |
| Ensure scribe present to regularly weigh blood-soaked swabs and call out blood loss when it reaches 1000mls, 1500mls, 2000mls, 2500mls, etc |
| Escalate care, assess clotting and treat according to local protocols as loss increases |

Once PPH has been diagnosed, the use of evidence-based **care bundles** can help health care staff to provide interventions in a systematic way (Kumaraswami and Butwick 2022). These typically consist of a uterotonic, uterine massage, tranexamic acid and IV fluids. Postnatal monitoring is also commonly included, using specific cut-offs to trigger escalation as well as prophylactic and therapeutic activities. Results of recent studies conducted in high-resource settings demonstrate that despite the recognised deficiencies, the implementation of these PPH bundles is safety, effective and associated with declined incidence of PPH-related morbidity (Althabe et al. 2020; Bell et al. 2021; De Tina et al. 2019; Shields et al. 2015; Skupski et al. 2017).

**UTEROTONICS IN PPH PREVENTION AND TREATMENT**

Uterotonics are the most common medication used at birth. They are clinically used to induce and augment labour but also to prevent and manage postpartum bleeding. Uterotonics include various categories of agents causing uterine contraction through different pathways. Detailed understanding of each medication is important and necessary, allowing clinicians to make the right choices for each stage of labour and minimising undesirable effects.

Oxytocin is the first-line choice for prophylaxis and treatment of PPH and appears in most guidelines across the world. According to the RCOG recommendations, the administration of oxytocin remains the key component of active management of the third stage of labour (RCOG 2017). Slow intravenous administration of 5IU oxytocin is recommended to prevent PPH for caesarean birth in preference to intramuscular injection of 10IU (RCOG 2017; Soltanifar and Russell 2012; WHO 2018). Heat-stable Carbetocin (known as Pabal® in the UK) is a synthesised oxytocin analogue with long-lasting effects and agonist properties. It is also recommended by WHO for PPH prevention as an alternative uterotonic in situations where the cost is comparable to the other (Nelson et al. 2017; WHO 2018). Carbetocin has also been shown to reduce the need for additional uterotonics when compared to oxytocin at elective caesarean birth (Onwochei et al. 2019) and is recommended for this purposes by NICE (NICE 2023)*.* For the treatment of PPH, these measures should be instituted in turn starting with slow intravenous administration of 10IU oxytocin (NICE 2023; RCOG 2017; WHO 2012), and followed by an infusion of 40IU oxytocin in either 500mls or 1000mls saline (RCOG 2017) (Fouche-Camargo 2022; WHO 2012) to give the oxytocin over 4-5 hours until the bleeding is under control.

Ergometrine/Methylergometrine is a powerful uterotonic that causes a prolonged tonic uterine contraction and is often combined with oxytocin as SyntometrineÒ (oxytocin 5IU and ergometrine 500mcg). The recommended dose and route of ergometrine for PPH treatment is 200-500mcg intramuscularly with a maximum of 1250 mcg (Fouche-Camargo 2022). Ergometrine causes a rapid increase in blood pressure and so should be used with great care in those with hypertension. Typical adverse effects are headaches, hypertension, nausea, and vomiting, and women receiving ergometrine should therefore be closely monitored. Many authorities suggest that ergometrine should be reserved for PPH treatment rather than used for prophylaxis due to its unfavourable adverse effect profile (Gallos et al. 2018; Laganà et al. 2023), but NICE includes it as a prophylaxis option for high risk women (NICE 2023)*.*

NICE updated its guidance in September 2023 and included a new table of uterotonics for PPH treatment (NICE 2023). The table varies the first line treatment according to the type of prophylaxis used and is a rational approach to care, even if there is no specific evidence to support or refute this approach (Table 3).

Prostaglandins (PGs) used in obstetric practice include PGE1 (Misoprostol), PGE2α (Carboprost) and PGE2 (Dinoprostone). Following oxytocin, they are frequently administered as a second-line treatment, especially if ergometrine is contraindicated. Common side effects of all PGs are fever, shivering, diarrhoea, nausea, and vomiting. Globally, the use of misoprostol in PPH prophylaxis and treatment has been the subject of much attention and research due to its low cost and not needing refrigeration. The recommended dose for prophylaxis 400-600µg orally, and 800µg sublingually or rectally for treatment (NICE 2023; RCOG 2017; WHO 2012; 2020). High fever and shivering are two most often side effects of misoprostol, but both rapidly respond to paracetamol (Durocher et al. 2010). The use of Dinoprostone is not generally considered for PPH even though a clinical trial in 2010 found that Dinoprostone is as effective as oxytocin in the prevention of PPH (Ozalp et al. 2010). However, stronger evidence is required to support the effectiveness of Dinoprostone in PPH prevention and treatment. Although Carboprost (Hemabate®, 0.25mg intramuscularly) is approved for the treatment of PPH, it is not recommended for prevention (WHO 2018). A large ongoing trial is comparing it first line use for PPH treatment to oxytocin and that will inform its role in PPH treatment. Due to the risk of acute bronchospasm, Carboprost should not be provided to women who have a history of asthma or substantial pulmonary disease (Gallos et al. 2018; Laganà et al. 2023).

**THE ROLE OF TRANEXAMIC ACID IN PPH PREVENTION AND TREATMENT**

In recent years, Tranexamic acid (TXA), an anti-fibrinolytic agent, began to be used in the treatment of acute bleeding in numerous situations due to its low cost, ease of administration and low incidence of side effects (Saccone et al. 2020; Sentilhes et al. 2018) and has now entered NICE guidance for use as a treatment for all women with PPH (NICE 2023). TXA is a successful intervention for reducing bleeding in pregnant women with PPH, and from a clinical perspective, it has the advantage of doing so regardless of the underlying cause (Shakur et al. 2017). Additionally, recent evidence illustrates that TXA can be used for both the prevention and treatment of PPH (Gedeno Gelebo et al. 2023; Lee et al. 2023).

**Table 3:** Suggested choice of uterotonic treatment according to the type of prophylaxis used.

|  |  |  |  |
| --- | --- | --- | --- |
| **Uterotonic used in the third stage of labour as prophylaxis** | **Suggested first-line treatment of postpartum haemorrhage** | **Suggested second-line treatment of postpartum haemorrhage** | **Additional treatments that can be offered, depending on clinical need** |
| No uterotonic used – physiological management | * Oxytocin plus ergometrine by intramuscular injection (if contraindicated, give carboprost), **or**
* Oxytocin infusion as soon as intravenous access is available
 | Carboprost intramuscular injection  | * Carboprost intramuscular injection (can be repeated at intervals not less than 15 minutes up to a maximum of 8 doses), **or**
* Misoprostol 800 micrograms sublingually or rectally (may be used earlier if intravenous route not available), **or**
* Carbetocin slow intravenous injection
 |
| Oxytocin alone | * Ergometrine intramuscular injection (if contraindicated give carboprost), or
* Oxytocin infusion as soon as intravenous access is available
 | Carboprost intramuscular injection | * Carboprost intramuscular injection (can be repeated at intervals not less than 15 minutes up to a maximum of 8 doses), or
* Misoprostol 800 micrograms sublingually or rectally (may be used earlier if intravenous route not available), or
* Carbetocin slow intravenous injection
 |
| Oxytocin plus ergometrine | * Carboprost intramuscular injection, or
* Oxytocin infusion as soon as intravenous access is available
 | Repeat carboprost after 15 minutes | * Carboprost intramuscular injection (can be repeated at intervals not less than 15 minutes up to a maximum of 8 doses), or
* Misoprostol 800 micrograms sublingually or rectally (may be used earlier if intravenous route not available), or
* Carbetocin slow intravenous injection
 |
| Carbetocin | Ergometrine intramuscular injection | Carboprost intramuscular injection | * Carboprost intramuscular injection (can be repeated at intervals not less than 15 minutes up to a maximum of 8 doses), or
* Misoprostol 800 micrograms sublingually or rectally
 |

A 2015 Cochrane review on the role of TXA in PPH **prophylaxis** shows that in addition to uterotonics, TXA can reduce postpartum blood loss, prevent PPH, and reduce the need for blood transfusions after both vaginal birth and Caesarean section in women who are at low risk of PPH (Novikova et al. 2015). Results from the systematic review with meta-analysis of randomised clinical trials conducted in 2022 also demonstrates the effectiveness of prophylactic TXA in reducing postpartum bleeding (Assis et al. 2022). Whilst there were concerns that universal TXA prophylaxis could increase the rate of thromboembolism, this side effect appears to be extremely rare (McQuilten et al. 2023). Authors emphasise the importance of further studies to accurately assess side effects and determining the optimal dose to achieve a therapeutic effect with the fewest side effects (Gedeno Gelebo et al. 2023).

Recent studies and systematic reviews have demonstrated that TXA is a successful **treatment** for PPH (Gedeno Gelebo et al. 2023; Sentilhes et al. 2018; Shakur et al. 2018). A Cochrane review demonstrates that the use of TXA in PPH treatment contributes to a reduced rate of death from bleeding and laparotomy to control bleeding, and without any sign of the dreaded increase in thromboembolic risk (Shakur et al. 2018). Data from the WOMAN trial suggest that TXA is most effective when given early after diagnosis. Surprisingly, despite reducing laparotomy and death, there was no effect on rates of hysterectomy, serious maternal morbidity or blood transfusion (Shakur et al. 2017). A review examining the cost-effectiveness of TXA concluded that in situations where PPH and PPH-related morbidity are common and TXA is inexpensive, it is likely to be cost-effective (Aziz et al. 2021). One of obstacles to women seeking TXA treatment is the requirement for intravenous injection. This can be a barrier for women giving birth in places where it is very difficult to administer an intravenous injection. Alternative TXA administration methods would make this life-saving medication available to more women (Ameh and Althabe 2022). Shakur-Still suggests that, based on the TXA pharmacokinetic profile, intramuscular administration should be preferable to intravenous injection due to the ease of administration and speed, given the requirement for slow intravenous injection over 10 mins (Shakur‐Still et al. 2022).

**USING THE THROMBOELASTOGRAM TO GUIDE HAEMATOLOGICAL MANAGEMENT**

Thromboelastography (TEG) was developed nearly 70 years ago by Hellmut Hartert, a German doctor, but it was not implemented into clinical practice until 25 years later. The initial purpose of this viscoelastic dynamic global test was to track alterations in coagulation and fibrinolysis related to liver transplantation. TEG is now implemented as a point-of-care device with applications in various therapeutic domains thanks to major improvements brought about by technological advancements over the past few decades (Othman and Kaur 2017).

For decades, the length of time taken for fresh blood to clot in a test tube has been used as a simple bedside test for disseminated intravascular coagulation. TEG is a development of that same technique. It works by placing a small needle in a vibrating vial of fresh blood. Initially, the needle moves little as the blood is completely liquid. However, as the clot forms, so the needle starts to move with the vial of blood, and this shows up on a graphic reader. The start of the deflection on the graph shows the initiation of the clot formation, and the widest part relates to the maximum strength of the clot before it begins to break down. The shape of the graph can be measured to calculate various aspects of the clotting cascade (Othman and Kaur 2017).

TEG has been used in maternity care for early diagnosis and treatment of coagulation disorders in PPH and has yielded promising results (Hartmann et al. 2018; Karlsson et al. 2014; Khanna et al. 2023; McNamara and Mallaiah 2019; Rigouzzo et al. 2020; Zhu et al. 2022). Results of the Karlsson study show that when compared to traditional laboratory testing, TEG provides rapid and clinically important information about haemostatic changes associated with massive PPH, revealing indications for specific blood product therapies at an earlier stage (Karlsson et al. 2014). TEG also provides a reliable detection of coagulation disorders (hypofibrinogenemia ≤2 g/L and/or thrombocytopenia ≤80,000/mm3), assisting clinicians in the rapid diagnosis and treatment of clotting disorders during the progression of PPH (Rigouzzo et al. 2020). Thus, TEG has a good diagnostic value for peripartum haemorrhage, playing an important role in PPH prediction and providing clinical evidence for PPH prevention, evaluation and treatment (Perelman et al. 2021; Zhu et al. 2022). It is now in widespread use in the UK as part of the OBSCYMRU protocol (Bell et al. 2021; Bell et al. 2020). The Figure 1 below provides a guide to its interpretation (MacIvor et al. 2012).

|  |  |
| --- | --- |
|  |  |
| 1. Normal thromboelastography and interpretation
 | 1. TEG patterns
 |

**Figure 1:** The interpretation of thromboelastography (MacIvor et al. 2012).

**FUTURE RESEARCH STRATEGIES IN PPH PREVENTION AND MANAGEMENT**

Recent studies have shown that **PPH prediction tools** have an important role to play in the improvement of maternal outcomes; many of them have been validated and implemented across the world. However, the use of prediction tools based on available risk factors still need to be used with caution given that the risk factors of PPH have changed over time and that PPH still occurs in women with almost no risk factors. Instead of stratifying the PPH risk prior to labour from low to high as at present, a specific ‘PPH risk index’ may provide a more nuanced and individualised approach to adjusting the PPH prevention and management strategy. This should also include risks specific to the setting (including low-income countries) and intrapartum risk factors (prolonged labour, CS or instrumental birth). This would improve PPH risk stratification, early and targeted interventions, patient-centred care, research and quality improvement. The development and validation of a continuous numerical PPH risk index should be developed, and studies carried out to optimise its accuracy and clinical utility.

**Treatment bundles** have shown their effectiveness in the management of PPH, significantly contributing to the reduced rate of haemorrhage-related mortality and morbidity. However, their application has some limitations. Current cut-offs used to trigger prevention and treatment actions seem to be effective in lower risk women but do not represent all groups of risk women. A pregnant woman with anaemia or underlying heart condition should, of course, receive interventions earlier than those with a normal haemoglobin. Therefore, it is necessary to have various cut-offs for initiating treatment, depending on women’s underlying health status as well as their level of PPH risk. Additionally, there are several barriers that may interfere with the bundle application. In low-income settings where the maternity units have a high throughput of births but are less well equipped, the implementation of bundles for all low-risk women would create a huge amount of work for healthcare staff. As a result, thresholds for care in protocols or bundles should be further researched so that clinicians can individualise care, adjusting them to match the underlying risk of bleeding in the women as well as the resources available in the unit.

**CONCLUSION**

Despite massive investments in maternal health services worldwide, PPH continues to remain a leading cause of maternal death. The use of uterotonics and TXA are being gradually optimized, helping to improve PPH outcomes. The development of PPH prediction tools and bundles of prophylaxis and treatment have contributed to the reduced incidence of PPH related mortality and morbidity. More research is now required to address the limitations of predictable tools and improve the effectiveness of protocols or bundles used in daily practice in various settings.

**KEY POINTS**

* Evidence-based tools and guidelines have shown promise in improving maternal outcomes, but the lack of consensus on PPH risk factors hinders the development of accurate prediction models.
* Accurate ongoing quantification of blood loss during the third stage of labour using objective measurement methods is crucial for timely diagnosis and appropriate management of PPH.
* Uterotonics and tranexamic acid have demonstrated effectiveness in PPH prevention and treatment, although further research is needed to optimise their use and mitigate potential side effects.
* Thromboelastography is a bedside dynamic test that provides rapid, clinically important information about changes in maternal clotting associated with PPH, enabling early diagnosis and treatment of coagulation disorders.
* Ongoing research efforts, including the development of individual-level PPH risk index and the utilisation of advanced statistical models and artificial intelligence, hold promise in improving prediction accuracy and individualised care for pregnant women at risk of PPH.

**REFLECTIVE QUESTIONS**

1. In your clinical practice, what triggers you to start treatment for PPH and why? Why are PPHs sometimes missed, and what can be done to overcome this?
2. How would the development of an individual-level PPH risk index help to guide individualised care for pregnant women? What changes in care would you advise to a mother if she scored as high risk?
3. What are the main challenges in implementing accurate quantification methods for blood loss, and how can these challenges be addressed to ensure timely PPH diagnosis and appropriate management?
4. What PPH prophylaxis do you recommend for women in your care and why?
5. What are the barriers to implementing thromboelastogram testing in clinical practice, and how can they be overcome to improve PPH management outcomes?

 **REFERENCES**

Abdul-Kadir R, McLintock C, Ducloy A-S, El-Refaey H, England A, Federici AB, Grotegut CA, Halimeh S, Herman JH, Hofer S et al. 2014. Evaluation and management of postpartum hemorrhage: Consensus from an international expert panel. Transfusion. 54(7):1756-1768.

ACOG. 2017. Practice bulletin no. 183: Postpartum hemorrhage. Obstet Gynecol. 130(4):e168-e186.

Maternal safety bundle for obstetric hemorrhage. 2019a. The American College of Obstetricians and Gynecologists; [accessed 2023 06 July]. <https://www.acog.org/community/districts-and-sections/district-ii/programs-and-resources/safe-motherhood-initiative/obstetric-hemorrhage>.

ACOG. 2019b. Quantitative blood loss in obstetric hemorrhage. Acog committee opinion no. 794. Obstet Gynecol. 134(6).

Alexander MV, Wang MJ, Srivastava A, Tummala S, Abbas D, Young S, Claus L, Yarrington C, Comfort A. 2023. Association between duration of intrapartum oxytocin exposure and obstetric hemorrhage. Archives of Gynecology and Obstetrics.

Althabe F, Therrien MNS, Pingray V, Hermida J, Gülmezoglu AM, Armbruster D, Singh N, Guha M, Garg LF, Souza JP et al. 2020. Postpartum hemorrhage care bundles to improve adherence to guidelines: A who technical consultation. Int J Gynaecol Obstet. 148(3):290-299.

Ameh C, Althabe F. 2022. Improving postpartum hemorrhage care: Policy, practice, and research. Int J Gynaecol Obstet. 158 Suppl 1:4-5.

Arora KS, Shields LE, Grobman WA, D'Alton ME, Lappen JR, Mercer BM. 2016. Triggers, bundles, protocols, and checklists–what every maternal care provider needs to know. Am J Obstet Gynecol. 214(4):444-451.

Assis IdC, Govêia CS, Miranda D, Ferreira RS, Riccio LG. 2022. Analysis of the efficacy of prophylactic tranexamic acid in preventing postpartum bleeding: Systematic review with meta-analysis of randomized clinical trials. Braz J Anesthesiol (English Edition).

Postpartum hemorrhage risk assessment table. 2017. Association of Women's Health Obstetric and Neonatal Nurses; [accessed 2023 06 July]. <https://cdn-links.lww.com/permalink/aog/b/aog_134_6_2019_10_06_kawakita_19-1065_sdc2.pdf>.

Aziz S, Rossiter S, Homer CSE, Wilson AN, Comrie-Thomson L, Scott N, Vogel JP. 2021. The cost-effectiveness of tranexamic acid for treatment of postpartum hemorrhage: A systematic review. Int J Gynaecol Obstet. 155(3):331-344.

Bamberg C, Dollen KN-v, Mickley L, Henkelmann A, Hinkson L, Kaufner L, Heymann Cv, Henrich W, Pauly F. 2016. Evaluation of measured postpartum blood loss after vaginal delivery using a collector bag in relation to postpartum hemorrhage management strategies: A prospective observational study. J Perinat Med. 44(4):433-439.

Bell SF, Collis RE, Pallmann P, Bailey C, James K, John M, Kelly K, Kitchen T, Scarr C, Watkins A et al. 2021. Reduction in massive postpartum haemorrhage and red blood cell transfusion during a national quality improvement project, obstetric bleeding strategy for wales, obs cymru: An observational study. BMC Pregnancy Childbirth. 21(1):377.

Bell SF, Kitchen T, John M, Scarr C, Kelly K, Bailey C, James K, Watkins A, Macgillivray E, Edey T et al. 2020. Designing and implementing an all wales postpartum haemorrhage quality improvement project: Obs cymru (the obstetric bleeding strategy for wales). BMJ Open Qual. 9(2):e000854.

Bingham D, Melsop K, Main E. 2010. Cmqcc obstetric hemorrhage hospital level implementation guide. CMQCC.

Bláha J, Bartošová T. 2022. Epidemiology and definition of pph worldwide. Best Practice & Research Clinical Anaesthesiology. 36(3):325-339.

Davis NL, Smoots AN, Goodman DA. 2019. Pregnancy-related deaths: Data from 14 us maternal mortality review committees. Education. 40(36):8-2.

De Tina A, Chau A, Carusi DA, Robinson JN, Tsen LC, Farber MK. 2019. Identifying barriers to implementation of the national partnership for maternal safety obstetric hemorrhage bundle at a tertiary center: Utilization of the delphi method. Anesth Analg. 129(4):1045-1050.

Dilla AJ, Waters JH, Yazer MH. 2013. Clinical validation of risk stratification criteria for peripartum hemorrhage. Obstet Gynecol. 122(1):120-126.

Durocher J, Bynum J, León W, Barrera G, Winikoff B. 2010. High fever following postpartum administration of sublingual misoprostol. BJOG: Int J Obstet Gynaecol. 117(7):845-852.

Ende HB, Lozada MJ, Chestnut DH, Osmundson SS, Walden RL, Shotwell MS, Bauchat JR. 2021. Risk factors for atonic postpartum hemorrhage: A systematic review and meta-analysis. Obstet Gynecol. 137(2):305.

Escobar MF, Nassar AH, Theron G, Barnea ER, Nicholson W, Ramasauskaite D, Lloyd I, Chandraharan E, Miller S, Burke T et al. 2022. Figo recommendations on the management of postpartum hemorrhage 2022. Int J Gynaecol Obstet. 157(S1):3-50.

Evensen A, Anderson JM, Fontaine P. 2017. Postpartum hemorrhage: Prevention and treatment. Am Fam Physician. 95(7):442-449.

Faysal H, Araji T, Ahmadzia HK. 2023. Recognizing who is at risk for postpartum hemorrhage: Targeting anemic women and scoring systems for clinical use. American Journal of Obstetrics & Gynecology MFM. 5(2, Supplement):100745.

Federspiel JJ, Eke AC, Eppes CS. 2022. Postpartum hemorrhage protocols and benchmarks: Improving care through standardization. Am J Obstet Gynecol.100740.

Forbes G, Akter S, Miller S, Galadanci H, Qureshi Z, Fawcus S, Hofmeyr GJ, Moran N, Singata-Madliki M, Dankishiya F et al. 2023. Factors influencing postpartum haemorrhage detection and management and the implementation of a new postpartum haemorrhage care bundle (e-motive) in kenya, nigeria, and south africa. Implementation Science. 18(1):1.

Ford JB, Patterson JA, Seeho SKM, Roberts CL. 2015. Trends and outcomes of postpartum haemorrhage, 2003-2011. BMC Pregnancy Childbirth. 15(1):334.

Fouche-Camargo JS. 2022. Chapter 18 - uterotonics and tocolytics. In:Mattison D, Halbert L-A, editors. Clinical pharmacology during pregnancy (second edition). Boston: Academic Press. p. 323-338.

Gallos ID, Papadopoulou A, Man R, Athanasopoulos N, Tobias A, Price MJ, Williams MJ, Diaz V, Pasquale J, Chamillard M et al. 2018. Uterotonic agents for preventing postpartum haemorrhage: A network meta‐analysis. Cochrane Database of Systematic Reviews. (12).

Gedeno Gelebo K, Mulugeta H, Mossie A, Geremu K, Darma B. 2023. Tranexamic acid for the prevention and treatment of postpartum hemorrhage in resource-limited settings: A literature review. Annals of Medicine and Surgery.

Glonnegger H, Glenzer MM, Lancaster L, Barnes RFW, von Drygalski A. 2023. Prepartum anemia and risk of postpartum hemorrhage: A meta-analysis and brief review. Clin Appl Thromb Hemost. 29:10760296231214536.

Green L, Knight M, Seeney F, Hopkinson C, Collins PW, Collis RE, Simpson NAB, Weeks A, Stanworth SJ. 2016. 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. 172(4):616-624.

Hancock A, Weeks AD, Lavender DT. 2015. 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. 15(1):230.

Hartmann J, Mason D, Achneck H. 2018. Thromboelastography (teg) point-of-care diagnostic for hemostasis management. Point of Care. 17(1):15-22.

Henriquez DDCA, Bloemenkamp KWM, van der Bom JG. 2018. Management of postpartum hemorrhage: How to improve maternal outcomes? J Thromb Haemost. 16(8):1523-1534.

Hire MG, Lange EMS, Vaidyanathan M, Armour KL, Toledo P. 2020. Effect of quantification of blood loss on activation of a postpartum hemorrhage protocol and use of resources. J Obstet Gynecol Neonatal Nurs. 49(2):137-143.

Huang C-r, Xue B, Gao Y, Yue S-w, Redding SR, Wang R, Ouyang Y-q. 2023. Incidence and risk factors for postpartum hemorrhage after vaginal delivery: A systematic review and meta-analysis. Journal of Obstetrics and Gynaecology Research. 49(7):1663-1676.

Karlsson O, Jeppsson A, Hellgren M. 2014. Major obstetric haemorrhage: Monitoring with thromboelastography, laboratory analyses or both? Int J Obstet Anesth. 23(1):10-17.

Kawakita T, Mokhtari N, Huang JC, Landy HJ. 2019. Evaluation of risk-assessment tools for severe postpartum hemorrhage in women undergoing cesarean delivery. Obstet Gynecol. 134(6):1308-1316.

Khanna P, Sinha C, Singh AK, Kumar A, Sarkar S. 2023. The role of point of care thromboelastography (teg) and thromboelastometry (rotem) in management of primary postpartum haemorrhage: A meta-analysis and systematic review. Saudi J Anaesth. 17(1):23-32.

Knight M. 2019. The findings of the mbrrace-uk confidential enquiry into maternal deaths and morbidity. Obstet Gynaecol Reprod Med. 29(1):21-23.

Knight M, Callaghan WM, Berg C, Alexander S, Bouvier-Colle MH, Ford JB, Joseph KS, Lewis G, Liston RM, Roberts CL et al. 2009. Trends in postpartum hemorrhage in high resource countries: A review and recommendations from the international postpartum hemorrhage collaborative group. BMC Pregnancy Childbirth. 9:55.

Kumaraswami S, Butwick A. 2022. Latest advances in postpartum hemorrhage management. Best Pract Res Clin Anaesthesiol. 36(1):123-134.

Laganà AS, Casarin J, Lembo A, Ervas E, Cromi A. 2023. Postpartum hemorrhage: Conservative treatments. In:Cinnella G, Beck R, Malvasi A, editors. Practical guide to simulation in delivery room emergencies. Cham: Springer International Publishing. p. 539-555.

Lee SH, Kwek ME-J, Tagore S, Wright A, Ku CW, Teong ACA, Tan AWM, Lim SWC, Yen DYT, Ang CYX et al. 2023. Tranexamic acid, as an adjunct to oxytocin prophylaxis, in the prevention of postpartum haemorrhage in women undergoing elective caesarean section: A single-centre double-blind randomised controlled trial. BJOG: An International Journal of Obstetrics & Gynaecology. 130(9):1007-1015.

Lilley G, Burkett-st-Laurent D, Precious E, Bruynseels D, Kaye A, Sanders J, Alikhan R, Collins PW, Hall JE, Collis RE. 2015. Measurement of blood loss during postpartum haemorrhage. Int J Obstet Anesth. 24(1):8-14.

MacIvor D, Rebel A, Hassan Z-U. 2012. 27 how do we integrate thromboelastography with perioperative transfusion management? \_3728 1386.. 1392. Transfusion. 53:1386-1392.

Main EK, Cape V, Abreo A, Vasher J, Woods A, Carpenter A, Gould JB. 2017. Reduction of severe maternal morbidity from hemorrhage using a state perinatal quality collaborative. Am J Obstet Gynecol. 216(3):298.e291-298.e211.

McNamara H, Mallaiah S. 2019. Managing coagulopathy following pph. Best Pract Res Clin Obstet Gynaecol. 61:106-120.

McQuilten ZK, Wood EM, Medcalf RL. 2023. When to use tranexamic acid for the treatment of major bleeding? Journal of Thrombosis and Haemostasis.

Natrella M, Di Naro E, Loverro M, Benshalom-Tirosh N, Trojano G, Tirosh D, Besser L, Loverro MT, Mastrolia SA. 2018. The more you lose the more you miss: Accuracy of postpartum blood loss visual estimation. A systematic review of the literature. J Matern-Fetal Neonatal Med. 31(1):106-115.

Neary C, Naheed S, McLernon D, Black M. 2021. Predicting risk of postpartum haemorrhage: A systematic review. BJOG: Int J Obstet Gynaecol. 128(1):46-53.

Nelson HA, Draycott T, Siassakos D, Yau CWH, Hatswell AJ. 2017. Carbetocin versus oxytocin for prevention of post-partum haemorrhage at caesarean section in the united kingdom: An economic impact analysis. Eur J Obstet Gynecol Reprod Biol. 210:286-291.

NICE. 2023. National institute for health and care excellence: Clinical guidelines. Intrapartum care. London: National Institute for Health and Care Excellence (UK).

Novikova N, Hofmeyr GJ, Cluver C. 2015. Tranexamic acid for preventing postpartum haemorrhage. Cochrane Database Syst Rev. (6).

Olsen O, Clausen JA. 2023. Planned hospital birth compared with planned home birth for pregnant women at low risk of complications. Cochrane Database of Systematic Reviews. (3).

Onwochei DN, Van Ross J, Singh PM, Salter A, Monks DT. 2019. Carbetocin reduces the need for additional uterotonics in elective caesarean delivery: A systematic review, meta-analysis and trial sequential analysis of randomised controlled trials. Int J Obstet Anesth. 40:14-23.

Othman M, Kaur H. 2017. Thromboelastography (teg). J Thromb Haemost.533-543.

Ozalp E, Tanir HM, Sener T. 2010. Dinoprostone vaginal insert versus intravenous oxytocin to reduce postpartum blood loss following vaginal or cesarean delivery. Clin Exp Obstet Gynecol. 37(1):53-55.

Perelman A, Limaye M, Blakemore J, Friedman S, Hoskins IA. 2021. 206 thromboelastography (teg) versus standard coagulation assays in the management of patients with postpartum hemorrhage. Am J Obstet Gynecol. 224(2):S138.

Pettersen S, Falk RS, Vangen S, Nyfløt LT. 2023. Exploring trends of severe postpartum haemorrhage: A hospital-based study. BMC Pregnancy and Childbirth. 23(1):363.

Powell E, James D, Collis R, Collins PW, Pallmann P, Bell S. 2022. Introduction of standardized, cumulative quantitative measurement of blood loss into routine maternity care. J Matern-Fetal Neonatal Med. 35(8):1491-1497.

Rajkomar A, Dean J, Kohane I. 2019. Machine learning in medicine. N Engl J Med. 380(14):1347-1358.

RCOG. 2017. Prevention and management of postpartum haemorrhage. BJOG: Int J Obstet Gynaecol. 124(5):e106-e149.

Rigouzzo A, Louvet N, Favier R, Ore M-V, Piana F, Girault L, Farrugia M, Sabourdin N, Constant I. 2020. Assessment of coagulation by thromboelastography during ongoing postpartum hemorrhage: A retrospective cohort analysis. Anesth Analg. 130(2):416-425.

Robinson D, Basso M, Chan C, Duckitt K, Lett R. 2022. Guideline no. 431: Postpartum hemorrhage and hemorrhagic shock. J Obstet Gynaecol Can. 44(12):1293-1310.e1291.

Ruppel H, Liu VX, Gupta NR, Soltesz L, Escobar GJ. 2020. Validation of postpartum hemorrhage admission risk factor stratification in a large obstetrics population. Am J Perinatol. 38(11):1192-1200.

Saccone G, Della Corte L, D’Alessandro P, Ardino B, Carbone L, Raffone A, Guida M, Locci M, Zullo F, Berghella V. 2020. Prophylactic use of tranexamic acid after vaginal delivery reduces the risk of primary postpartum hemorrhage. The Journal of Maternal-Fetal & Neonatal Medicine. 33(19):3368-3376.

Sade S, Weintraub AY, Baumfeld Y, Kluwgant D, Yohay D, Rotem R, Pariente G. 2022. Trend changes in the individual contribution of risk factors for postpartum hemorrhage over more than two decades. Matern Child Health J. 26(11):2228-2236.

Say L, Chou D, Gemmill A, Tunçalp Ö, Moller A-B, Daniels J, Gülmezoglu AM, Temmerman M, Alkema L. 2014. Global causes of maternal death: A who systematic analysis. Lancet Glob Health. 2(6):e323-e333.

Sentilhes L, Winer N, Azria E, Senat MV, Le Ray C, Vardon D, Perrotin F, Desbriere R, Fuchs F, Kayem G et al. 2018. Tranexamic acid for the prevention of blood loss after vaginal delivery. New England Journal of Medicine. 379(8):731-742.

Shakur‐Still H, Grassin‐Delyle S, Muhunthan K, Ahmadzia HK, Faraoni D, Arribas M, Roberts I. 2022. Alternative routes to intravenous tranexamic acid for postpartum hemorrhage: A systematic search and narrative review. Int J Gynaecol Obstet. 158:40-45.

Shakur H, Beaumont D, Pavord S, Gayet-Ageron A, Ker K, Mousa HA. 2018. Antifibrinolytic drugs for treating primary postpartum haemorrhage. Cochrane Database Syst Rev. 2(2):Cd012964.

Shakur H, Roberts I, Fawole B, Chaudhri R, El-Sheikh M, Akintan A, Qureshi Z, Kidanto H, Vwalika B, Abdulkadir A et al. 2017. Effect of early tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with post-partum haemorrhage (woman): An international, randomised, double-blind, placebo-controlled trial. Lancet. 389(10084):2105-2116.

Shields LE, Wiesner S, Fulton J, Pelletreau B. 2015. Comprehensive maternal hemorrhage protocols reduce the use of blood products and improve patient safety. Am J Obstet Gynecol. 212(3):272-280.

Skupski DW, Brady D, Lowenwirt IP, Sample J, Lin SN, Lohana R, Eglinton GS. 2017. Improvement in outcomes of major obstetric hemorrhage through systematic change. Obstet Gynecol. 130(4):770-777.

Soltanifar S, Russell R. 2012. The national institute for health and clinical excellence (nice) guidelines for caesarean section, 2011 update: Implications for the anaesthetist. Int J Obstet Anesth. 21(3):264-272.

Thams AB, Larsen MH, Rasmussen SC, Jeppegaard M, Krebs L. 2023. Incidence of postpartum hemorrhage and risk factors for recurrence in the subsequent pregnancy. Archives of Gynecology and Obstetrics. 307(4):1217-1224.

Turkoglu O, Friedman P. 2023. Evaluation during postpartum hemorrhage. Clinical Obstetrics and Gynecology. 66(2):357-366.

Weeks A. 2015. The prevention and treatment of postpartum haemorrhage: What do we know, and where do we go to next? BJOG: Int J Obstet Gynaecol. 122(2):202-210.

WHO. 2012. Who recommendations for the prevention and treatment of postpartum haemorrhage. Geneva: World Health Organization.

WHO. 2018. Who recommendations uterotonics for the prevention of postpartum haemorrhage: Web annex 7: Choice of uterotonic agents. World Health Organization.

WHO. 2020. Who recommendation on routes of oxytocin administration for the prevention of postpartum haemorrhage after vaginal birth. Geneva: World Health Organization.

Zhu X, Tang J, Huang X, Zhou Y. 2022. Diagnostic value of fibrinogen combined with thromboelastogram in postpartum hemorrhage after vaginal delivery. Am J Transl Res. 14(3):1877.