DEVELOPMENT OF AN ALGORITHM FOR POSTPARTUM HEMORRHAGE RESUSCITATION

by

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As members of the DNP Project Committee, we certify that we have read the DNP project prepared by Rylee Marie Apodaca, titled Development of an Algorithm for Postpartum Hemorrhage Resuscitation and recommend that it be accepted as fulfilling the DNP project requirement for the Degree of Doctor of Nursing Practice.

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Final approval and acceptance of this DNP project is contingent upon the candidate's submission of the final copies of the DNP project to the Graduate College.

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To my grandparents. For your constant love and devotion over the years and willingness to go above and beyond your role. I would not be where I am today without you.

And finally, God. He has brought me to it and through it.

DEDICATION

To my Papa in heaven, I love you.

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ABSTRACT

The United States has the highest rates of maternal mortality and morbidity in the developed world with postpartum hemorrhage being a leading cause. This Doctor of Nursing Practice (DNP) project was set out to identify evidence-based research regarding the medical care of mother's experiencing a postpartum hemorrhage and to develop a resuscitation algorithm for anesthesia providers at a facility lacking a concrete process. The first phase of the project involved the development of an algorithm using a literature review of current evidence and recommendations provided by the American College of Obstetricians and Gynecologists current guideline for a Level III trauma center in Mesa, Arizona. During the second phase, the participants graded the algorithm, agreed that the development algorithm was high quality, and could move towards dissemination. The principle investigator disseminated the results and an educational presentation about PPH to the anesthesia providers at their monthly meeting. The Kurt Lewin change theory guided the implementation and integration of the algorithm. The material was well received and feedback on the presentation and developed algorithm was requested. There were no further suggestions made by the team and it ensured that medications suggested in the algorithm were available in the formulary. The chief of the department plans to integrate the algorithm into their OB anesthesia manual and several copies of the algorithm were posted throughout on the unit for quick and convenient access during a crisis response. It was suggested that ongoing education and evaluation of the current algorithm be introduced for continued success. Translation of research into clinical practice continues to be a challenge; however, the presented algorithm serves to bridge the gap between research and clinical practice with the intent to improve patient outcomes in this unique population.

INTRODUCTION

Every woman is entitled to a safe birthing experience. Despite extensive medical advances made over the past two decades, the United States (U.S.) is the only country where maternal deaths and injuries have continued to rise, with some of the highest rates of maternal deaths in the developed world (Association of Women's Health, Obstetric, and Neonatal Nurses [AWHONN], 2017). In the U.S. there are 26.4 deaths per every 100,000 lives births, compared to 9.2 deaths per every 100,000 in the United Kingdom, who is the second leading in maternal deaths in the developed world (Kassebaum, 2016). These numbers are surprising considering Finland and Denmark have some of the lowest rates of maternal morbidity in developed countries at 4.2 and 3.8 deaths per 100,000 women, respectively (Kassebaum, 2016). The evidence suggests that primary postpartum hemorrhage (PPH) is the leading preventable cause of maternal morbidity and mortality in the U.S. (Belfort, 2019).

Background

Postpartum hemorrhage excessive bleeding or blood loss with associated signs of hypovolemia in the first 24 hours following the delivery of a baby (Belfort, 2019). The 2017 updated guideline (Appendix D) by the American College of Obstetricians and Gynecologists (ACOG) (2017) defines PPH as blood loss exceeding 1000 milliliters (ml) for both vaginal and cesarean delivery. There are four stages of hemorrhage, stage 0-III. Stage 0 can be defined as the immediate post-delivery period with less than 1000 ml of blood loss for vaginal delivery and cesarean delivery (ACOG, 2017). During Stage 0, the mother has vital signs within normal limits. Stage 0 follows the third stage of active labor. Stage I hemorrhage is defined as blood loss greater than 1000 ml for vaginal or cesarean section (C-section) with vital sign instability, Stage

II hemorrhage is continued bleeding with changing vital signs and blood loss up to 1500 ml, and Stage III hemorrhage is blood loss greater than 1500 ml (ACOG, 2017). While the immediate postpartum period is often chaotic and transition from one stage to the next can be sudden, assessment of the current stage of hemorrhage is vital to appropriate treatment and intervention.

Maternal Risk Factors

Some parturients pose a greater risk to experiencing PPH including those with placenta previa, placental abruption, multiple pregnancies, gestational hypertension, prolonged labor, overdistended uterus, induced labor, forceps or vacuum assisted delivery, infection, and obesity (AWHONN, 2017). Although identifying high-risk individuals is crucial, 20% of PPHs occur in women with no known risk factors (Evensen, Anderson, & Fontaine, 2017). Prevention of PPH starts at identifying a high-risk individual, whereas treatment begins at the recognition of excessive bleeding. Tachycardia is the earliest sign of PPH followed my hypotension, nausea, vomiting, oliguria, and chest pain (Evensen et al., 2017). The four T's have been used to identify specific causes. These include uterine tone (atony), thrombin (coagulopathy), trauma, and tissue (retained placenta) (Evensen et al., 2017). Although the normal progression of labor involves the spontaneous return of the uterine tone, reduced uterine tone or uterine atony remains the leading cause of PPH (Evensen et al., 2017). To begin appropriate management to prevent maternal morbidity, a PPH resuscitation algorithm should be initiated upon recognition of symptoms and blood loss. Although PPH algorithms and protocols are now described as a standard of care, some facilities still fail to implement a targeted and systematic response to PPH.

Complications Related to PPH

Obstetrical complications occurring prior to birth or in the intermediate postpartum phase of labor that contribute to PPH include the following conditions:

Uterine atony. Loss of the tone of the uterine musculature after the birth of a child that results in excessive bleeding

Placenta previa. A condition where the placenta lies low in the uterus, partially or completely covering the cervix leading to potential bleeding.

Placenta abruption. Occurs when the placenta separates from the inner wall of the uterus before birth, depriving the baby of oxygen and nutrients and leading to heavy bleeding in the mother.

Gestational hypertension. A form of high blood pressure associated with pregnancy. Gestational hypertension is association with an increased risk in PPH.

Significance

From 1987 to 2014, maternal morbidity has more than doubled from 7.2 to 18 deaths per every 100,000 live births in the U.S. (Center for Disease Control and Prevention [CDC], 2018). The U.S. saw a sharp rise in rates of PPH from 1994 to 2006 and although rates of associated mortality have decreased since the late 1980's, severe maternal morbidity related to transfusion related complications and peripartum hysterectomies has continued to radically rise, increasing almost 200% since 1993 (ACOG, 2017; CDC, 2017). Although the CDC (2018) does not draw in conclusion for the increased mortality, the report does show that 11.5% of pregnancy related deaths between 2011 and 2014 were attributed to hemorrhage.

The consequences of PPH alongside maternal morbidity include increased medical costs and prolonged hospitalizations (CDC, 2017).

Internationally, more than 830 women expire every day from preventable complications related to pregnancy and childbirth, such as infection, bleeding, and high blood pressure associated with pregnancy compared to only two to three women daily in the U.S (AWHONN, 2017; World Health Organization [WHO], 2018). This number still provides room for growth and improvement, especially considering the U.S. is a developed country, and leading standard of care worldwide. Even in the midst of exceptional medical resources, the U.S. continues to have large ethnic, socioeconomic, and geographic disparities, with maternal African American women having three to four times greater deaths than women of all other ethnic groups (AWHONN, 2017).

PPH occurs in 3% to 5% of deliveries, most commonly after cesarean deliveries, accounting for 12% of maternal deaths in the U.S. (Evensen et al., 2017). In the last 10 years, there has been a 183% increase in postpartum mothers requiring a blood transfusion following the delivery of a baby (ACOG, 2017). While this sharp increase may be attributable to maternal age, pre-pregnancy obesity, coexisting medical conditions, and even the recognition of PPH, assessing resources and developing a comprehensive plan are important for the continued reduction of PPH related mortality and morbidity (ACOG, 2017; CDC, 2017). Every 10 minutes a woman experiences a pregnancy related complication, with PPH being the leading cause (AWHONN, 2017). This adds up to more than 125,000 women in the U.S. affected yearly (AWHONN, 2017). Current research suggests that over 5% of mothers will develop PPH and more than half will die from untreated PPH (AWHONN, 2017).

Local Problem

From 2011 to 2015, 141 maternal deaths were reported in Arizona with the majority occurring in Hispanic and African American populations (Arizona Department of Health Services, 2017). In addition, 24% of these deaths were due to PPH with more than 85% occurring within minority populations (Arizona Department of Health Services, 2017). An obstetric (OB) unit at a local community hospital has over 700 births each year and an increased number of minority and high-risk births. In addition, the hospital did not have a PPH algorithm in place.

Over the years, the increasing complexity of patient care has resulted in an increased need for policies and procedures. Policies and protocols result in a safer, more effective and algorithmic approach to patient care, improving patient outcomes (ACOG, 2015). The implementation of PPH guidelines have historically had a positive effect on PPH prevention, diagnostics and management (Nadisauskiene et al., 2016). It leads to a more conservative and methodical approach to the treatment of PPH and ultimately, can decrease deaths as well as postpartum anemia and postpartum hysterectomy rates due to uterine atony (Savirón-Cornudella et al., 2018).

Problem Statement

Postpartum hemorrhage accounts for the majority of preventable maternal deaths. Lack of a PPH algorithm can lead to a delay in identifying and treating a preventable complication. The purpose of this project was to create and implement a systematic resuscitation algorithm for a local facility with the aim of increasing the probability of recognizing and responding to

a PPH. Development of a guideline for stakeholders involved in the care of OB patients is an initiative to prevent maternal mortality and morbidity at this local facility.

Purpose

The purpose of this DNP project was to develop a resuscitation algorithm for PPH for anesthesia providers at a local hospital in the Phoenix area.

Aims and Objectives

The primary aim of the project was to increase anesthesia providers' knowledge about managing PPH. Secondary aims were the adoption of the algorithm for practice with the goal for approval as a policy and procedure in the anesthesia and obstetrics manual.

Stakeholders

Optimal management of PPH occurs when various providers from multiple specialties recognize the potential for PPH to occur and elicit an algorithm that allocates specific tasks for each individual and a protocol to be followed (Ring & Landau, 2018). Stakeholders considered for the project included OB nurses, obstetricians, anesthesia providers, nurse managers, hospital pharmacists, and staff within the blood bank and laboratory department. Expectant mothers are pertinent external stakeholders.

Project Question

This project aimed to answer, 'can a high quality PPH resuscitation algorithm be developed and adopted by anesthesia providers at a facility?'

Theoretical Framework

Kurt Lewin Organizational Change Theory

A theoretical framework is one of the most important aspects of the research process. It is the foundation from which all knowledge is constructed, serving as the rationale for the study and providing a base for the literature review, methods, and analysis (Grant & Osanloo, 2014). The Kurt Lewin's change theory examines three specific stages, providing a high-level approach to change. Although criticized for its overly simplistic nature, Kurt Lewin developed a theory that gives organizations a framework to seamlessly implement change (Cummings, Bridgman, & Brown, 2016).

In order for change to take place within an organization, certain elements must be established including a direction for a practice change, effective leadership, and a culture that promotes change (Gesme & Wiseman, 2010). Lewin's change theory describes three stages: unfreezing, change, and refreezing (Cummings et al., 2016). The general concept of Lewin's change theory is that driving forces facilitate change and cause a shift in the equilibrium (Cummings et al., 2016). This DNP student worked as the driving force within the facility, attempting to shift the equilibrium and create a shared vision amongst the OB staff.

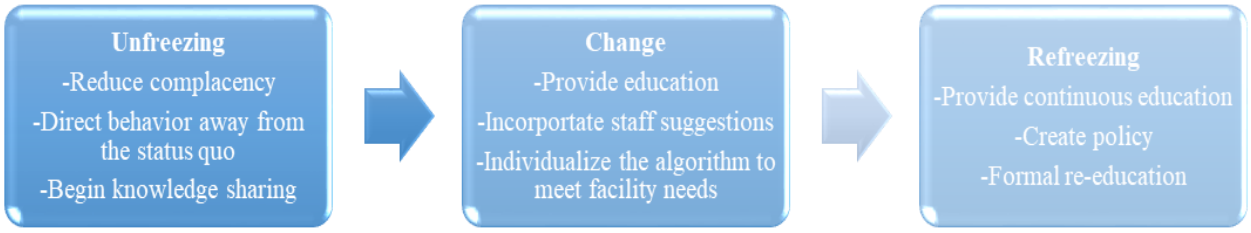


FIGURE 1. The stages of Kurt Lewin's organizational change theory.

Concepts

Unfreezing

During the unfreezing or equilibrium stage, one must surpass the natural resistance to change and increase awareness of how the current practices are hindering the organization (Cummings et al., 2016). At the facility, the complacency with a lack of protocol needed to be overcame. Lewin's change theory describes several ways that resistance can be overcome. They include increasing the driving forces that direct behavior away from the status quo, decreasing the restraining forces negatively affecting movement, or a combination of the two (Cummings et al., 2016). This can be accomplished through knowledge sharing and with the help of a stimulating leadership style. The DNP student worked to increase the driving forces to direct behavior away from the current practices and increase understanding through knowledge sharing. The DNP student also facilitated open conversation with anesthesia providers reviewing current practices and addressing concerns.

Change

Change includes transitioning phase to a new state of being, marked by the execution of the change and is overall the hardest stage to overcome (Cummings et al., 2016). Feelings of uncertainty, fear, and defiance often hinder this stage and could result in a rejection of the change altogether (Cummings et al., 2016). The DNP student presented evidence-based recommendations to the staff and addressed concerns with action plans and revisions. The algorithm was tailored to meet provider and facility needs.

Refreezing

Refreezing is the formal reinforcement of the change (Cummings et al., 2016). The change becomes the standard operating procedure and steps are taken to ensure that the facility does not revert to old ways of doing (Cummings et al., 2016). This stage can be solidified by moving the algorithm into policy, education, and continual reinforcement and re-education. The anesthesia provider provided education to OB staff and anesthesia providers regarding the new guideline. Plan for continual education was discussed with the chief anesthesiologist to ensure longevity.

Synthesis of Evidence

Literature Search

A literature review was conducted to identify the current evidence in identifying high-risk mother's and the management of PPH (Appendix I). The research databases Cochrane, Cumulative Index to Nursing and Allied Health Literature (CINAHL), and the American College of Obstetricians and Gynecologists' database were utilized to identify the current literature. Key terms used for the search included: *pregnancy, bleeding, maternal risk factors, postpartum hemorrhage, obstetric hemorrhage, mass transfusion, crystalloid replacement, maternal anesthetic management, maternal mortality, uterotonic agents, uterine atony, active management labor, retained placenta, and obstetric trauma.* The terms "and" and "or" were used to broaden search criteria. Inclusion criteria comprised literature in the English language, publications within the past five years, and studies within the U.S. While only 15 randomized control trials within the past five years were produced, altogether 251 articles were constructed. Broadening inclusion criteria to articles in the last 10 years and international studies resulted in

resulted in 372 articles including randomized control trails, protocols, clinical practice guidelines, and evidence-based recommendations. Finally, 10 articles were chosen based on recent timeframe, randomized control trials, and study size.

Maternal Risk Factors

There are well established maternal and OB risk factors that have been found to play a major role in the incidence of PPH. Risk factors can be separated into two categories: admission risk (Figure 2) and intrapartum/antenatal risk. These risk factors can be incorporated into a PPH algorithm and be useful in assisting anesthesia providers in identifying high-risk mother's during the pre and intrapartum period.

Admission risks can be further separated into low, medium, and high-risk categories. Low risk individuals include those with no previous uterine incision, single pregnancy, less than four vaginal births, no history of PPH, and a body mass index (BMI) <30 (Lisonkova et al., 2016). Moderate risk includes prior c-section or uterine surgery, maternal age greater than 35, more than four deliveries, multiple gestation, large uterine fibroids, chorioamnionitis, preeclampsia, and BMI greater than 30 (Combs, Murphy, & Laros, 1991; Lisonkova et al., 2016). High-risk individuals include those with placenta previa, accreta, increta, or percreta, a starting hematocrit less than 30%, bleeding upon admission, known coagulopathy or anticoagulant therapy, and a history of PPH (Combs et al., 1991; Lisonkova et al., 2016; Kramer et al., 2013). Placenta accreta had the highest hysterectomy rate at 70% (Hu et al., 2017).

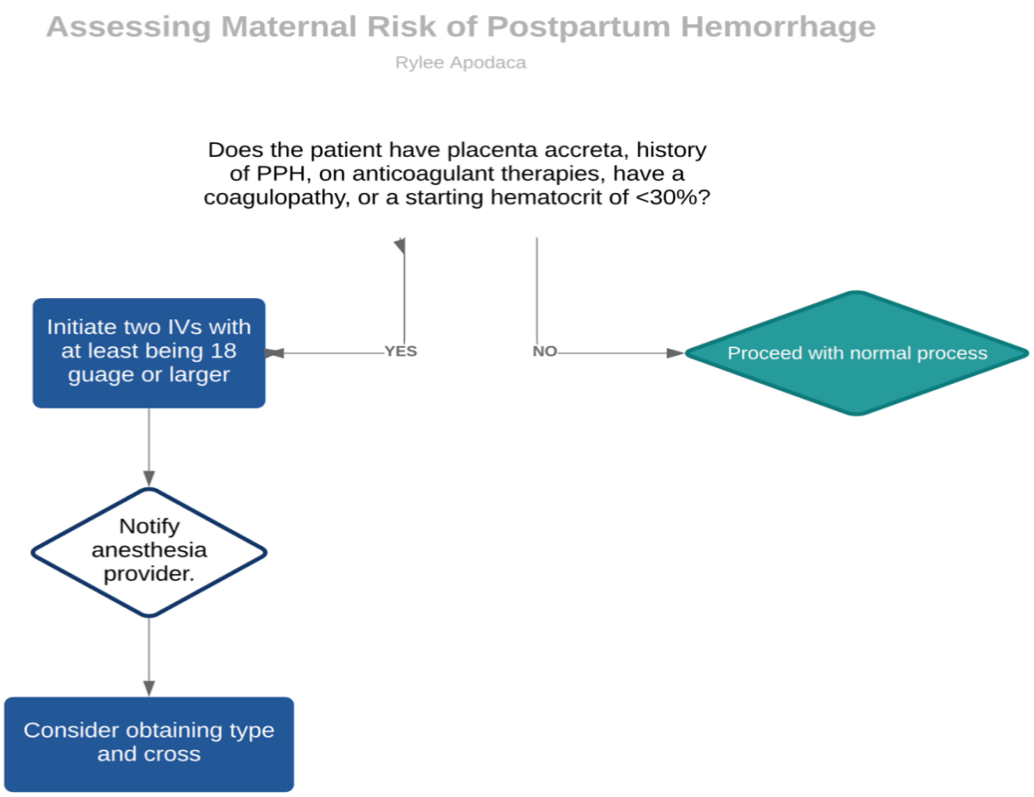


FIGURE 2. Assessment of risk for PPH based on admission factors. (Adapted from *Atonic postpartum hemorrhage: Blood loss, risk factors, and third stage management* by Lisonkova, S., Mehrabadi, A., Allen, V., Bujold, E., Crane, J., Gaudet, L,…Joseph, K., 2016; *Factors associated with postpartum hemorrhage with vaginal birth* by Combs, C., Murphy, E., & Laros, R, 1991.)

The National Partnership for Maternal Safety and Council on Patient Safety in Women's Health Care suggest assessing risk on admission and throughout the birthing process as other risk factors may develop throughout the laboring process (ACOG, 2017). Low intrapartum/antenatal risk includes uncomplicated vaginal delivery and no genital tract trauma. Intermediate risk includes a cesarean birth, prolonged labor >12 hours, rapid labor, use of magnesium sulfate infusion, prolonged use of oxytocin, use of forceps or vacuum, genital tract trauma, and shoulder dysplasia (ACOG, 2017). High risk includes hematocrit less than 30% with an accompanying

intermediate risk factor(s), retained placenta, platelets less than 100,000 mg/dL, retained placenta, and uterine rupture (ACOG, 2017; Lisonkova et al., 2016).

Stages of Hemorrhage

The stages of PPH can be broken into four individual stages, Stage 0 through Stage III with increased blood loss and instability with progression (ACOG, 2017).

Stage 0 Hemorrhage

Stage 0 hemorrhage follows the third stage of active labor and is defined as the immediate post-delivery period with less than 1000 ml of blood loss for vaginal delivery and c-section (ACOG, 2017). Active management of the third stage of labor includes a prophylactic uterotonic agent, early cord clamping, and controlled cord traction to deliver the placenta (Begley et al., 2019). Active management of the third stage of labor reduces the risk of severe primary PPH, anemia post birth, maternal blood loss at birth, and the need for maternal blood transfusion (Begley et al., 2019).

Stage I Hemorrhage

Stage I hemorrhage is defined as blood loss greater than 1000 ml for vaginal or C-section with vital sign instability. If this is identified, comprehensive vital signs including pulse oximetry should be recorded every five minutes along with a recording of cumulative blood loss. Supplemental oxygen, 5-7 L/min by facemask should be administered to optimize oxygen delivery to organs. Foley catheter should be inserted with the intent of monitoring urine output and decompressing the bladder for fundal massage (ACOG, 2017). Intravenous access should be ensured or obtained, ideally with a 16- or 18-gauge catheter in anticipated for fluid administration.

Protocol for Stage I Hemorrhage

Laboratory values. While shock index indicators such as heart rate, blood loss, and hemoglobin are often used to determine the need for transfusion, Era et al. (2014) found that the specificity of these indicators as decision factors was not always high. A fibrinogen levels is one of the most sensitive indicators to transfuse packed red blood cells (PRBCs) or fresh frozen plasma (FFP) (Era et al., 2014). Fibrinogen levels greater than 100 mg/dL should be maintained during PPH management (Shields, Lee, Druzin, McNultyt, & Mason, 2009).

Volume replacement. Intravenous crystalloid fluid replacement is routinely replaced at a 2:1 ratio, however, large volume crystalloid (greater than 500 ml) replacement that been associated with increased mortality in the hypotensive trauma patient (Chang & Holcomb, 2017). Thus, crystalloid resuscitation greater than one liter should warrant further investigation of alternative volume replacement. Early definitive hemorrhage control and mass transfusion with damage control resuscitation are the preferred treatment for severe hemorrhagic shock (Chang & Holcomb, 2017).

Tranexamic acid. Tranexamic acid (TXA) is a competitive inhibitor of plasminogen activation and reduces bleeding by inhibiting the breakdown of fibrinogen and fibrin clots (WHO, 2017). TXA should be considered a treatment for PPH when initial medical therapy fails (ACOG, 2017; Xu, Gao, & Ju, 2012). A loading dose of four grams over one hour at the identification of PPH followed by an infusion has been found effective in reducing blood loss associated with PPH (Xu et al., 2012). The WHO (2017) has also identified one gram of TXA intravenously over 10 minutes after initial diagnosis and a second gram after 30 minutes if bleeding continues to reduce mortality and morbidity associated with PPH. Side effects of TXA

are mild and transient including nausea and hypotension (Xu et al., 2012). While absolute contraindications to TXA include a history of thromboembolic or ischemic event, deep vein thrombus, and acute myocardial infarction, benefit over immediate risk must be identified and is left up to the provider discretion (Xu et al., 2012).

Uterotonic agents. A uterine tonic agent is a drug used to increase the tone of the uterus and should be the first line treatment for PPH caused by uterine atony (ACOG, 2017). Uterotonic agents include oxytocin, ergot alkaloids, and prostaglandins. Outside of recognized contraindications, no agent has been found to have greater efficacy than others for treatment of uterine atony (ACOG, 2017). Common agents include oxytocin 10 - 40 units intravenously, methergine 0.2 milligrams (mg) intramuscularly, 15-methyl prostaglandin F 0.25 mg intramuscularly, and Misoprostol 600-1000 micrograms (mcg) orally, sublingually, or rectally (ACOG, 2017).

Oxytocin. *Oxyt*ocin stimulates the upper segment of the myometrium to contract, which constricts spiral arteries and decreases blood flow through the uterus (Evensen et al., 2017). Oxytocin is a first line treatment against PPH because it is at least as effective as ergot alkaloids or prostaglandins, yet it has fewer side effects (Evensen et al., 2017). Side effects include nausea, vomiting, irregular heart rhythm, hypertension, and uterine rupture (Evensen et al., 2017). It can be injected intravascularly or intramuscularly.

***Methergine*.** Methergine, also known as methylergonovine, is an ergot alkaloid that causes generalized smooth muscle contraction in both the upper and lower segments of the uterus (Evensen et al., 2017). Because ergot alkaloid agents raise blood pressure, they are

contraindicated in women with preeclampsia or hypertension (Evensen et al., 2017). Other adverse effects include nausea and vomiting.

Prostaglandins. Prostaglandins enhance uterine contractility and cause vasoconstriction (Evensen et al., 2017). The prostaglandin most commonly used is 15-methyl prostaglandin or hemabate (Evensen et al., 2017). Hypersensitivity is the only absolute contraindication, but hemabate should be used with caution in patients with asthma or hypertension (Evensen et al., 2017). Side effects include nausea, vomiting, diarrhea, hypertension, headache, flushing, and pyrexia. (Evensen et al., 2017)

Misoprostol. Misoprostol is a synthetic prostaglandin analogue that increases uterine tone (Evensen et al., 2017). Misoprostol is effective in the treatment of PPH, but side effects limit its use. Doses range from 200 to 1,000 mcg depending on the route. Larger doses are associated with more side effects, including shivering, pyrexia, and diarrhea (Evensen et al., 2017). Although misoprostol is widely used in the treatment of PPH, the U.S. Food and Drug Administration do not approve it for this indication (Evensen et al., 2017).

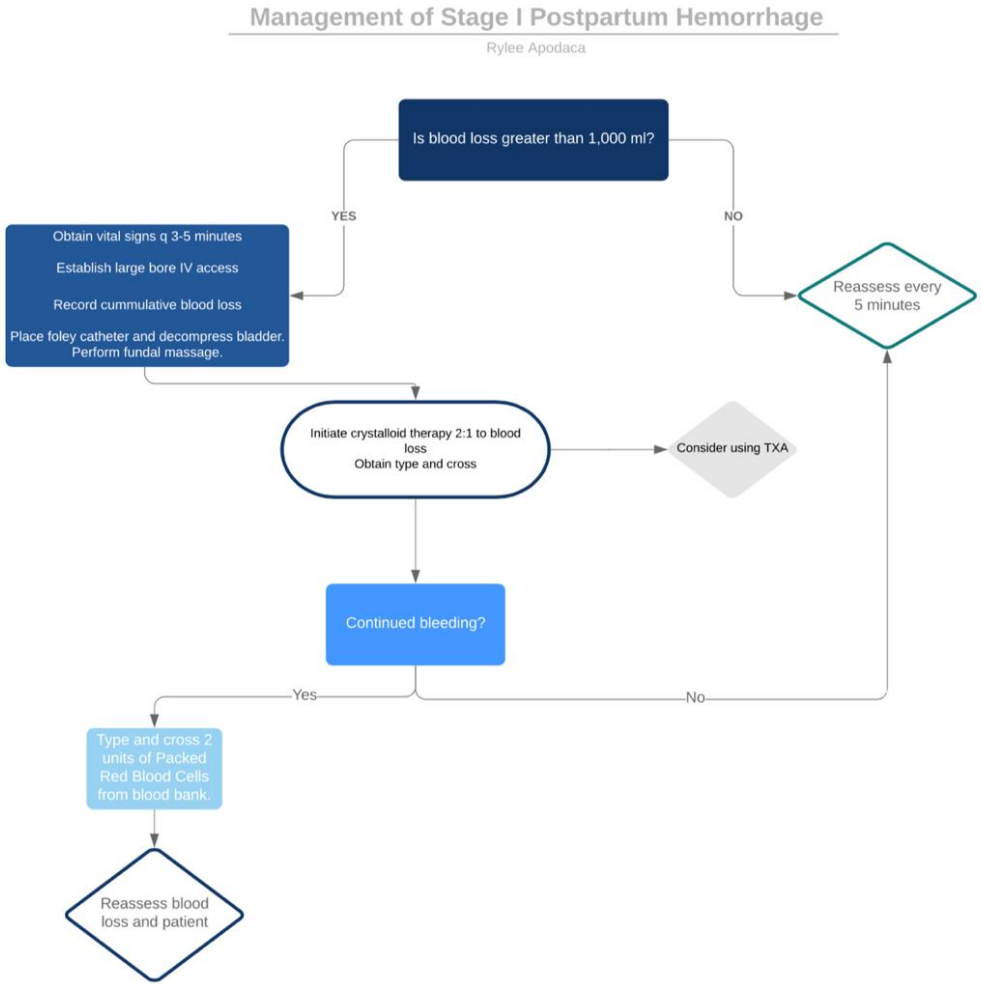


FIGURE 3. Management of Stage I PPH. (Adapted from *Tranexamic acid for the prevention of postpartum hemorrhage* by Xu, J., Gao, W., & Ju, Y, 2012; *Postpartum hemorrhage* by American College of Obstetricians and Gynecologists, 2017; *Optimal fluid therapy for traumatic hemorrhagic shock* by Chang, R. & Holcomb, J., 2017.)

Stage II Hemorrhage

Stage II hemorrhage is continued bleeding with changing vital signs and blood loss up to 1500 ml. During this stage, a second intravenous access should be established. If not already present, the patient should be transferred to the operating room (OR). Temperature regulation should remain a high priority to reduce bleeding. Utilize warming devices if feasible such as a fluid warming device (John & Harper, 2014).

Volume replacement. Blood loss greater than 30% of the total body volume requires replacement of volume with blood product (Lee et al., 2015). Ava, Ducloy-Bouthors, Rugeri, and Gris (2014) recommend transfusing a minimum of two units of PRBCs during stage II hemorrhage per clinical signs and to maintain a hematocrit of 21% to 24%.

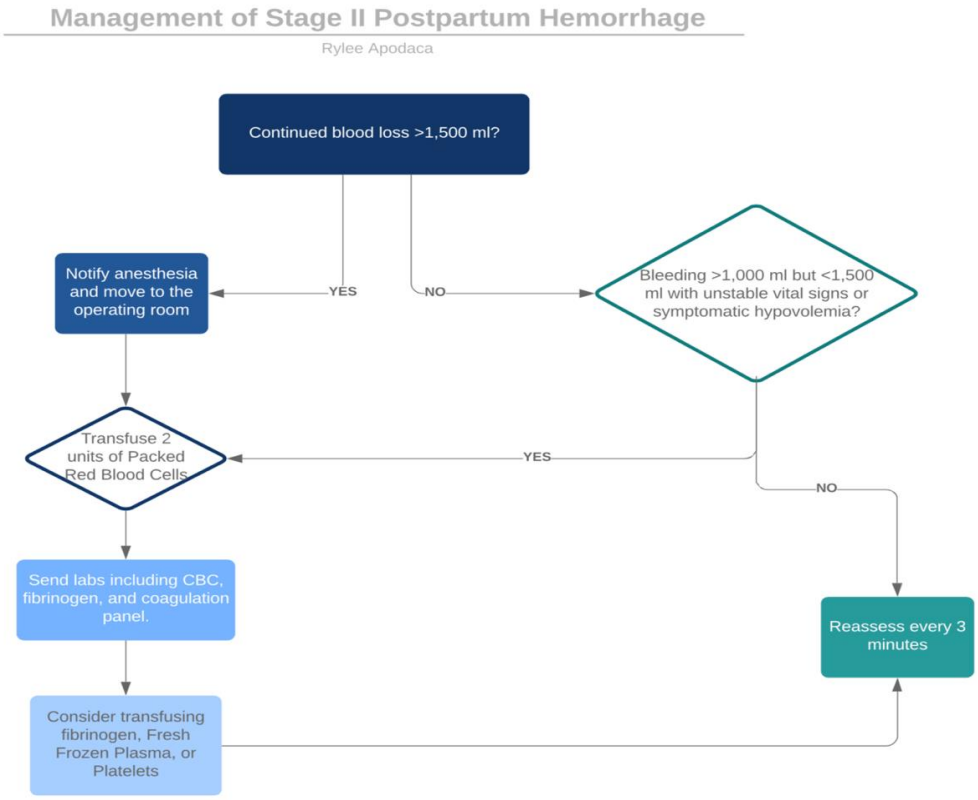


FIGURE 4. Management of Stage II PPH. (Adapted from *Postpartum hemorrhage* by American College of Obstetricians and Gynecologists, 2017; *Anesthetic management of severe or worsening postpartum hemorrhage* by Aya, A., Ducloy-Bouthors, A., Rugeri, L., & Gris, J., 2014; *Blood product replacement* by Lee, R., Shields, L., Mason, H., Rollins, M., Gorlin, J., Druzin, M., & McNulty, J, 2015.)

Stage III Hemorrhage

During Stage III hemorrhage, a massive transfusion protocol (MTP) should be initiated, and the patient should be aggressively transfused (Shields et al., 2009). Generally, management should be least invasive methods to more aggressive interventions including hysterectomy

(ACOG, 2017; Hu et al., 2017). While maternal MTPs contradict, a PRBC, FFP, and platelet transfusion ratio of 6:4:1, 4:4:1, and 1:1:1 are all supported within the evidence (ACOG, 2017; Ava et al., 2014; Shields et al., 2009).

Massive transfusion protocol. MTP includes three to six units of PRBC prepared to maintain a patient's hematocrit at 21% to 24% and hemoglobin 7% to 8% (Lee et al., 2015). If type and crossmatch has not been completed, uncross-matched group 'O' negative blood should be transfused (Lee et al., 2015). FFP contains nearly all coagulation factors and early transfusion with FFP should be initiated (Lee et al., 2015). Early transfusion with FFP has been found to correlate with improved survival rates from hemorrhage after trauma (Chang & Holcomb, 2017). Platelets should be transfused when platelet levels are less than 100,000 and should be maintained at 50,000 to 100,000 mg/dL (Ava et al., 2014). If fibrinogen levels are less than 100-125 mg/dL with ongoing bleeding, fibrinogen concentrate should be used (Lee et al., 2015).

Strengths, Weaknesses and Gaps of Literature Review

The literature review included multiple studies, which concluded high quality evidence regarding the care of mothers in the postpartum period.

Strengths

A seven-level hierarchy presented by Polit and Beck (2012) was utilized to allocate a level of evidence based on the strength and quality of the evidence provided. Evidence retrieved included randomized control trials (Level II), cohort studies and non-randomized control trials (Level III), retrospective and case studies (Level IV), and reappraised, secondary systematic reviews (Level I). Various systematic reviews and meta-analyses are available; nevertheless, the

majority contain data greater than 10 years old. There is extensive data regarding treatments and associated risk factors. Studies are performed over long periods and are multi-centered.

Weaknesses

Levels of evidence based on the source was fair concerning a lack of randomized control trials related to a preponderance of benefit over harm. Weaknesses identified in the literature included limited number of case control studies with the majority being retrospective case reviews. A large portion of the studies found was done outside of the U.S. questioning their application to the U.S. health system. Due to ethical constraints of potentially harming a mother or child, there is a lack of robust studies with randomization and large sample size, however, the value of discussion and analysis within this population is vital to advancement. Much of the current literature is limited to single site retrospective studies, literature reviews, and cohort studies that lack in sample size, which challenges transferability of the literature. Furthermore, studies varied in defined PPH parameters. For example, one study may consider PPH with a blood loss of 500 ml or more for vaginal and cesarean deliveries, while another considered less than 1000 ml for a cesarean delivery and greater than 500 for a vaginal delivery.

Gaps

Additionally, much of the literature reviewed is pooled with hemorrhagic trauma and unspecific to the obstetric population, which warrants special consideration. Most studies lacked a control group and a multitude of patient factors and histories make it difficult to transfer literature. There is also limited information available regarding crystalloid replacement in the obstetric patient and while one study is underway, results are not available. There is conflicting

data regarding transfusion methods and studies comparing outcomes with transfusion ratios within the obstetric population were not found.

METHODS

Project Design

The development of the PPH guideline was comprised of two phases: Phase I - Systematic development of an algorithm adopted from the ACOG clinical guidelines for PPH and other current evidence was developed by the principle investigator (PI); and Phase II - Expert consultants appraised the algorithm using the AGREE II tool for grading of evidence (Appendix E). The goal of the quality improvement project was to enhance maternal outcomes through the development of an algorithm and dissemination of education.

AGREE II Tool

The AGREE II tool provides a systematic strategy to assist practitioners in assessing the quality, rigor, and transparency of a developed guideline (Brouwers et al., 2013). The AGREE II tool is a free platform available online and assessible by appraisers at their own convenience. It is comprised of six key domains and two overall assessment guides. These six domains include: 1) Scope and purpose, 2) Stakeholder involvement, 3) Rigor of development, 4) Clarity of presentation, 5) Applicability, and 6) Editorial independence (Brouwers et al., 2013).

Scope and practice. The scope and practice domain are concerned with the overall aim of the guideline and the target population.

Stakeholder involvement. Stakeholder involvement focuses on the extent to which the guideline was developed by appropriate stakeholders and represents the views of its projected users.

Rigor and development. Rigor relates to the process used to gather evidence and the methods used to formulate recommendations.

Clarity of presentation. Clarity is in regard to the language, structure, and format of the guideline and its feasibly.

Applicability. Applicability pertains to the barriers to implementation, strategies to improve uptake, and resource implications of applying the guideline.

Editorial independence. Editorial independence is concerned with the formulation for the recommendations being unbiased with minimal conflict of interests.

My AGREE PLUS Platform

The My AGREE PLUS platform is a free, online, electronic platform that allows appraisers to collaborate and evaluate a particular practice guideline using the AGREE II assessment tool (Brouwers et al., 2010). The My AGREE PLUS platform (Appendix F) allows users to complete and track all of their online AGREE II appraisals. Users signed up for the platform using their email addresses, which was retrieved during time of recruitment.

Setting and Participants

The algorithm was developed for an anesthesia group-providing anesthesia at a facility in the Mesa area, which is a 178-bed, Level III trauma center with 12 operating rooms, two labor & delivery suites with one dedicated OR for C-sections. There was an average of 75 births per month at the facility with a projected increase over the next several years. There were five full-time anesthesia providers and two student nurse anesthetists who provided anesthesia for the OB department during the time of recruitment and implementation

The developed algorithm was created for all to follow with the intent to decrease avoidable morbidity and mortality resulting from PPH. Participants for this project included interprofessional collaborators in the fields of obstetrics, pharmacy and anesthesia. There were two groups appraising the algorithm for quality. The first group included two content experts; an obstetrician and a pharmacist, who were recruited by professional connections to perform the initial review and appraisal of the algorithm. A two-week time limit was set to review the algorithm and sources and provide open feedback and suggestions using the AGREE II tool as a guide. Feedback was provided via telephone and follow-up was made after recommended suggestions were ensued.

The second group consisted of anesthesia providers experienced in obstetric anesthesia. Recruitment of anesthesia providers was identified by the chief anesthesiologist at the project site who sent out an initial email to identified anesthesia providers introducing the PI, information about the project, commitment details, and a tentative timeline (Appendix A). Following the initial email, further correspondence was from the PI. The e-mail was sent to five anesthesia providers, two of which responded with interest in participating in the project. Recruitment took place over a two-week period, with a 33% response rate.

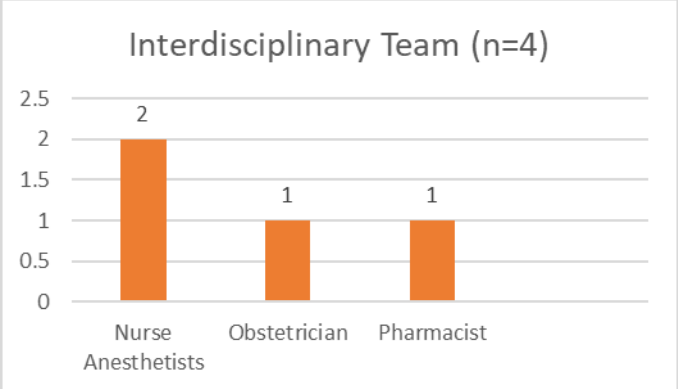


FIGURE 5. Critical appraisers.

Data Collection

Project data collection for the second phase of this project began after organization (Appendix C) and University of Arizona IRB approval (Appendix J). The My AGREE PLUS platform was utilized to evaluate and assess the developed algorithm by the interdisciplinary panel. When users completed the appraisal, they received a link to the AGREE II results summary. Scores for the algorithm were written on a pre-designed form (Appendix B) organized with item numbers and a score for ease of use. The AGREE II tool (Appendix E) was comprised of 23 key items organized within six domains and two overall guideline assessments. The student analyzed the concluded data.

Assessment Scoring

The two global guideline assessments are: 1) rate the overall quality of this guideline and 2) I would recommend this guideline for use to determine if the algorithm contains quality evidence to be implemented (Brouwers et al., 2013). The algorithm and guidelines will be analyzed and then amended based on overall assessment score. Each of the AGREE II items and the two global rating items are rated on a Likert seven-point scale, from '1' representing *strongly disagree* to '7' representing *strongly agree*. Scores increase as more criteria are met. A score between '2' and '6' was assigned when the reporting of the AGREE II item did not meet the full criteria or considerations.

To promote standardization of scoring, participants were required to complete a brief online tutorial on the AGREE II tool prior to assessing the developed algorithm. Each panel member was required to sign a written statement (Appendix E) that confirmed his/her completion of the online tutorial before assessment of the developed algorithm. Three of the four

participants completed the AGREE II tool tutorial and algorithm assessment scoring within a 24-hour period. One participant required 72 hours due to technological problems and difficulty navigating the online tool. Contact was made with the participant within 12 hours of the reported issue and resolution was attained; extension was provided due to the surrounding circumstances.

Data Analysis

A quality score was calculated for each of the six domains, independently. The domain scores were calculated by summing up all scores of individual items in each domain and scaling the total as a percentage of the maximum possible score for that domain (AGREE Next Steps Consortium, 2017). The final scores were calculated by summing up the scores of individual items in each domain and scaling the total as a percentage of the maximum possible score. A maximum and minimum possible score were calculated for each domain. Lastly, the scaled domain scores were calculated using the (Obtained score – Minimum possible score) / (Maximum possible score – Minimum possible score) x 100. The domain scores are useful for comparing guidelines and can help guide whether a guideline should be recommended for use, however, there is no set minimum score or patterns of scores across domains to differentiate between high-quality and poor-quality guidelines (Brouwers et al., 2013). The final score was reported in a percentage for each domain with a quality threshold of domain scores higher than 80% indicating a high-quality algorithm.

Ethical Considerations

The purpose of the project was explained with full disclosure and all parts of this DNP project were made available to participants.

Respect for Persons

Participant's anonymity and confidentiality was maintained throughout the utilization of the AGREE PLUS tool. There was explanation that study outcomes will not result in judgment, criticism, or misuse of information. After completion of the project, My AGREE PLUS users were able to terminate their AGREE II accounts and any printed collection data was discarded in protected health information trash bins available at the housing facility.

Beneficence

Described as a moral obligation to act in kindness and do well, the principal beneficence was demonstrated by treating all participating individuals with kindness and respect. Full transparency in regard to project purpose and potential implications for future research was disclosed.

Justice

All participants were treated judiciously, with no distinction made between participants based on personal characteristics, competence, or merit. With the intent to demonstrate fairness, all participants were given the same questionnaire.

RESULTS

The AGREE II online guideline appraisal provided individual scores for all 23 questions along with the opportunity for appraisers to add personal comments. A cumulative score for each of the six domains resulted with a final overall guideline assessment rating the quality of the developed guideline. The seven-point AGREE II score calculator and decision rules was utilized to calculate the combined score of all appraisers and determine guideline quality. The detailed

results of the appraisal can be found in Figure 5. A quality threshold of greater than 80% was assigned to each domain indicating that revisions were not needed.

The overall quality of the developed guideline was assessed and resulted in a combined score of 90.8%, representative of a high-quality guideline. Demonstrating low discrepancy between appraisers, the standard deviations for all domains were less than 0.5%. The overall combined score of the six domains were 90%, 98%, 82%, 84%, 94%, and 97% (Figure 5) respectively, indicating that no action is necessary to revise the developed algorithm.

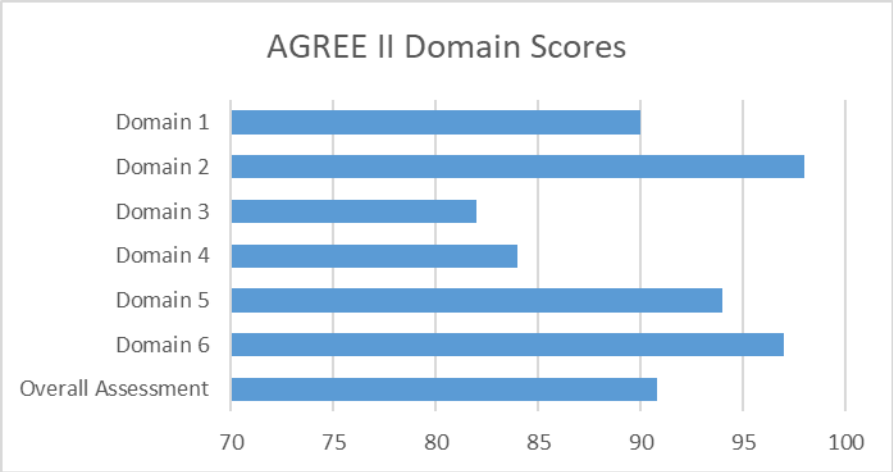


FIGURE 6. AGREE II domain scores.

Appraiser Comments

One advantage to the online AGREE II tool is the ability for appraisers to comment within each domain appraised and provide feedback. Constructive commentary to enhance the overall quality of the developed CPG are listed below.

Domain 1

One participant stated, “author clearly state the purpose and goal for the project.”

Domain 2

One participant stated, “specify which staff members will be involved.”

Domain 3

One participant stated, “ensure hemorrhage levels match the evidence and throughout the algorithm.”

Appraisers overall judgment regarding recommended use of the developed algorithm resulted with an answer of ‘Yes,’ to the recommended use.

DISCUSSION

Strengths

The ability for appraisers to add free text comments provided valuable information and insight on the quality of the algorithm. In Domain 3, changes included clear delineation of different hemorrhage stages. An interdisciplinary appraisal team increases an algorithms transferability and reliability of the data collected. The algorithm was developed to create a high quality PPH resuscitation algorithm with the goal of knowledge sharing and increasing adoption amongst anesthesia providers. To goal of the algorithm was to promote the relay of current, evidence-based information in regard to the resuscitation care of mothers experiencing PPH, to improve outcomes and ultimately, to reduce maternal mortality and morbidity. This DNP project addresses a current facility need and a gap and practice and provides a systematically developed high-quality algorithm to assist anesthesia in identifying and resuscitating a mother experiencing a current hemorrhage.

Limitations

One limitation in the study tool is the tool does not allow an appraiser to choose “not applicable” for an AGREE II item that may not be applicable. This may be reflected in the score for Domain 5, potential resource implications, which received a score of 87%. In Domain 5,

appraisers were asked to evaluate the potential resource implications of applying the recommendations, however, the proposed algorithm does not propose a treatment, but instead organizes the treatment approach.

Interpretation of the algorithm based on domain scores is ambiguous, as there is limited data to link specific overall assessment scores with algorithm quality and success (Brouwers et al., 2010).

Recommendations for Practice

PPH remains the leading cause of premature maternal mortality worldwide. PPH occurs unpredictably and has been described as the "equal opportunity killer," affecting mothers of all socioeconomic classes, races, ages, and creed (Edhi, Aslam, Naqvi, & Hashmi, 2013). Anesthesia providers are increasingly being called upon as first responders to assist in the management of patients with severe PPH (Shaylor et al., 2017). There is objective evidence and extensive research concerning PPH management, treatment, and prevention, as well as overwhelming evidence supporting the application of PPH algorithms and guidelines in practice to minimize maternal mortality and morbidity. Through systematic review of current evidence, an algorithm was developed to aid anesthesia providers in the resuscitation of a mother experiencing PPH. This algorithm was developed with the intent to increase awareness of PPH, decrease response times, and improve overall maternal outcomes.

Dissemination of the project was accomplished using a PowerPoint presentation at an anesthesia staff meeting at the local Mesa facility. While there are various PPH algorithm available, the following algorithm was designed with the needs of the facility in mind (Appendix H). This scholarly DNP project aimed to provide education on PPH and relay current evidence-

based advice for PPH resuscitation measures. The adoption and integration of the developed algorithm resulted in increased provider confidence and a globally posted crisis response for PPH displayed widely on the OB unit of the facility. The PI is working towards getting the algorithm placed on the anesthesia carts in the OB operating rooms for quick access during crisis response. Previous practice for PPH was unorganized and management was inconsistent. With an algorithm and educational presentation for anesthesia providers, future PPH management can be implemented according to the algorithm.

Adoption of the algorithm should be evaluated on a rolling basis through focus group assessment during the first six months of implementation to determine if anesthesia providers are utilizing the developed algorithm and to identify any barriers to use. A procedure for monitoring and updating the algorithm should be put in place to ensure the algorithm is updated with current evidence. An algorithm is only sustainable if there is a continual study of evolving evidence and modernization of recommendations based on arising evidence.

Dissemination

Dissemination is essential to sustainable practice change and the development of future practice. Once the algorithm was graded, results were disseminated to the anesthesia group at their monthly meeting. All parts of the algorithm were reviewed with all the anesthesia providers at the meeting to educate them about each of the steps to take for PPH. Project findings were shared in the January monthly newsletter for Diversity in Nurse Anesthesia Mentorship Program. The project leader also presented the project in digital format at an October diversity conference in Fort Worth, Texas, as well as provide the project in its entirety for future student nurse

anesthetists to use as an exemplar. This project was also disseminated at the Arizona Association of Nurse Anesthetists 2020 Fun and Sun conference.

DNP Essentials

This DNP project incorporated three significant elements of the DNP essentials.

DNP Essential III

Clinical scholarship and analytical methods for evidence-based practice is demonstrated in this DNP project through the integration of knowledge from various sources across disciplines for the improvement of health outcomes and fulfills this essential. Critically appraising the existing evidence and facilitating its translation into clinical practice as evidenced by the synthesis of evidence validates proficiency of this essential.

DNP Essential V

The DNP student exhibited advocacy in health care policy by developing and providing leadership for a facility through active participation and contribution towards hospital wide policy and procedures.

DNP Essential VI

Interprofessional collaboration for improving patient and population outcomes is represented in this project through the facilitation of an effective interprofessional team and demonstrates this project leader's ability to be an effective team leader.

Conclusion

The developed CPG provides providers with a synthesis of research findings and strong, evidence-based recommendations regarding the care of a mother experiencing PPH. Translation of research into clinical practice remains to be a challenge in healthcare, however, the developed

algorithm serves to bridge the gap between research and clinical practice to improve patient outcomes in this unique population. Future implications include dissemination of the developed algorithm to ancillary staff including OB registered nurses and obstetricians who work closely with laboring mothers. To continue to improve and strengthen the algorithm, women's health care providers, obstetricians, midwives, and gynecologists, as well as registered nurses, should join the interdisciplinary team.

APPENDIX A:

INVITE AND DISCLOSURE EMAIL

Invite and Disclosure Email

Hello,

You are invited to participate in a DNP project about the creation of an algorithm for postpartum hemorrhage. The algorithm will be graded using the Appraisal of Guideline for Research and Evaluation (AGREE) II tool.

The link for the AGREE II tool and tutorial will be provided to you via email. Recommendations will be graded by you using the Appraisal of Guideline for Research and Evaluation II tool. Commitment of the project includes short project introduction (5 minutes), AGREE II tool online tutorial (15 minutes), analyses of algorithm utilizing the AGREE II tool (variable), and recommendations for amendments (15 minutes). You will have two weeks to complete the AGREE II tool online tutorial and algorithm assessment.

This project is being conducted by Rylee Apodaca, a DNP-CRNA student through the University of Arizona College of Nursing.

I look forward to hearing from you all.

APPENDIX B:

AGREE II ASSESSMENT TOOL

AGREE II ASSESSMENT TOOL

Domain 1. Scope and Purpose		**1 SD**	**2**	**3**	**4**	**5**	**6**	**7 SA**
1	The overall objective (s) of the guideline is (are) specifically described.							
2	The health question (s) covered by the guideline is (are) specifically described.							
3	The population to whom the guideline is meant to apply is specifically described.							
Domain 2. Stakeholder Involvement		**1 SD**	**2**	**3**	**4**	**5**	**6**	**7 SA**
4	The guideline development group includes individuals from all relevant professional groups.							
5	The views and preferences of the target population have been sought.							
6	The target users of the guideline are clearly defined.							
Domain 3. Rigor of Development		**1 SD**	**2**	**3**	**4**	**5**	**6**	**7 SA**
7	Systematic methods were used to search for evidence.							
8	The criteria for selecting the evidence are clearly described.							
9	The strengths and limitations of the body of evidence are clearly described.							
10	The methods for formulating the recommendations are clearly described.							
11	The health benefits, side effects, and risks have been considered in formulating the recommendations.							
12	There is an explicit link between the recommendations and the supporting evidence.							
13	The guideline has been externally reviewed by experts before its publication.							
14	A procedure for updating the guideline is provided.							
Domain. Clarity of Presentation		**1 SD**	**2**	**3**	**4**	**5**	**6**	**7 SA**
15	The recommendations are specific and unambiguous.							
16	The different options for management of the condition or health issue are clearly presented.							
17	Key recommendations are easily identifiable.							
Domain 5. Applicability		**1 SD**	**2**	**3**	**4**	**5**	**6**	**7 SA**
18	The guideline describes facilitators and barriers to its application.							
19	The guideline provides advice and/or tools on how the recommendations can be put into practice.							
20	The potential resource implications of applying the recommendations have been considered.							

21	The guideline presents monitoring and/ or auditing criteria.							
Domain 6. Editorial Independence		**1 SD**	**2**	**3**	**4**	**5**	**6**	**7 SA**
22	The views of the funding body have not influenced the content of the guideline.							
23	Competing interests of guideline development group's members have been recorded and addressed.							

SD (strongly disagree) **SA** (strongly agree)

Overall Guideline Assessment
For each question, please choose the response which best characterized the guideline assessed

		1 Lowest quality	**2**	**3**	**4**	**5**	**6**	**7 Highest quality**
1	Rate the overall quality of this guideline							
		YES		YES, with modifications			NO	
2	I would recommend this guideline for use							

APPENDIX C:

SITE AUTHORIZATION FORM

Greater Anesthesia Solutions
1301 South Crimson Road
Mesa, Arizona 85209

5/3/2019

University of Arizona Institutional Review Board
c/o Office of Human Subjects
1618 E Helen St
Tucson, AZ 85721

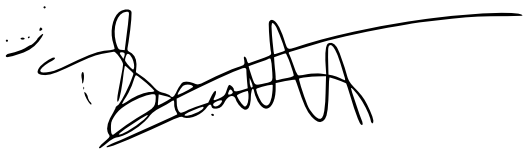
Please note that Ms. Rylee Apodaca, UA Doctor of Nursing Practice student, has permission of Greater Anesthesia Solutions to conduct a quality improvement project at the facility for her project, "Development of an Algorithm for Postpartum Hemorrhage."

Ms. Apodaca will develop an algorithm for anesthesia providers at Greater Anesthesia Solutions with the input, in part, of two CRNA's from one of the primary practice sites, Mountain Vista Hospital Medical Center. This will include communications conducted off site as agreed upon from both parties. Ms. Apodaca's activities will be completed by November 30, 2019.

Ms. Apodaca has agreed to provide and present the final upon completion to the anesthesia stakeholder of Greater Anesthesia Solutions providers.

If there are any questions, please contact my office.

Signed,



Dr. Ned Sciortino
Medical Director of Anesthesia

APPENDIX D:

ACOG PPH PRACTICE BULLETIN

Website URL: https://clinicalinnovations.com/wp-content/uploads/2017/10/ACOG_Practice_Bulletin_No_183_Postpartum-Hemorrhage-2017.pdf

The American College of Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

ACOG PRACTICE BULLETIN

Clinical Management Guidelines for Obstetrician–Gynecologists

NUMBER 183, OCTOBER 2017 *(Replaces Practice Bulletin Number 76, October 2006)*

Committee on Practice Bulletins—Obstetrics. This Practice Bulletin was developed by the American College of Obstetricians and Gynecologists' Committee on Practice Bulletins–Obstetrics in collaboration with Laurence E. Shields, MD; Dena Goffman, MD; and Aaron B. Caughey, MD, PhD.

Postpartum Hemorrhage

Maternal hemorrhage, *defined as a cumulative blood loss of greater than or equal to 1,000 mL or blood loss accompanied by signs or symptoms of hypovolemia within 24 hours after the birth process, remains the leading cause of maternal mortality worldwide (1). Additional important secondary sequelae from hemorrhage exist and include adult respiratory distress syndrome, shock, disseminated intravascular coagulation, acute renal failure, loss of fertility, and pituitary necrosis (Sheehan syndrome).*

APPENDIX E:

AGREE II ASSESSMENT TOOL AND USER MANUAL EDUCATIONAL TRAINING COMPLETION CONFIRMATION FORM

AGREE II Assessment Tool and User Manual Educational Training Completion Confirmation

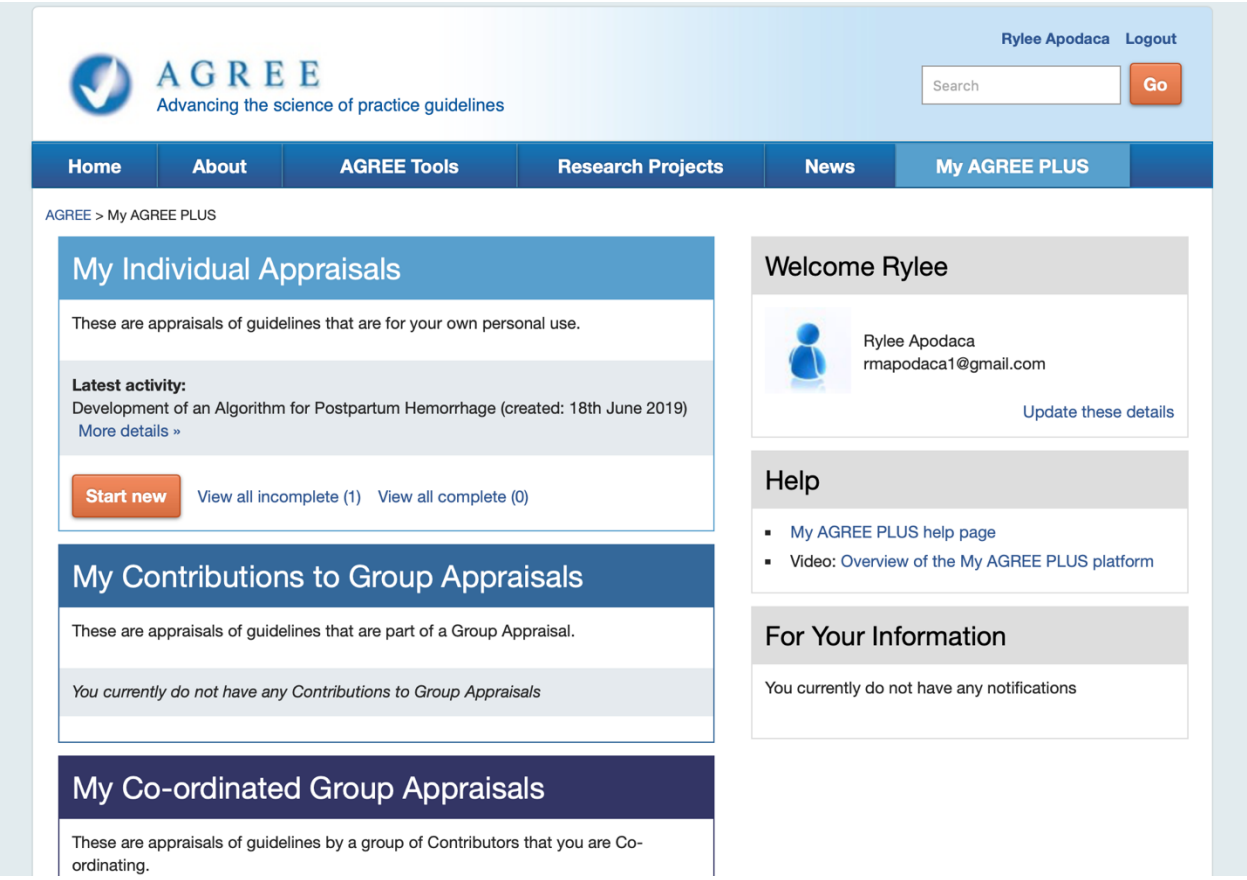
This letter serves to confirm that I, _____
have been provided a copy of the AGREE II assessment tool and user manual. That I have completed the AGREE II assessment tool online tutorial and been provided access to the AGREE II practice exercise in preparation for completing a formal appraisal of the developed Clinical Practice Guideline for Breastfeeding after Anesthesia.

_____ _____

Signed Name Date

APPENDIX F:

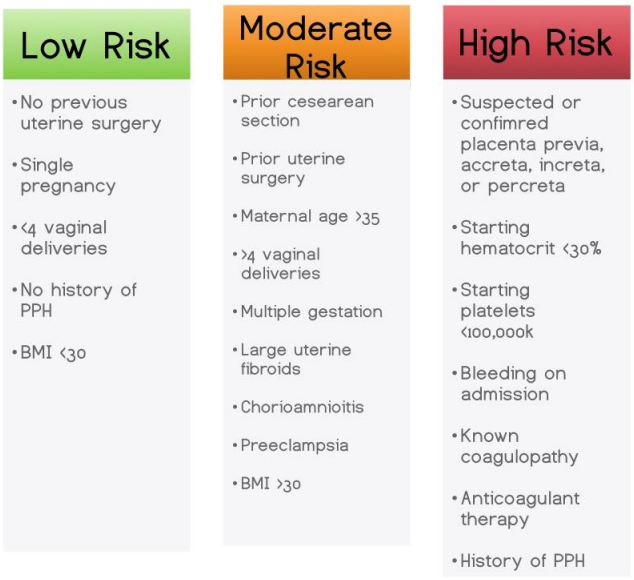
MY AGREE PLUS PLATFORM


Rylee Apodaca Logout
AGREE
Advancing the science of practice guidelines
Search
Go
Home
About
AGREE Tools
Research Projects
News
My AGREE PLUS
AGREE > My AGREE PLUS
My Individual Appraisals
These are appraisals of guidelines that are for your own personal use.
Latest activity:
Development of an Algorithm for Postpartum Hemorrhage (created: 18th June 2019)
More details »
Start new
View all incomplete (1)
View all complete (0)
My Contributions to Group Appraisals
These are appraisals of guidelines that are part of a Group Appraisal.
You currently do not have any Contributions to Group Appraisals
My Co-ordinated Group Appraisals
These are appraisals of guidelines by a group of Contributors that you are Co-ordinating.
Welcome Rylee
Rylee Apodaca
rmapodaca1@gmail.com
Update these details
Help
My AGREE PLUS help page
Video: Overview of the My AGREE PLUS platform
For Your Information
You currently do not have any notifications

APPENDIX G:

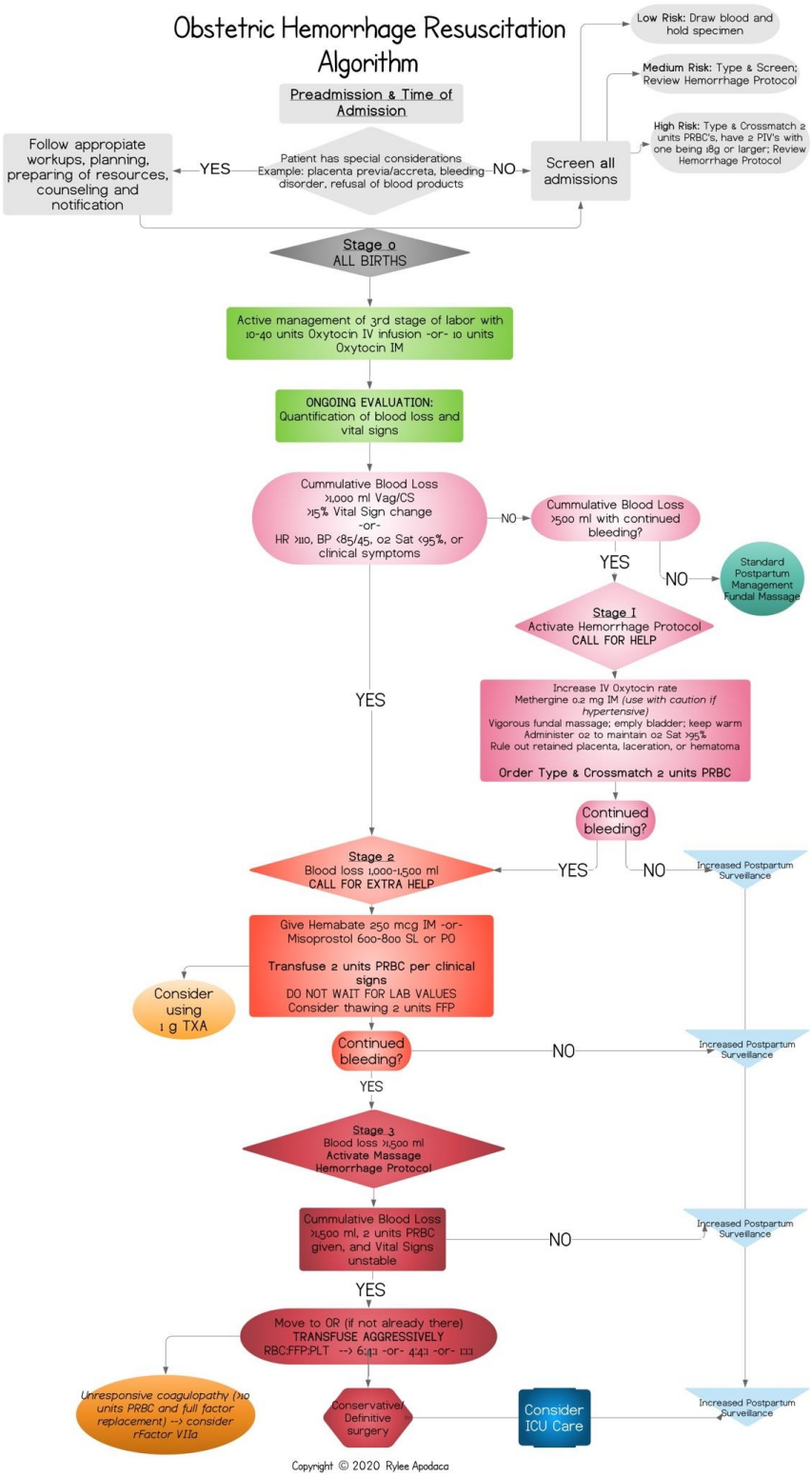
PREADMISSION PPH RISK ASSESSMENT TOOL

Preadmission Postpartum Hemorrhage Risk Assessment



APPENDIX H:

OBSTETRIC HEMORRHAGE RESUSCITATION ALGORITHM


Obstetric Hemorrhage Resuscitation Algorithm
Preadmission & Time of Admission
Patient has special considerations Example: placenta previa/accreta, bleeding disorder, refusal of blood products
YES
Follow appropiate workups, planning, preparing of resources, counseling and notification
NO
Screen all admissions
Low Risk: Draw blood and hold specimen
Medium Risk: Type & Screen; Review Hemorrhage Protocol
High Risk: Type & Crossmatch 2 units PRBC's, have 2 PIV's with one being 18g or larger; Review Hemorrhage Protocol
Stage 0
ALL BIRTHS
Active management of 3rd stage of labor with 10-40 units Oxytocin IV infusion -or- 10 units Oxytocin IM
ONGOING EVALUATION:
Quantification of blood loss and vital signs
Cummulative Blood Loss >1,000 ml Vag/CS >15% Vital Sign change -or- HR >110, BP <85/45, O2 Sat <95%, or clinical symptoms
NO
Cummulative Blood Loss >500 ml with continued bleeding?
YES
NO
Standard Postpartum Management Fundal Massage
Stage I
Activate Hemorrhage Protocol
CALL FOR HELP
Increase IV Oxytocin rate
Methergine 0.2 mg IM (use with caution if hypertensive)
Vigorous fundal massage; emply bladder; keep warm
Administer O2 to maintain O2 Sat >95%
Rule out retained placenta, laceration, or hematoma
Order Type & Crossmatch 2 units PRBC
YES
Continued bleeding?
Stage 2
Blood loss 1,000-1,500 ml
CALL FOR EXTRA HELP
YES
NO
Increased Postpartum Surveillance
Give Hemabate 250 mcg IM -or- Misoprostol 600-800 SL or PO
Transfuse 2 units PRBC per clinical signs
DO NOT WAIT FOR LAB VALUES
Consider thawing 2 units FFP
Consider using 1 g TXA
Continued bleeding?
NO
Increased Postpartum Surveillance
YES
Stage 3
Blood loss >1,500 ml
Activate Massage Hemorrhage Protocol
Cummulative Blood Loss >1,500 ml, 2 units PRBC given, and Vital Signs unstable
NO
Increased Postpartum Surveillance
YES
Move to OR (if not already there)
TRANSFUSE AGGRESSIVELY
RBC:FFP:PLT --> 6:4:1 -or- 4:4:1 -or- 1:1:1
Unresponsive coagulopathy (>10 units PRBC and full factor replacement) --> consider rFactor VIIa
Conservative/ Definitive surgery
Consider ICU Care
Increased Postpartum Surveillance
Copyright © 2020 Rylee Apodaca

APPENDIX I:

SYNTHESIS OF EVIDENCE

Project Question: What is the evidence-based management of various stages of PPH?

Author/Article	Research Question	Design	Sample (N)	Data Collection (Instruments/Tools)	Findings
Aya, A., Ducloy-Bouthors, A., Rugeri, L., & Gris, J. (2014) Anesthetic management of severe or worsening postpartum hemorrhage	The purpose of the study is to explore the anesthetic management of the patient experiencing severe PPH.	Review of literature	A search and consensus of the available literature on blood product replacement during PPH and analysis of 9 current massive hemorrhage protocols	Keywords related to the anesthetic and critical care practice and obstetrical management were used in various combinations Guidelines from several societies and organizations were read	Hematocrit should be maintained 21-24% During stage II hemorrhage, two units of PRBC should be released from blood bank Do not delay transfusion of fresh frozen plasma (FFP) waiting for laboratory results Transfuse platelets when platelet levels are 50,000-100,000. Utilize Rh negative platelets in Rh negative mothers For massive PPH, use a ratio of PRBC to FFP to platelets 6:4:1. If bleeding continues, consider changing to 4: 4: 1 ratio. RBC to FFP ratio not to exceed 3:2.
Begley, C., Gyte, G., Devane, D., McGuire, W., Weeks, A., & Biesty, L. (2019) Active versus	The purpose of the project is to compare the effects of active versus expectant management of the third stage of labor	Randomized and quasi-randomized controlled trials comparing active versus expectant	Eight studies from Cochrane Pregnancy and Childbirth's Trials Register, Clinicaltrials.gov, and the WHO International Clinical Trials Registry	A random-effects model was used in the analysis. Two review authors independently assessed the studies for inclusion, assessed risk of bias, carried out data extraction and assed	It is uncertain whether active management of labor reduces the risk of maternal PPH. Mothers with a hemoglobin <9 following birth, active management of third stage may

Author/Article	Research Question	Design	Sample (N)	Data Collection (Instruments/Tools)	Findings
expectant management for women in the third stage of labour	on severe PPH and maternal/infant outcomes.	management of the third stage of labor	Platform. Eight studies with a data analysis of 8892 women were analyzed. The studies were all from hospitals, seven in high-income countries and one in a lower income country.	the quality of the evidence using the GRADE tool.	reduce anemia post birth. Active management reduces maternal blood loss at birth and reduces the rate of primary blood loss >500 ml. Active management reduces the need for maternal blood transfusion. Active management of the third stage of labor increases maternal diastolic blood pressure, vomiting, afterpains, and use of analgesics after birth.
Ducloy-Bouthers, A., Jude, B., Duhamel, A., Broisin, F., Hulssouud, C., Keita-Meyer, H., Mandelbrot, L., Tillouche, N., Fontaine, S., Le Goueff, F., Depret-Mosser, S., Vallet, B., Susen, S. (2011) High-dose tranexamic acid reduces blood loss in postpartum	The purpose of the study was the determine whether the administration of high-dose tranexamic acid at the time of diagnosis of PPH could reduce blood loss	Randomized, controlled, multi-center, open-label trial	144 women with PPH and blood loss >800 ml following vaginal delivery Randomly assigned to receive TXA (loading dose 4 g over 1 hour then an infusion over 6 hours) or not. PRBC and colloids could be used according the guidelines	Anonymous data was managed by an independent operator following double data acquisition Results were expressed as means +- standard deviation in cases of normal distribution and as medians and interquartile ranges Normality was tested using the Shapiro-Wilk test Comparisons between groups were performed using the x2 test or Fisher's	Blood loss was significantly lower in the TXA group than in the control group (median blood loss 173 verses 221 ml in the controls group) (p=0.041). In the TXA group, bleeding duration was shorter and progression to severe PPH and PRBC transfusion was less frequent than in controls. Invasive procedures were performed in 4 women in the TXA group vs 7 controls PPH stopped after only

Author/Article	Research Question	Design	Sample (N)	Data Collection (Instruments/Tools)	Findings
hemorrhage				exact test for categorical variables For numerical variables, Student's t-test in cases of normal distribution and the Mann Whitney U test otherwise. Blood loss was measured utilizing an under buttocks drape with a graduated collection pouch with close consideration to not overestimate blood loss due to antiseptic or saline solutions.	uterotonics and PRBC transfusion in 93% of women in the TXA group versus 79% of the controls Mild transient side effects occurred more in the TXA group versus the control group
Era, S., Matsunaga, S., Matsumura, H., Murayama, Y., Takai, Y., Seki, H. (2015) Usefulness of shock indicators for determining the need for blood transfusion after massive obstetric hemorrhage	The purpose of the study was to analyze patients with massive obstetric hemorrhage (MOH) to determine usefulness of the indicators of shock including the shock index (SI) in evaluating the need for blood transfusion	Retrospective study	80 emergency referral patients who had received blood transfusion at the department between January 2009 and July 2011	Computer software JMP version 10.0 was used for statistical analysis. Correlations were evaluated using Spearman's rank correlation coefficient. The strength of the correlation of each shock indicator with the amount of blood transfused was ranked using Spearman's rank correlation coefficient-ρ. The Kruskal–Wallis test was used to compare median values. $P < 0.05$ was considered as a statistically	Although the SI showed significant positive correlation with blood transfusion volume for RBC and FFP in patients with dilutional coagulopathy, a stronger correlation was seen with the fibrinogen level and Japan Society of Obstetrics and Gynecology disseminated intravascular coagulation Score (JSOG DIC). The strongest correlation was seen between RBC transfusion volume and fibrinogen level, and between FFP transfusion

Author/Article	Research Question	Design	Sample (N)	Data Collection (Instruments/Tools)	Findings
				significant difference.	volume and JSOG DIC score followed by fibrinogen level. In multivariate analysis, only fibrinogen level was significantly associated with both RCC and FFP massive transfusion. Many study patients had severe disease as measured by each criterion, and the percentages of indicators with high severity were as follows: estimated blood loss, 47.5%; fibrinogen level, 58.8%; hemoglobin, 40.0%; JSOG DIC score, 46.3%; and SI, 41.2%. The specificity of these indicators as decision factors was not always high, and no difference was found among them.
Hu, J., Yu, Z., Wang, P., Shi, C., Yang, H. (2017) Clinical analysis of postpartum hemorrhage requiring massive transfusions at a tertiary center	The purpose of the study was to define the clinical features, risk factors, causes, and outcomes of massive transfusion due to severe PPH and within the past 10 years.	Retrospective data analysis	136 PPH patients who were >28 weeks of gestation in the OB unit at Peking University First Hospital from Jan 2006 to Feb 2015.	The Pearson's Chi-square and Fisher's exact tests were used to compare the frequency distributions among the categorical variables of the clinical features.	Uterine atony was the main cause of massive transfusion There was a rising trend to placental abnormalities, especially placenta accreta, in the second 5-year group 23 women underwent hysterectomy

Author/Article	Research Question	Design	Sample (N)	Data Collection (Instruments/Tools)	Findings
					Placenta accreta had the highest hysterectomy rate (70%) No maternal deaths were observed.
Lisonkova, S., Mehrabadi, A., Allen, V., Bujold, E., Crane, J., Gratton, R., Ladhani, N., Olatunbosun, O., Joseph, K. (2016) Atonic postpartum hemorrhage: blood loss, risk factors, and third stage management.	Quantify the association between risk factors and atonic postpartum hemorrhage	Case Control Study Multicenter medical chart abstraction study	393 cases of atonic postpartum hemorrhage and 393 controls without postpartum hemorrhage. 766 women in total	Chart review in eight tertiary hospitals in Canada between January 2011 and December 2013. Information about maternal characteristics such as obstetric history, pregnancy, labor, and delivery was abstracted from the charts. Trained medical record abstractors used standardized forms to enter the data into the customized software (Research Electronic Data Capture). Interim analyses were performed to detect discrepant values.	Factors associated with atonic postpartum hemorrhage included cesarean section, nulliparity, vaginal birth after cesarean section, vitamin and analgesic use during pregnancy, preeclampsia, and use of magnesium sulfate were associated with atonic postpartum hemorrhage. Use of oxytocin, artificial rupture of membranes, and forceps delivery increased the odds of atonic postpartum hemorrhage.
Shields, L., Lee, R., Druzin, M., McNultyt, J., Mason, H. (2009) Blood product replacement: Obstetric hemorrhage	To cover new science of massive transfusion findings and protocols. A comprehensive review of blood component replacement therapy in the	Literature review	Covers the new science of mass transfusion 9 massive hemorrhage protocols tailored to obstetrics were evaluated	All of the protocols were developed in consultation with obstetric and hematology experts and analyzed by experts in the field	Majority of protocols recommended six units of PRBC's be prepared and available. Hematocrit should be maintained 21-24% minimum. PRBC should increase hematocrit 3-4% in a 70 kg patient; however, increase may be less due to the volume of distribution. Any patient with

Author/Article	Research Question	Design	Sample (N)	Data Collection (Instruments/Tools)	Findings
	context of significant maternal hemorrhage.				continued bleeding after initial measures have failed (Stage II) should have 2 units of PRBCs released from blood bank. Consider O-negative un-crossmatched blood if type and cross is being competed. Any patient in Stage 3 hemorrhage should have massive transfusion protocol initiated. Using a high ratio of PRBC to FFP (1.5:1 of 1:1) has been shown to significantly improve surgical from hemorrhage Initial request for 4 units of AB-FFP are recommended. Transfuse platelets when platelet level 50,000-100,000. Platelets should be used as a guide. Some protocols suggest higher platelet counts for initiating transfusion and maintaining appropriate levels. Administer Rh-negative platelets to patients who are Rh-negative blood type. If fibrinogen levels <100-125 with ongoing bleeding, fibrinogen should be used in addition to FFP. For transfusion during massive PPH, using a ratio of PRBC to FFP to platelets of 6:4:1 should be used. If

Author/Article	Research Question	Design	Sample (N)	Data Collection (Instruments/Tools)	Findings
					bleeding continues, consideration should be given to increasing the amount of FFP to a ratio of 4:4:1. Repeat labs every 30 minutes until patient stable.
Stephens, B., Sethna, F., & Crispin, P. (2017) Postpartum obstetric red cell transfusion practice: A retrospective study in a tertiary obstetric centre	To determine whether postpartum red cell transfusion practices are consistent with best practice and to identify opportunities for improvement	Retrospective audit of postpartum red cell transfusions conducted at a tertiary level obstetric unit	3235 women who delivered in 2013 at Centenary Hospital for Women and Children, a tertiary level obstetric unit	Parameters collected included maternal characteristics, antenatal laboratory data (haemoglobin (Hb) levels, red cell indices and results of iron studies) and intrapartum events including the length and complications of labour, mode of delivery and estimated blood loss. Blood transfusion details such as location of transfusion, the prescriber and clinical decision maker, timing and the number of red cell units' transfused and subsequent change in Hb were collected.	Anemic women prior to delivery received a postpartum blood transfusion (58.5%) compared with 17.8% of non-anemic women. When these anemic women experienced a PPH, they lost a greater volume of blood than those women without anemia (1252 ± 947 mL vs 1031 ± 548 mL, $P < 0.02$). In the PPH population, both moderate (1000–1499 mL) and severe (>1500 mL) blood loss following delivery was associated with an increased risk of blood transfusion (OR 4.34, CI 2.28–8.26, $P < 0.01$ and OR 16.17, CI 8.58–30.46, $P < 0.01$ respectively). Of all the initial transfusion decisions, 22% were for actively bleeding patients, predominantly made by anesthetists. Decisions to transfuse within 12 hours of delivery were more likely to have an appropriate trigger than later transfusions (OR 9.64 CI 2.73–34.08, $P < 0.01$). 53% of initial transfusions used an appropriate

Author/Article	Research Question	Design	Sample (N)	Data Collection (Instruments/Tools)	Findings
					trigger. The rate of appropriate target Hb did not significantly vary, time of transfusion post-delivery or location. Most transfusions (52%) had a post-transfusion Hb > 90 g/L with 25% of transfusions resulting in a Hb > 100 g/L. 40% of the second transfusions used an appropriate trigger and 50% achieved the appropriate post-transfusion target Hb. Only 14% of initial transfusions were prescribed a single unit transfusion. Specific management of PPH to minimize blood loss was primarily by syntocinon infusion (86.5%), followed by ergometrine (48.5%) and misoprostol (30.6%). Transfer for further management in the operating room occurred 17% of the time. Primary operative management included manual removal of placenta (12.6%), balloon tamponade (4.1%), B-Lynch suture (2.4%) and hysterectomy (1.1%).
The American College of Obstetricians and Gynecologists in collaboration with Shields, L., Goffman, D., & Caughey, A. (2017)	The purpose of the practice bulletin is to discuss the risk factors associated with PPH as well as its evaluation, prevention, and active	Review of literature	A search and consensus of the available literature on managing PPH	Appraisal of the current evidence and information about risk of PPH and the prevention and management of PPH. Medline, Cochrane library, and ACOG's own internal resources and documents were used to	Once as PPH is identified, rapid physical examination should occur to identify the cause. Uterine tonic agents should be the first line treatment for PPH caused by uterine atony.

Author/Article	Research Question	Design	Sample (N)	Data Collection (Instruments/Tools)	Findings
Postpartum hemorrhage	management.			conduct a literature search to locate relevant articles between 2000 and 2017. Studies were reviewed and evaluated for quality using the methods outline by the United States Preventative Services Task Force.	When uterine tonic fails to control PPH, prompt escalation to other interventions and escalation of care and support personnel are indicated. Tranexamic acid should be considered as a treatment for PPH when initial medical therapy fails. Ensure the existence of a multidisciplinary response team and a staged protocol to include guidelines for escalation of care and functioning a massive transfusion protocol. Generally, management should be least invasive methods to more aggressive interventions including hysterectomy. Utilize fixed ratios of blood products if transfusion is required.
Xu, J., Gao, W., & Ju, Y. (2012) Tranexamic acid for the prevention of postpartum hemorrhage after	The purpose of the study was to determine the efficacy of tranexamic acid (TXA) in reducing blood loss in	A randomized, double-blind, case-controlled study	174 primipara mothers undergoing cesarean section 88 of them given 10 mg/kg TXA immediately before	Blood loss was calculated from blood collected and measured during two pertinent periods: (1) placental delivery to the end of cesarean section and (2) end of cesarean section to 2	Blood loss from placental delivery to the end of the cesarean section did not differ between groups. P= 0.17. Blood loss in the period between cesarean section and 2-

Author/Article	Research Question	Design	Sample (N)	Data Collection (Instruments/Tools)	Findings
cesarean section: a double-blind randomization trial	patients after cesarean section.		cesarean section and 86 whom TXA was not given.	hours postpartum.	hour postpartum period was significantly lower p <0.01 in the TXA group 46.6 and 84.7 in the control group. PPH stopped in 65 women in the control group and 81 in the TXA group.

APPENDIX J:

THE UNIVERSITY OF ARIZONA INSTITUTIONAL REVIEW BOARD APPROVAL LETTER

THE UNIVERSITY OF ARIZONA
Research, Discovery & Innovation

Human Subjects Protection Program

1618 E. Helen St.
P.O Box 245137
Tucson, AZ 85724-5137
Tel: (520) 626-6721
http://rgw.arizona.edu/compliance/home

Date:	August 01, 2019
Principal Investigator:	Rylee Apodaca
Protocol Number:	1907849958
Protocol Title:	Development of an Algorithm for Postpartum Hemorrhage
Determination:	Human Subjects Review not Required

Documents Reviewed Concurrently:

HSPP Forms/Correspondence: *Apodaca Determination of Human Research 07 23 19.pdf*

Regulatory Determinations/Comments:

- Not Research as defined by 45 CFR 46.102(l): As presented, the activities described above do not meet the definition of research cited in the regulations issued by U.S. Department of Health and Human Services which state that "Research means a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities. For purposes of this part, the following activities are deemed not to be research."

The project listed above does not require oversight by the University of Arizona.

If the nature of the project changes, submit a new determination form to the Human Subjects Protection Program (HSPP) for reassessment. Changes include addition of research with children, specimen collection, participant observation, prospective collection of data when the study was previously retrospective in nature, and broadening the scope or nature of the study activity. Please contact the HSPP to consult on whether the proposed changes need further review.

The University of Arizona maintains a Federalwide Assurance with the Office for Human Research Protections (FWA #00004218).

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