UNIVERSITY OF THE WESTERN CAPE

FACULTY OF COMMUNITY AND HEALTH SCIENCES

RESEARCH REPORT

Title: A systematic review of best practices in the acute management of postpartum haemorrhage in primary maternity care settings

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ABSTRACT

Background: Postpartum haemorrhage (PPH) is one of the most preventable causes of maternal death, yet it still ranks as one of the main conditions responsible for maternal mortality. PPH occurs at a stage when a mother is the least likely to receive care, and mothers often do not survive to be referred to a more specialised level of care. This is compounded by the patient not being able to warn healthcare providers timeously about their condition and healthcare providers lacking training resulting in a lack of accuracy in diagnosis, lack of resources, and differing methods of treatment. Due to the lack of consensus in available treatment options, and the paucity of research aimed at clinical interventions for midwives at the primary care level, this research report aimed to investigate the evidence in order to establish the best practices and evidence for clinical interventions to manage postpartum haemorrhage for midwives at the primary care level. This is to ensure that the continuing education for midwives in practice is based on evidence to keep their skill set current and expose practitioners to the latest evidence based care.

Aim: To systematically review all available published evidence for the acute non-pharmaceutical, non-surgical, management of PPH for use by midwives at a primary maternity care setting.

Method: A systematic review of available published evidence was conducted using standard systematic review methodology. A detailed search strategy with specific inclusion and exclusion criteria based on the PI[C]O was conducted. Literature searches revealed 150 systematic reviews on the topic, after which a decision was made to perform a review of the systematic reviews. Sixteen studies were included for full-text analysis and quality

assessment. All included articles were subjected to the AMSTAR-2 quality assessment tool. Twelve were excluded, due to being of low or critically low quality. Four reviews were included in the analysis. Due to low homogeneity, the results were presented in table format and no quantitative synthesis was concluded.

Findings: Although many systematic reviews for the management of postpartum haemorrhage exist, they mainly describe the evidence for surgical and pharmaceutical interventions which fit within the scope of medical practitioners. Interventions for midwives at the primary care level include nipple stimulation and uterine massage which were non-significant. Non-pneumatic anti-shock garments were significant to reduce maternal mortality. Self-administered oxytocin was not significant.

Recommendations: It is recommended that further high-quality research is done to establish accurate methods to diagnose and treat postpartum haemorrhage for midwives, at the primary care level.

DECLARATION

I declare that, "A systematic review of best practices in the acute management of postpartum haemorrhage in primary maternity care settings", is my own work, and has not been submitted for any degree or examination in any other university, and that all the sources I have used or quoted have been indicated and acknowledged by complete references.

FULL NAME: Haaritha Binkowski (Boltman)

SIGNATURE:

DATE: December 2018

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SURAH AT TALAQ [65:3]

أنت لا تختار عائلتك. إنهم هدية من الله لك. كما أنت بالنسبة لهم.

In the memory of my father AlHaj Muhammad Hashim, you instilled a love of learning in me, which will be with me until I die. Truly, those have knowledge, realise how little they know. I would not be here without you.

In the memory of my dearly departed brother AlHaj Humayd bin Muhammad Hashim, who left us suddenly in February 2017. You are missed every day, with every word I type. This is for you.

With my love, to my mother, who has borne and birthed me – your sacrifices are deeply acknowledged in my soul. I could not do this without you. I cannot thank you, but I will live my gratitude in every action to and for you, in this life and the next. You are my life.

To my husband, Lev Sergeivich. Люблю тебя всем сердцем, всей душою. Для тебя, ради тебя и за тебя жизнь моя! And my beloved baby daughter, you are the light of my eyes, the joy of my life. I hope you can see that you can do anything – I hope I am an example to you.

To my brother, Alhufaath Alhaj Abdul Haadee bin Muhammad Hashim, the love you create with your hands and the protection you bestow on us with your presence is priceless.

To the rest of my friends and family – I love you all, and thank you for being part of my journey as an academic and as a mother.

And finally, to Professor Jennifer Chipps. Thank you would be premature – we have a long road to walk, you and I. I hope I still learn much more from you, but for this beginning step, I thank you.

LIST OF ABBREVIATIONS

PPH – Postpartum haemorrhage

C/S- caesarean section

NVD –normal vertex delivery

RCT- Randomised controlled Trial

SR- Systematic Review

ICU: Intensive Care Unit

NS: Not significant

S: Significant

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CHAPTER ONE

ORIENTATION TO THE STUDY

1.1. Introduction

The aim of this chapter is to set the foundation for the thesis. This chapter includes an overview of the literature, purpose, aims and background to the study and a summary of the research methodology. This is done in partial fulfilment of a structured Masters in Nursing (Nursing Education) by manuscript format.

1.2. Background to the study

Postpartum haemorrhage (PPH) is one of the most preventable causes of maternal death, yet it still ranks as one of the main conditions responsible for maternal mortality (Ajenifuja et al., 2010). It is one of the major causes of maternal death in South Africa, and this trend is reflected worldwide in varying degrees across both developing and developed countries (Ajenifuja, Adepiti, & Oguniyi, 2010; Saving Mothers Report, 2015). PPH can be defined as more that 500ml of blood lost from the vagina within 24 hours of delivery (WHO, 2012). Severe PPH is defined as a blood loss of more than 1000ml in the same time period (WHO, 2012). It has serious adverse effects on maternal health.

In 2015, the 2011 -2013 Saving Mothers Report on maternal deaths in South Africa reported that deaths due to obstetric haemorrhage was one of the top three causes of maternal mortality in that tri-ennium. This is unchanged in the 2017 Saving Mothers Report, which reports on the years 2014-2016 (Saving Mothers Report, 2017). It was reported that 30.4% of all maternal deaths during this period were due to obstetric haemorrhage, and it was preventable in 89% of all cases (Saving Mothers Report, 2015; Saving Mothers Report,

2017). This report also highlighted that poor clinical assessment was amongst the top health provider related errors, and a contributing factor to the issue (Saving Mothers Report, 2015; Saving Mothers Report, 2017).

In South Africa, primary maternity care in the public sector is administered at midwife obstetric units, by midwives, in settings where there are no operating theatres and referral is through emergency services to a secondary or tertiary level of care. It should be viewed with concern that the South African Confidential Enquiries in Maternal Deaths Report (2012) states that the majority of deaths due to PPH (94.2%) occurred at public hospitals, and that about a third of (30.7%) PPH related deaths were due to inadequately trained doctors or nurses, especially at the primary level of care (Saving Mothers Report, 2012). In addition to poorly trained personnel, the scope of practice of midwives is limited. Unless a registered midwife has a prescribing license, they may not administer any medications, or perform any surgeries, with the exception of oxytocin: "*7.3 A registered midwife shall, in the case of postpartum haemorrhage when a medical practitioner is not available or pending the arrival of the medical practitioner, administer not more than 10 units of oxytocin at a time by intramuscular injection, but the administration may be repeated at intervals if and when necessary*"(South African Nursing Council: R 2488, 1990). Midwives may also not perform any surgical management of PPH, and the facilities at which they practice in the low-resource, primary health and maternity care settings, often do not have operating theatres attached to them.

Apart from death, PPH can cause adult respiratory distress syndrome, coagulation disorders, shock, hysterectomy and subsequent loss of fertility (ACOG, 2017). As bleeding after

delivery is expected, women often do not realise the seriousness of their condition until it is too late and they do not survive to be referred to another level of care (Nangalia & Thaddeus, 2004; Ogunjimi, Ibe & Ikorok, 2012; ACOG, 2017). In addition to a patient not being able to warn healthcare providers timeously about their condition and healthcare providers lacking training, the situation is compounded by a lack of accuracy in diagnosis, lack of resources, and differing methods of treatment (Lombaard & Pattinson, 2006; Ogunjimi, Ibe & Ikorok, 2012).

1.3. Problem statement

PPH has been shown to be the major cause of maternal mortality in South Africa (Saving Mothers Report, 2012; Saving Mothers Report, 2015; Saving Mothers Report, 2017). PPH occurs at a stage when a mother is least likely to receive care. They often do not survive to be referred to a more specialised level of care or the seriousness of their condition is not identified until they have developed clinical syndromes, resulting in serious morbidity, and in most cases, death (Nangalia & Thaddeus, 2004; ACOG, 2017).

Research has shown that the diagnosis and management of PPH is complex, with the primary challenge being with the visual assessment of blood loss (Rath, 2011). Most of the primary maternity care in South Africa is provided by midwives, and the overall quality of care during the management of PPH is poor (Boltman-Binkowski, 2015). Midwives also have a scope of practice which does not enable them to administer or prescribe medications or perform any surgeries. These midwives are required to manage this complex clinical syndrome using non-pharmaceutical and non-surgical methods.

The primary aim of this study was to systematically review and synthesise current evidence on the acute non-surgical, non-pharmaceutical management of PPH in order to make recommendations on evidence based management of PPH by midwives at the primary maternity care level.

1.4. Significance of the study

This study may provide evidence-based non pharmaceutical, non-surgical clinical strategies for midwives in practice, to use when they are required to manage PPH. In addition, it may have an impact on the education of midwives, of new, clinically effective ways to manage PPH – both at under and post-graduate level. The methodology used in the study may inform nurses and midwives to perform similar studies in their own areas of practice and to base their clinical practice on evidence. The results from the study may allow policy-makers to review the current midwifery scope of practice to include strategies which are evidence-based. The study may also reveal gaps and limitations in evidence in order to provide further areas for research.

1.5. Aim

To systematically review and synthesise all current best practice evidence for the acute non-pharmaceutical, non-surgical, management of PPH in order to make recommendations on non-surgical, non-pharmaceutical management of PPH by midwives at the primary health care level.

1.6. Definition of Terms

Table: Definition of Terms

Term	Definition	Operational Definition (In this study)
Best Practice	A set of systematically developed and researched statements which inform and shape clinical practice (Nelson, 2014)	Best practices refer to clinical practices which have been informed by systematic evaluated research evidence.
High resources setting	High resource setting can be defined as an area where there is no financial hindrance to accessing healthcare (facilities, infrastructure, medications, trained personnel or equipment), either on a personal or societal level. It is the converse of the definition of a low-resource setting (Moahi, Bwalya & Sebina, 2017)	A setting where there are no financial barriers on a societal level to accessing essential maternity care.
Low resource setting	A healthcare delivery area where a lack of finances lead to limited access to facilities, medications, trained personnel, infrastructure and equipment. This lack of finances may be individual or societal (Moahi, Bwalya & Sebina, 2017)	Limited access to healthcare due to societal lack of finances – leading to limited access to resources essential to deliver and receive essential maternity care.
Postpartum haemorrhage	According to the WHO, PPH is defined as a loss of more than 500ml of blood per vagina, within 24 hours of delivery. Severe PPH is defined as 1 litre or more of blood loss within 24 hours of delivery (WHO, 2012)	General definition of PPH will be applied, regardless of mode of delivery
Primary maternity care settings	Primary health care is defined as a set of principles underlying the health care system which ensures that basic healthcare is accessible by all members of the population (WHO World Health Report, 2008)	Clinical settings where obstetric healthcare is delivered in the community, within a primary health care system

1.7. Summary of methodology

Standard systematic review methodology was applied ensure the scientific quality of the review using the guidelines set out in The Preferred Reporting Items for Systematic Reviews (PRISMA) checklist (see Appendix D). The stages in completing the review were as follows:

- Stage one- systematic search of the literature:

A comprehensive search of fifteen databases was done in August 2017, to ensure the inclusion of all relevant articles (details of databases and search can be found in Chapter Three). This search revealed quite a number of systematic reviews on the management of postpartum haemorrhage. Following this, the search terms were refined and restricted to systematic reviews. Key terms for the search included synonyms of (*postpartum haemorrhage* Or *bleeding after delivery)* And (*management* Or *assessment* Or *medication* Or

pharmaceuticals Or *diagnosis* Or *prediction test)* And (*Systematic Review* Or *Randomized controlled trial, quasi-experimental study* Or *relevant evaluation study)* AND *>2007*. In addition, reference lists of the articles were further searched for literature.

- Stage two – abstract screening:

In order to reach a complete list of abstracts, the Endnote 7 reference manager software was used to identify and delete duplicates and irrelevant data from the search. Titles were then examined by the student and supervisor for inclusion, based on specified inclusion and exclusion criteria (Table 1.). The student and supervisor then screened the abstracts for selection of systemartic reviews to be included in the review based on the PI[C]OS as specified in Table 1. Any disagreements for inclusion between the student and supervisor would be referred to a third reviewer. Full-text articles were obtained from the abstracts and further examined against the PI[C]OS.

- Stage Three - Quality assessment:

All included full-text articles were subjected to a quality assessment. The latest version of the "A MeaSurement Tool to Assess systematic Reviews" (AMSTAR), the AMSTAR-2 tool was used to measure the quality of included reviews. The AMSTAR-2 tool had 16 items, but no overall score is allocated, according to the user guide for the AMSTAR-2 tool (Shea, et al; 2017). Reviews were excluded from the analysis if they were identified as having low or critically low levels of quality.

- Stage Four and Five – Data extraction/ Data analysis:

Data were extracted and entered into an excel sheet for analysis. Data were analysed and presented in table format and no quantitative synthesis was conducted.

1.8. Structure of thesis

The thesis will be presented in five chapters. Chapter One contains the background, problem statement, aim and significance of the study. Chapter Two presents a detailed literature review focussing on the available management guidelines as well as the current pharmaceutical and surgical management of PPH. Chapter Three explains the methodology, as well as quality assessment strategies used in this study. In Chapter Four, the results and discussion is presented in manuscript format. Chapter Five outlines the limitations, discussions and recommendations for the study.

1.9. Conclusion

This chapter has presented an outline of the background and problem statement in this study. It has also provided an understanding of the terms which are used throughout the study, as well as the possible significance the study may have.

CHAPTER TWO

LITERATURE REVIEW

2.1. Introduction

As the study is a detailed systematic review of the literature, this chapter provides a summary of issues related to the management of PPH. There are three parts to this literature review: the first provides a context and background to the review, the second focuses on current pharmaceutical and surgical management strategies for PPH and the third examined all the available management guidelines.

2.2. Literature Review Methodology

This literature review has been conducted using a systematic search process. Each of the sections of this literature review has their own methodology, which will be summarised as follows:

- Context and background:

Focused searches were done through the World Health Organization online resources, Google Scholar, Cochrane, Science Direct and Epistomonikos. Search terms which were used were according to what was required for the background, and exclusion criteria did not apply.

- Pharmaceutical and surgical management:

Studies were purposefully selected on the basis of whether they were systematic reviews on the pharmaceutical management or an article on the surgical management of postpartum haemorrhage. Non-english studies were excluded. Outcomes, participants and comparisons

were not focused on, as it was aimed to describe the interventions in this section of the literature review.

- Summary of all evidence-based guidelines:

All the the requirements for a defined PICO could not be met, as this was not a systematic review, but the principles of the search process were applied in order for this section of the summary review to be methodologically sound. The potential for included studies based on conventional criteria would be immense so purposive sampling was applied to obtain clinical guidelines used internationally in the management of postpartum haemorrhage (Schreiber & Stern 1997; Dixon-Woods, Cavers, Agarwal, et al. 2006). Studies were purposefully selected for review on the basis of whether they were an English language, evidence- based clinical guideline on the management of postpartum haemorrhage currently used in clinical practice. Clinical guidelines in their nature are usually qualitative, hence motivating for qualitative strategies being applied in this review. Comparisons and outcome measures were not considered, as guidelines usually do not contain these aspects.

An extensive electronic search was carried out to ensure that all relevant literature was included in the review. The initial search was done on the major electronic biomedical databases like PubMed, EBSCO, Medline, Google Scholar, Science Direct, Academic Search Premier, and the Cochrane Controlled Trials register. The bibliographies of articles were consulted to ensure that all the relevant trials were included in the review. Key terms for the search included evidence-based guidelines, postpartum haemorrhage, bleeding after delivery, management, and clinical protocol. Key words and terms were used in isolation but also in combination with each other. Full articles were obtained online when available or

ordered through the library facilities of the University of the Western Cape. The study selection was undertaken independently by the researcher and the guidelines were included only if they met the inclusion criteria. Only seven out of 15 articles detailing clinical guidelines met the eligible inclusion criteria. The quality of guidelines were not assessed for inclusion, as it was not the purpose of the summary to follow the full systematic review process, rather to present a summary of the current practice in a systematic manner.

After the data were extracted from the studies and entered into the data collection sheet, common themes were identified, and the results were tabulated, in order to present a consensus around the current management options for midwives. Consensus in this summary was noted as four or more out of seven studies agreeing on a specific outcome (over 50%).

2.3. Context and background to the study

2.3.1. Definition of PPH

PPH is defined by the World Health Organization (WHO) as more than 500 ml of blood loss per vagina during the first 24 hours after birth (WHO, 2009; Rath, 2011; Kerr & Weeks, 2016). Severe PPH is defined as more than 1000 ml of blood loss per vagina after birth (Rath, 2011; Kerr & Weeks, 2016). There is a distinct difference in primary and secondary PPH, with primary occurring in the first 24 hours after birth, and secondary PPH occurring from 24 hours to six weeks after delivery (Kerr & Weeks, 2016). Due to issues with measurement of blood loss, the definitions of PPH have recently broadened to include clinical signs and symptoms of shock, even though the blood loss is estimated at less than the 500ml (Rath, 2011; Kerr & Weeks, 2016). The mode of birth is also considered when making a diagnosis of

PPH, as caesarean section births are associated with a much higher blood loss than vaginal births (Rath, 2011). The intent with this study is to focus on primary PPH (first 24 hours after birth), as primary care midwives primarily see birthing mothers for their labour and up to six hours after birth (Boltman-Binkowski, 2015).

2.3.2. PPH and maternal mortality

Haemorrhage is the highest cause of maternal death worldwide, with PPH causing 480 000 reported maternal deaths internationally between 2003 and 2009 (Say, et al; 2014). The majority (479 000) of these deaths occur in developing regions with just under half of deaths caused by PPH in Sub-Saharan Africa (200 000 deaths) (Say, et al; 2014; Saving Mothers Report, 2017).

In South Africa, PPH has consistently ranked as one of the top five causes of reported maternal mortality (Saving Mothers Report, 2012; Saving Mothers Report, 2015; Saving Mothers Report, 2017). It is important to note that the Enquiry into Maternal Death Reports (Saving Mothers Reports) only obtains data from health institutions across South Africa, and does not report on maternal deaths outside of institutions. The 7th Enquiry into Maternal Death Report has reported that deaths due to obstetric haemorrhage are at 16.9% of the total maternal deaths in South Africa, as compared the 15.8% in the previous report (Saving Mothers Report, 2017). The 6th Enquiry into Maternal Death Report findings state that in South Africa, deaths due obstetric haemorrhage have increased 24.7% from an institutional maternal mortality rate of 19.51 per 100000 live births in 2002-2004 to an institutional maternal mortality rate of 24.32 per 100000 live births in 2011-2013 (Saving Mothers

Report, 2015). This is one of the only causes of maternal deaths which have risen in the documented period.

2.3.3. Causes and risk factors for PPH

Causes of PPH are multiple, as this is a complex clinical syndrome. The most obvious cause is birth injury to the genital tract, but the most significant cause is uterine atony (Ononge, Mirembe, Wandabwa & Campbell, 2016). There are also other causal factors, like coagulation failure of the haematological system, which occurs in the end stage of untreated hypertensive disorders in pregnancy (Hemolysis, Elevated Liver enzymes, Low platelet count Syndrome, or HELLP syndrome) (Ononge, Mirembe, Wandabwa & Campbell, 2016).

Large, multi-country studies on the risk factors for PPH have revealed that large disparities exist between the incidences of PPH in low and high income areas, despite a high rate of administration of oxytocic medication in both settings (Sheldon, et al., 2014). Specific risk factors for this condition, apart from low income, are associated with age, parity, gestational age, induction of labour, and mode of birth - caesarean section (Sheldon,et al., 2014). In addition, women with a history of PPH were more likely to experience PPH in a subsequent pregnancy (Oberg, Hernandez-Diaz, Palmsten, Almqvist & Bateman, 2014). Overall, a history of PPH, caesarean section birth, non-administration of oxytocic medication, low income geographic locations, increased parity, primigravidity and multiple pregnancy have been shown to be associated with an increased risk of PPH (Ononge, Mirembe, Wandabwa & Campbell, 2016).

2.3.4. Challenges with Diagnosis and Management of PPH

In South Africa, a postpartum mother is discharged from maternity care services six hours after a normal vaginal delivery if they are deemed to be in a stable condition, and that, amongst others, no active vaginal bleeding is occurring (National Department of Health, 2015). However, PPH may occur any time within the first 24 hours after delivery (Kerr & Weeks, 2016). Furthermore, women have come to see vaginal bleeding after delivery as normal and may not have the tools to distinguish initially when the bleeding is a cause for concern (Wioski, 2015). They may only become aware of seriousness of the condition when they are already in clinical shock, and are least likely to receive care (Fawcus & Moodley, 2011; Nangalia & Thaddeus, 2004). These patients often do not survive their first contact with the primary maternity care clinic, and do not make it to be referred to a secondary level of care (Fawcus & Moodley, 2011; Saving Mothers Report, 2017).

At the health care facility during the first six hours after delivery, the mother is often left with minimal medical assistance, as the floor plan of the primary care midwife obstetric units dictate that postpartum mothers are left at the back of the facility while the midwives on duty are caring for women in labour at a different area (Boltman-Binkowski, 2015). PPH then occurs silently and with no warning to the healthcare providers (Mathai, Gulmezoglu & Hill, 2007).

The diagnosis of PPH should be based on the visual assessment of this blood loss after delivery, however studies indicate that visual assessment of blood loss is inaccurate when used as the only diagnostic tool (Larsson et al., 2006; Natrella et al., 2017). There are other methods of diagnosing PPH which are more expensive and time-consuming and may not be

suitable for use in a primary care facility, for example testing the haematocrit levels or adding measurement bags to bedding (Atukunda, et al., 2016).

To compound the issue of accurate diagnostic techniques, there is a lack of appropriately trained healthcare providers to manage PPH with the National Department of Health (NDOH), reporting that 27% of deaths related to obstetric haemorrhage were due to the lack of adequately trained personnel (Saving Mothers Report, 2015). It was reported that the overall quality of care in the management of PPH by midwives was poor, as basic resuscitation measures were only instituted in half of the cases measured, and most midwives realised that they were not competent to manage PPH independently (Rousseau, et al., 2016). This is concerning as most of the care at primary facilities are led by midwives.

2.3.5. South African Midwifery Scope of Practice

South African midwives have a limited scope of practice. Unless a registered midwife has a prescribing license, they may not administer any medications, with the exception of oxytocin:

"7.3 *A registered midwife shall, in the case of postpartum haemorrhage when a medical practitioner is not available or pending the arrival of the medical practitioner, administer not more than 10 units of oxytocin at a time by intramuscular injection, but the administration may be repeated at intervals if and when necessary*"(South African Nursing Council: R 2488, 1990). In addition, primary care midwives in South Africa do not perform any surgical interventions, and most primary care facilities do not have an operating theatre attached the facility (Boltman-Binkowski, 2015).

2.4. Specific Management of Postpartum Haemorrhage

Management options for postpartum haemorrhage are varied, and an overall review of the literature revealed a number of systematic reviews on the topic. They could be grouped under pharmaceutical, surgical, and non-pharmaceutical interventions. An overview of the surgical and pharmaceutical interventions will be presented, as it was excluded from the review – due to the previously explained, limited scope of practice of midwives in South Africa. As the non-pharmaceutical interventions are included in the systematic review, they will be found in Chapter Three and Four in this study.

2.4.1 Pharmaceutical interventions

Twenty nine systematic reviews on pharmaceutical interventions were found through the literature search. The reviews found on pharmaceutical interventions are classified as follows:

Table 1: Pharmaceutical interventions not included in analysis by number

Management intervention	Number of reviews found
Carbetocin	3
Misoprostol	14
Tranexamic Acid	12

Each of the pharmaceutical interventions will be explained:

- Carbetocin

This drug composition is a human oxytocin synthetic analogue, with a mechanism of action similar to oxytocin and is used in the treatment of PPH following caesarean section. It has a longer half-life than oxytocin, and therefore a prolonged pharmaceutical effect (Hasan, 2018). It can be administered intramuscularly or intravenously (Hasan, 2018). Dosages from

20 – 100 µg have been found to be effective (Mannaerts, Van der Veeken, Coppejans & Jacquemyn, 2018).

In the three reviews found, findings revealed that carbetocin may be a useful alternative to oxytocin, although further studies are warranted. Jin et al (2016) reported a reduced need for additional uterotonics when carbetocin was added to the standard postpartum treatment. Although nausea, vomiting and arterial hypotension were found to be adverse effects of oxytocin administration, carbetocin would have been thought to have similar effects as an analogue. A recent, albeit small, randomised controlled trial reported a possible (but not clinically significant) incidence of lower nausea was found with carbetocin (Mannaerts, Van der Veeken, Coppejans & Jacquemyn, 2018). The complete lists of reviews on the use of carbetocin are included in Appendix A at the end of the report.

- Misoprostol/Prostaglandins

Misoprostol is a synthetic prostaglandin, which requires individual mention. It was initially used in the treatment of ulcers, due to its action on the smooth muscle. It was then found that it has excellent properties to contract the uterus, and is still used in early terminations of pregnancy (under 7 weeks gestation). It is also used as an induction agent for post-dates pregnancy, and recently has successfully been used in the treatment of PPH. It is available in tablet form, in 200 – 400 micrograms per tablet. Dosages of 600 micrograms via rectum were shown to be effective in the treatment of PPH (Hofmeyr, Gülmezoglu, Novikova & Lawrie, 2013). The reviews show a favourable indication that this drug, because it is not heat sensitive and does not require knowledge of injection to administer, may be of use in primary maternity settings (Tan, et al., 2016) Although this drug has the potential to be used

in primary maternity care facilities, it is not within the midwifery scope of practice to dispense these drugs at the time of writing this study. It has been reported that use of misoprostol has been associated with fevers due to the effect of the prostaglandins, although they did not lead to hospitalisation (Durocher, Bynum, León, Barrera & Winikoff, 2010). The complete list of reviews on the use of misoprostol are included in appendix A at the end of the report.

- Tranexamic Acid

Tranexamic acid acts on the physiological mechanism of bleeding by utilising plasmin to impede the process of the enzymatic breaking down of fibrinogen and fibrin. Tranexamic acid reduces mortality rates in women with PPH, regardless of mode of birth, with no significant adverse effects (Shakur, et al., 2017). There have been no significant adverse effects for the action of tranexamic acid on bleeding (Shakur, et al., 2017). The complete list of reviews on the use of tranexamic acid are included in appendix A at the end of the report.

2.4.2 Surgical Interventions

The literature search revealed thirty two articles which either had management options related to the pre and post caesarean care, or specific management interventions. The list of articles was included in Appendix B at the end of the study.

The articles found on surgical interventions can be categorised as follows:

Table 2: Number of articles with surgical interventions

Management intervention	Number of articles found
Uterine compression sutures	3
Hysterectomy	4
Pelvic or uterine artery embolisation	10
Outcomes of surgical management of PPH	6
Caesarean Section	7
Anaesthetic management of PPH	2

Articles on the outcomes of the surgical management of PPH did not cover specific surgical techniques but looked at the fertility and menstrual outcomes of patients following surgery for management of PPH. Articles grouped under caesarean section examined various factors: general surgical management, intraoperative cell salvage, as well as the risk of emergency peripartum hysterectomy. Anaesthetic management was included in the surgical grouping, but did include actual surgical interventions for the management of PPH. Each of the actual surgical management interventions (uterine compression sutures, hysterectomy and uterine artery embolization) will be explained, as part of this section of the literature review.

- Uterine compression sutures

In 1997, the use of uterine compression sutures was introduced by B-Lynch, and was further refined by medical practitioners (Matsubara, Yano, Ohkuchi, Kuwata, Usui & Suzuki, 2013). This practice involves accessing the uterus surgically and inserting a suture in various ways in order to 'tighten' the uterus, to achieve homeostasis (Matsubara et al., 2013). An incision is usually made in the lower uterine segment and a suture is passed through the anterior wall of the lower segment, looped around the fundus of the uterus and inserted in the posterior wall of lower segment again. This forms a shape which looks like braces, used to hold up

pants (Matsubara et al., 2013). It is also the reason this is known as a 'brace' suture (Matsubara et al., 2013). Advantages of this method are that the uterus remains intact in order to maintain fertility after the haemorrhage. Disadvantages of this technique are that the uterus must be accessed surgically, through an abdominal incision (Matsubara et al., 2013), but it has proven to be effective in treating postpartum haemorrhage, especially in cases of uterine atony (Matsubara et al., 2013).

- Hysterectomy

Hysterectomy involves the removal of the uterus, surgically, usually through a lower uterine segment incision (de la Cruz et al., 2015). The removal of the ovaries may or may not happen simultaneously, depending on the surgeon (de la Cruz et al., 2015). A hysterectomy ensures that the area of bleeding is completely removed from the mother, and if adequate fluid resuscitation is performed – is a lifesaving procedure (Fawkus and Moodley, 2011). The use of hysterectomy as a management intervention for postpartum haemorrhage is more than likely a last resort to save the mother's life, and instituted when all other measure have failed – due to complete failure of fertility after the procedure (de la Cruz et al., 2015). The primary disadvantage is obviously complete loss of fertility, and hormonal changes which may result from the removal of the ovaries (de la Cruz et al., 2015).

- Uterine artery embolization

This procedure is usually performed by a radiologist who specialises in invasive procedures using contrast mediums – an interventional radiologist (Aoki et al., 2018). The radiologist uses a catheter to insert micro-particles into the uterine vessels, to occlude the blood supply to the uterine body (Aoki et al., 2018). This is done through the femoral or radial artery, and

requires the use of special equipment like an ultrasound as well as specialised personnel (Aoki et al., 2018). The blood vessels absorb the blockage within 4-6 weeks and blood flow to the uterine body is confirmed by Doppler testing (Aoki et al., 2018). It is a uterine- sparing technique, but also may be prone to affecting fertilisation if the incorrect vessels are blocked, or have no effect on the haemorrhage (Aoki et al., 2018). Severe morbidity as a result of uterine necrosis has also been reported with the use of this technique (Pirard et al., 2002; Poujade, 2013)

2.5. Available Guidelines on PPH: a summary review

This section of the literature review will provide a summary of available guidelines, which looks at the management of PPH. This will illustrate a consensus of the management options available, and also provide an insight to the review.

2.5.1 Consensus areas between guidelines

- Identifying risk factors and etiology

Early identification of risk factors enables high-risk mothers to be referred to a higher level of care and causal factors for PPH enable the midwife to proceed in managing PPH accurately. Only two out of six guidelines documented the anatomy and physiology of the uterus. Five out of six presented both the primary and secondary causes of postpartum haemorrhage, while four also included the risk factors of this condition. One guideline did not mention either causes or risk factors. There is a consensus across guidelines that both primary and secondary causes of postpartum haemorrhage, as well as risk factors, are an important step in the management of postpartum haemorrhage (Table 3).

Table 3: Results – guidelines stating causes and risk factors

	States Anatomy and Physiology of the Uterus	States Primary Causes of PPH	States Secondary Causes of PPH	States Risk Factors
ACOG Practice Bulletin, 2006 (United States)	No	Yes	Yes	Yes
Saving Mothers: Essential Steps in the Management of Common Conditions associated with Maternal Mortality, 2007 (South Africa)	No	Yes	Yes	No
Education Material for teachers of Midwifery, 2008 (World Health Organization)	Yes	Yes	Yes	Yes
National Women's Health Clinical Guideline, 2009 (New Zealand)	No	No	No	No
Monograph on the Prevention of Post Partum Haemorrhage, 2010 (South Africa)	No	Yes	Yes	Yes
FIGO Guidelines, 2012 (FIGO Safe Motherhood and Newborn Health Committee – International)	Yes	Yes	Yes	Yes

- Criteria for diagnosis

Diagnostic criteria are the basis of clinical decision-making. Six of the seven guidelines defined postpartum haemorrhage as blood loss of over 500ml. One did not include a definition of PPH. Three guidelines admitted that there are difficulties with visual estimation of blood loss, but only one (separately from the ones who mentioned difficulty) provided a guide to the estimation of blood loss. Two guidelines also referred to the measurement of decrease in haematocrit levels (Table 4). Six guidelines differentiated between primary and secondary PPH, while only four mentioned vaginal bleeding after birth compared to Caesarean section (Table 4).

Table 3: Criteria for diagnosis

	Blood loss over 500ml	Decrease in haematocrit	Visual Estimation of blood loss	Differentiates between primary and secondary PPH	Differentiates between bleeding after vaginal birth and Caesarean section
ACOG Practice Bulletin, 2006 (United States)	Yes	Yes	Yes	Yes	No
Mousa & Alfirevic, 2007 (Cochrane Review)	Yes	No	Yes	Yes	Yes
Saving Mothers: Essential Steps in the Management of Common Conditions associated with Maternal Mortality, 2007 (South Africa)	No	No	Yes	No	No
Education Material for teachers of Midwifery, 2008 (World Health Organization)	Yes	No	Provides recommendation on how to accurately estimate blood loss	Yes	Yes
National Women's Health Clinical Guideline, 2009 (New Zealand)	Yes	No	Yes	Yes	No
Monograph on the Prevention of Post Partum Haemorrhage, 2010 (South Africa)	Yes	No	States inaccuracy in visual estimation	Yes	Yes
FIGO Guidelines, 2012 (FIGO Safe Motherhood and Newborn Health Committee – International)	Yes	No	States inaccuracy in visual estimation	Yes	Yes
Score (number of guidelines agreed)	6/7	1/7	4/7	6/7	4/7

- Initial evaluation

There was a general consensus between the guidelines in the in the initial assessment of a patient who has PPH. These steps could be performed by a midwife at the primary level of care. All the guidelines agree that visual assessment of the lower genital tract should be performed (Table 5). Four guidelines agree that a full assessment of the condition should be

made, including vital signs, as well as obtaining a blood sample for cross matching in case of blood transfusion.

Aspects of management which, in addition to the above, were only mentioned in single guidelines were: administration of oxygen; pueperial sepsis; an ultrasound for retained products of conception; and also a clot observation test.

Table 4: Initial evaluation and further diagnostic steps

	Initial assessment	Visual assessment of lower genital tract	Further diagnostic steps
ACOG Practice Bulletin, 2006 (United States)	-	Yes	Ultrasonography for retained placental products, clot observation test
Mousa & Alfirevic, 2007 (Cochrane Review)	-	Yes	-
Saving Mothers: Essential Steps in the Management of Common Conditions associated with Maternal Mortality, 2007 (South Africa)	-	Yes	Suturing, draw blood for crossmatch and fresh frozen plasma
Education Material for teachers of Midwifery, 2008 (World Health Organization)	Full assessment of the condition including vital signs	Yes	Draw blood for crossmatch
National Women's Health Clinical Guideline, 2009 (New Zealand)	Full assessment of the condition including vital signs	Yes	Draw blood for crossmatch. Only guideline to administer oxygen
Monograph on the Prevention of Post Partum Haemorrhage, 2010 (South Africa)	Full assessment of the condition including vital signs	Yes	Draw blood for crossmatch
FIGO Guidelines, 2012 (FIGO Safe Motherhood and Newborn Health Committee – International)	Full assessment of the condition including vital signs	Yes	Draw blood for crossmatch
Score (number of guidelines agreed)	4/7	7/7	Draw blood for crossmatch – 5/7

- Initial management steps

All the initial management steps documented in the guidelines do not require expensive equipment, but do require some basic knowledge. Midwives at primary care level would easily be able to carry out these steps. Six out of seven guidelines agreed that emptying the

bladder was one of the first steps to managing PPH (Table 6). Evaluation of uterine tone was found to be important (6 out of 7 guidelines), while fundal massage was only found in five of seven guidelines.

Table 5 : Initial management steps

	Emptying of the bladder	Evaluation of uterine tone	Fundal massage
ACOG Practice Bulletin, 2006 (United States)	Yes	Yes	No
Mousa & Alfirevic, 2007 (Cochrane Review)	No	No	No
Saving Mothers: Essential Steps in the Management of Common Conditions associated with Maternal Mortality, 2007 (South Africa)	Yes	Yes	Yes
Education Material for teachers of Midwifery, 2008 (World Health Organization)	Yes	Yes	Yes
National Women's Health Clinical Guideline, 2009 (New Zealand)	Yes	Yes	Yes
Monograph on the Prevention of Post Partum Haemorrhage, 2010 (South Africa)	Yes	Yes	Yes
FIGO Guidelines, 2012 (FIGO Safe Motherhood and Newborn Health Committee – International)	Yes	Yes	Yes
Score (number of guidelines agreed)	6/7 agreed	6/7	5/7

- Pharmaceutical Management

Pharmaceutical management of PPH concentrates on uterotonic pharmaceutical agents. They can be administered orally, intravenously (IV) or via intramuscular injection (IMI). Most of these drugs are light (ergot alkaloids) or heat-sensitive (oxytocin). There are three first-line drug therapies recommended for the treatment of PPH. The therapies include intravenous oxytocin, followed by intramuscular injection of an ergot alkaloid, and then rectal administration of misoprostol. All seven guidelines agreed on all three first-line therapies, but there were some differences in dosages and routes. Two out of seven guidelines differed in term of dosage of oxytocin, but the consensus appeared to be reached

above 20 IU of oxytocin in one litre of intravenous fluid (Table 7). The same result was found for the administration of ergometrine. All seven guidelines agreed that it should be administered intramuscularly, but one guideline specified a lower dosage, while another did not specify any dosage. Misoprostol administration was also advocated by all seven guidelines , with the dosages varying between 600 and 1000 mcg, per rectum. Only one guideline suggested a sublingual administration of misoprostol.

Table 6: Pharmaceutical management

	Oxytocin IVI	Ergot Alkaloid	Misopristol
ACOG Practice Bulletin, 2006 (United States)	Oxytocin 10 – 40 IU IVI one litre normal saline	Methylergonovine (ergometrine) (IM, 0.2 mg)	Misoprostol (800 – 1000 micrograms (mcg) rectally)
Mousa & Alfirevic, 2007 (Cochrane Review)	Oxytocin IVI– dosage not specified	Ergometrine, dosage not specified	Misoprostol, dosage & route not specified
Saving Mothers: Essential Steps in the Management of Common Conditions associated with Maternal Mortality, 2007 (South Africa)	Oxytocin 20 IU in one litre IV fluids	Ergometrine 0.5 mg IM	Misoprostol 600 mcg rectally
Education Material for teachers of Midwifery, 2008 (World Health Organization)	Oxytocin 20 IU in one litre IV fluids	Ergometrine 0.5 mg IM	Misoprostol 800 mcg rectally
National Women's Health Clinical Guideline, 2009 (New Zealand)	Oxytocin 20 IU in one litre Plasmalyte fluid	Ergometrine 0.5 mg IM	Misoprostol 800 mcg rectally
Monograph on the Prevention of Post Partum Haemorrhage, 2010 (South Africa)	Oxytocin 20 IU in one litre Ringers Lactate fluid 20 IU	Ergometrine 0.5 mg IM	Misoprostol 600 mcg rectally
FIGO Guidelines, 2012 (FIGO Safe Motherhood and Newborn Health Committee – International)	Oxytocin 20 IU IVI one litre normal saline	Ergometrine 0.5 mg IM	Misopristol 800 mcg sublingually
Score (number of guidelines agreed)	7/7	7/7	7/7

- Further management

Further non-surgical management strategies varied from administration of prostaglandins, which are not commonly available at primary care level, to applying special haemostatic compression belts. The management strategy most applicable to primary care was the suggestion of a 'balloon tamponade', which entailed the insertion of a fluid-filled glove into the vagina to ensure uterine contraction through compression of the uterus.

2.5.2 Consensus of results of summary of guidelines

The results of the summary review conclude that current management guidelines for PPH contain at least the following factors for consideration:

- Background knowledge about the risk factors for postpartum haemorrhage as well as the primary and secondary causes of postpartum haemorrhage.
- Diagnostic criteria based on a visual estimation of blood loss of more than 500ml, even though this has proven to be inaccurate. In addition, diagnostic criteria should differentiate between primary and secondary haemorrhage as well as bleeding after normal vaginal delivery compared to post-caesarean section.
- Initial assessment of the extent and cause of the condition, which would be obtained through information from vital signs, assessing the lower genital tract, and then further, drawing of a blood sample for crossmatch in case a transfusion is required.
- Management steps which would initially be required are emptying the bladder, assessing the uterine tone, and fundal massage.
- Pharmaceutical management would be focused on three major types of drug therapies –intravenous oxytocics (20 IU in one litre of intravenous fluid), ergot administration (0,5 mg intramuscularly) followed by misopristol 600 mcg rectally.
- Further management would depend on the kind of resources that are available in the setting, but referral to a higher level of care at this stage is imperative, while also maintaining uterine contraction through compression.

The results of this summary review show that there are specific management strategies which may be helpful for midwives to focus on. The management strategies which were presented at the end of the integrative summary include aspects of prevention, assessment, acute/initial management and pharmaceutical management steps. According to the South African midwifery scope of practice, all of these are relevant, except for the administration of pharmaceutical and surgical treatments. The results from the summary review will also be used to inform the inclusion and exclusion criteria and PIOS for the systematic review in this study. This can be found in Chapter Three and Four in this report.

2.6 Conclusion

The detailed review of the literature revealed a number of systematic reviews on the management of PPH and the decision between the supervisor and student was made to do a review of systematic reviews on the non-surgical, non-pharmaceutical management of PPH. This can be found in Chapter Three and Four of this study.

CHAPTER THREE

METHODOLOGY

3.1. Introduction

This chapter will present the systematic review methodology which was used in this study. The search strategy, search process, quality assessment, data extraction and data analysis will be outlined. An initial search of the literature revealed a number of systematic reviews on postpartum haemorrhage and so it was decided that a review of systematic reviews will be conducted.

3.2. Research Approach/Design

In this study, a systematic review of reviews of available published evidence was conducted, following PRISMA guidelines. Systematic reviews typically fall into two categories, of which the aggregative methods have received much scientific attention in the past few years. Conventional reviews are usually aggregative and are primarily concerned with synthesising certain forms of evidence through the application of scientific strategies such as meta-analysis, and require clear definition of the research question as well as some similarity between the phenomena, so that results can be summarised or pooled. In this study, a systematic review of reviews of available published evidence was conducted, following PRISMA guidelines.

The methodology followed five stages: a comprehensive literature search, followed by a title and abstract screen based on the PI[C]OS, then a detailed quality assessment and finally the data extraction and analysis. In order to guide the conduct of a review, two main

reporting guidelines are primarily used. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses or (PRISMA), is a minimum set of requirements for reporting the stages that were completed in the review, while the Quality of Reporting of Meta-analyses or QUOROM statement is similar (Pussegoda, 2017). In this study, the PRISMA guidelines for reporting will be used, as the QUOROM statement was updated to the PRISMA guidelines in 2009. PRISMA is thus the minimum set of requirements for reporting the stages that were completed in a review. The stages of the review are based on the guidelines set out in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses or PRISMA (Moher, Liberati, Tetzlaff & Altman, 2009).

There are 27 items in the PRISMA checklist (see Appendix D). Item 1-4 of the PRISMA guidelines are covered in the previous sections of this study. They require that: the report be identified as systematic review, the abstract is a structured summary containing full details of the study, and that rationale and objectives for the study are clearly outlined (Moher, Liberati, Tetzlaff & Altman, 2009).

Items 5-16 of the PRISMA guideline checklist outline the standards for the methods of the study, and are as follows: “protocol and registration, eligibility criteria, information sources, search, study selection, data collection process, data items, risk of bias in individual studies, summary measures, synthesis of results, risk of bias across studies and additional analyses” (Moher, Liberati, Tetzlaff & Altman, 2009). For this study, the research protocol has already been passed through the official structures of the University of the Western Cape, and is a registered protocol for the purposes of completing this thesis. The eligibility criteria for inclusion and exclusion in the study are clearly laid out in this chapter in section 3.3. Review

Question/ PI[C]OS. Item 7-16 of the PRISMA reporting guideline will be laid out in the rest of this chapter, and will contain detailed explanations of each of the criterion.

3.3. Review Question/ PI[C]OS

The following review question arose:

What are the most effective acute non-pharmaceutical, non-surgical management strategies (I) to decrease negative health outcomes (O) for women with PPH (P)?

PRISMA reporting guidelines require a well-defined PICOS for every systematic review. The PICOS acronym stands for (P): participant, (I): intervention, (C): control/comparison, (O): outcome, (S): study type. PICOS requires that the person, problem or participant be well described, the intervention searched for to be formulated, comparison or control to be clear, and the outcomes to be stated (Schardt, Adams, Owens et al., 2007). As this was a review of systematic reviews, there was no comparison or control, and so the PI[C]OS for the study was defined. Following the review question and the results from the literature review (see Chapter Two), the following PI[C]OS was applied for this study:

Table 7: PI[C]OS Criteria applied

	Inclusion	Exclusion
Participants	Women with primary PPH post normal vaginal delivery	Women with secondary PPH, women with antepartum bleeding, women with vaginal bleeding of non-pregnancy causes, women with PPH post caesarean section delivery
Intervention	Non pharmaceutical management steps on the management of PPH, initial assessment steps (general physical assessment, visual assessment of the diagnostic tract, further diagnostic steps) of PPH, Oxytocic related interventions for PPH, only	Pharmaceutical management (tranexamic acid, prostaglandins, carbetocin), surgical management (uterine compression sutures, hysterectomy, uterine artery embolization, caesarean section, anaesthetic management practices), management of third stage of labour
Outcomes	Decreased risk of death Decreased adverse effects from blood loss such as adult respiratory distress syndrome, coagulation disorders, shock, hysterectomy and subsequent loss of fertility.	Adverse outcomes post-surgical intervention for postpartum haemorrhage (bleeding, necrosis, shock, coagulation disorders).
Types of study	Systematic reviews: reviews with a quantitative review process, English language	Reviews without a systematic review process, Primary studies, non-english language

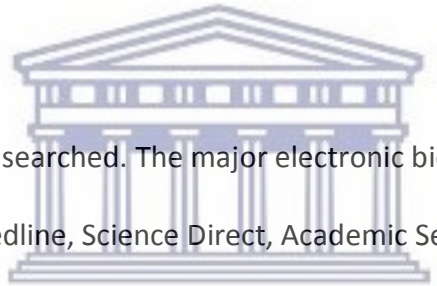
3.4. Search strategy

A comprehensive electronic search was carried out to ensure that all relevant published quantitative reviews or primary evaluative studies were included in the review. The initial search was done on Google Scholar to revise and finalise the search terms and to identify the existence of current systematic reviews addressing components of the review question. At least 150 systematic reviews were found, resulting in refining the original study and to restrict the study to systematic reviews, excluding primary studies.

The scope of the search was not restricted to South Africa, as there were only 10 systematic reviews found on the non-pharmaceutical, non-surgical management of postpartum haemorrhage, and not all the primary studies included in these reviews were from South Africa. The paucity of evidence led to the inclusion of all the reviews, internationally as well.

In addition initial searches revealed that prior to 2007, there were a lack of systematic reviews on the management of PPH (Oakley, 2005). The study was thus delineated to the inclusion of international studies, from the year 2007 to present.

Key terms for the search included synonyms of (*postpartum haemorrhage* Or *bleeding after delivery)* And (*management* Or *assessment* Or *medication* Or *pharmaceuticals* Or *diagnosis* Or *prediction test)* And (*Systematic Review)* AND *>2007*. Key words and terms were used in isolation but also in combination with each other. MeSH terms were also used. The full electronic search strategy as well as the dates of the search can be found in Appendix E at the end of this report.



Fifteen major databases were searched. The major electronic biomedical databases including PubMed, EBSCO, Medline, Science Direct, Academic Search Complete, CINAHL, JBI, Science Direct, Global Library of Women's Medicine, Allied and Complementary Medicine Database, British Nursing Index, EMBASE, Sage Journals Online, SCOPUS and the Cochrane Controlled Trials register were searched. Epistomonikos was used to confirm the results of the search at the end of the search process. All results found in Epistomonikos were also found in the initial search.

3.5. Study selection

Using the search terms, all possible published paper titles were identified and downloaded into a reference manager database (End Note 7). Using the Endnote functionality, the programme was used to identify a list of duplicate titles. Each duplicate was manually examined, and if an actual duplicate was found, one copy of the duplicate was deleted from

Endnote. After duplicates were deleted, a full title list was downloaded from Endnote into Excel. Titles of papers were classified as irrelevant if they did not include PPH or PPH-related topics. All irrelevant titles were manually removed from the Excel sheet at the first stage of the selection process. Due to use of the reference management software, the search and selection process was able to be documented.

Both reviewers then examined the full title list in the excel sheet, based on the PI[C]OS applied in the study (Table 1). Titles were excluded if they did not meet the PI[C]OS and categorized with reason for the exclusion. Any discrepancies were resolved by discussion between the two reviewers. At the end of this process, a list of included article titles were obtained from the excel sheet. The abstracts of all included titles were obtained, using Endnote. The abstracts were further examined by both reviewers again, against the PI[C]OS, and abstracts which did not meet the PI[C]OS were categorised as excluded, with reasons (see Appendix H). The full articles were then obtained, in order to be assessed for quality before being included for analysis in the review.

3.6. Quality Assessment

All systematic reviews that met the PI[C]OS criteria were evaluated for methodological quality, and the AMSTAR-2 tool was used to evaluate methodological quality of the reviews. Inter-rater reliability will be assured by two reviewers agreeing on the scientific aspects of the study – from quality assessment, inclusion and exclusion of studies to data capturing and analysis (Ten Ham-Baloyi & Jordan, 2016). The quality ratings were done by 2 reviewers (student and supervisor). No discrepancies for inclusion or exclusion were required to be resolved by referral to a third reviewer.

There is an increasing amount of systematic reviews being published in order to support healthcare policy and interventions (Shea et al., 2017). Accepting results from a single systematic review without critically examining the manner in which the review was conducted poses a risk to the patient if health decisions are based on such reviews. It becomes vital to review the manner in which a review was conducted.

An important factor to consider is that a critical appraisal tool is different from a reporting guideline. Reporting guidelines are used as a step-by-step process to report the actual conduct of the review, while critical appraisal tools are for ensuring the quality of the articles which are included in the review. In the literature, five main quality assessment tools were revealed to be applied to assess the quality of systematic reviews. Early tools in the 1980's, included the Mulrow and the Sacks criteria, but it was only in 1991 that the first validated tool for the assessment of quality of systematic reviews was presented by Oxman and Guyat (Pussegoda, 2017). This was known as the Overview of Quality Assessment Questionnaire (OQAQ).

In 2007, the "A MeaSurement Tool to Assess systematic Reviews" (AMSTAR) was developed, with 10 items. This version of the AMSTAR tool improved on the OQAQ as it addressed new quality criteria like examining for sources of bias (Pussegoda, 2017; Shea et al.,2017). Subsequent to this, an 11 item version of the AMSTAR, the AMSTAR-R (AMSTAR-Revised) was published by a different group of authors to the AMSTAR.

A newer version of the AMSTAR with 16 items (AMSTAR-2) was published in 2017, by the same group of authors as the initial AMSTAR. Both the AMSTAR and AMSTAR-2 are

acknowledged as validated, reliable tools to assess the quality of systematic reviews. The primary difference between the AMSTAR and AMSTAR-2 is that the AMSTAR-2 can be applied to systematic reviews which contain randomised controlled trials and those reviews which contain non-randomised studies (Shea, et al; 2017). Research acknowledges the difficulty in establishing the reliability and validity of the critical appraisal tools (Ten Ham-Baloyi & Jordan, 2016), and therefore, AMSTAR- 2 was utilised to ensure that quality of the included systematic reviews in this study (see Appendix C).

- Quality assessment scores

The user guide for the AMSTAR-2 maintains that the overall quality assessment should not be assigned a score, rather areas of critical and non-critical weakness in the studies should be identified. Based on the overall areas of critical and non-critical weakness identified in a study, a comprehensive judgement between two reviewers are made on whether or not to include the review in the analysis. This also applied to this study. The assessment of quality was based on the following explanation:

Table 8: Quality Assessment Score AMSTAR-2.

Quality Score	Explanation
High	0/1 non-critical weakness
Moderate	More than one non-critical weakness; no critical flaws
Low	One critical flaw with or without non critical weaknesses
Critically Low	More than one critical flaw with or without non-critical weakness

Critical weaknesses were categorised as follows:

Table 9: AMSTAR-2 Critical weakness criterion

AMSTAR-2 Item Number	AMSTAR-2 Criterion (as stated in Shea, et al (2017))
2	Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?
4	Did the review authors use a comprehensive literature search strategy?
7	Did the review authors provide a list of excluded studies and justify the exclusions?
9	Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?
11	If meta-analysis was performed, did the review authors use appropriate methods for statistical combination of results?
13	Did the review authors account for RoB in primary studies when interpreting/discussing the results of the review?
15	If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?

Non critical weaknesses were categorised as follows:

Table 10: AMSTAR-2 Non- Critical weakness criterion

AMSTAR-2 Item Number	AMSTAR-2 Criterion (as stated in Shea, et al (2017))
3	Did the review authors explain their selection of the study designs for inclusion in the review?
5	Did the review authors perform study selection in duplicate?
6	Did the review authors perform data extraction in duplicate?
8	Did the review authors describe the included studies in adequate detail?
10	Did the review authors report on the sources of funding for the studies included in the review?
12	If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?
14	Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?

Quality assessments were completed independently by both reviewers, and the results of the assessments were compared for agreement. Based on the criteria set out above, reviews were excluded from the study if both reviewers agreed that the quality of the review was moderate, low and critically low.

3.7. Data Extraction

Data were extracted from full text papers only. The data from each publication was extracted and entered into an Excel spread sheet. Authors of individual reviews were not contacted for further information due to time constraints and the scope of the review being for the completion of a mini-thesis research report.

The first stage of data extraction was to identify the individual review characteristics. Study characteristics like country, period of data collection, birth setting of review, facility characteristics, funding, design of included studies, number of databases searched, grey literature searched, number of primary studies included in review, and number of randomised controlled trials included in analysis, quality assessment, countries of primary studies included in review, recognitions of bias, and limitations of the study were extracted per review. This was done to examine whether there would be similarities or differences between reviews at this stage, and also to provide a summary of the selection of the systematic reviews included in the study.

The second stage of data extraction was to extract detailed information per review, based on the inclusion and exclusion criteria and PICO of the reviews. An example of the data extraction sheet can be found in Appendix F at the end of this study.

- Data Synthesis

Systematic reviews typically fall into two categories, of which the aggregative methods have received much scientific attention in the past few years (Dixon-Woods, Cavers, Agarwal et al. 2006). Conventional reviews are usually aggregative and are primarily concerned with

synthesising certain forms of evidence through the application of scientific strategies such as meta-analysis, and require clear definition of the research question as well as some similarity between the phenomena, so that results can be summarised or pooled. It lends itself to the quantitative school of thought (Dixon-Woods, Cavers, Agarwal et al. 2006). This method has the limitation that the theory presented in the study cannot be interpreted and analysed, giving rise to recent research focusing on interpretative synthesis (Dixon-Woods, Cavers, Agarwal et al. 2006). This method is focused on interpreting the theory base of the study, and is inductive in nature. It is mainly used to interpret qualitative studies (Dixon-Woods, Cavers, Agarwal et al. 2006).

For this study, the included data were only presented in table format. The heterogeneity between reviews included in this study were high, and homogeneity of the outcome data were low. Interventions were not similar- and there were not more than one review per intervention, so it was not possible to combine reviews based on intervention or outcome. Outcomes were also not similar between reviews (see results Chapter Four). The clinical recommendations based on the strength of evidence are also presented.

3.8. Ethics

The review protocol was registered by the Senate Higher Degrees Committee of the University of the Western Cape. Although ethical approval was applied for, through the Human Science Social Science Ethics Committee, as it is a systematic review, the student was advised that the study did not have to be approved through this committee. General ethical standards on acknowledging and referencing original author guidelines will be followed. This is done to treat the original author contributions ethically and fairly (Boddy et

al., 2018). All information already in the public domain will be utilised (Boddy et al., 2018). This will ensure that the confidentiality of the primary study participants will remain confidential.

The scientific rigour of a systematic review also assures that the review is conducted ethically. There are various ways to ensure scientific rigour of systematic review, and for this review, the PRISMA checklist was closely followed. This was done in order to ensure that standards used for writing the review were objective and that the review could be replicated again, if following the same steps set out in this review. As there are no human subjects or interactions at the core of this study, the principles of beneficence do not apply. Although these principles do not apply, care has been taken to approach the research study in an ethical manner (Boddy et al., 2018).

3.9. Conclusion

In this chapter, the application of the systematic review methodology in this study was outlined. The measures to ensure quality of the included reviews were described in detail, and the ethical considerations for the review were described. This ensures that the methods for this review are scientific, rigorous, and that it was conducted in an ethical manner.

CHAPTER FOUR

RESULTS AND DISCUSSION

4.1. Introduction

The following chapter will present the results and the discussion of the study in manuscript format for submission to the African Journal of Nursing and Midwifery using the author guidelines. A total of sixteen reviews were found of which four (4) reviews were separate reviews and were included. Details can be found in in abstract of article. For ease of reading, the manuscript submission (4.2) has been started on a separate page.

4.2. Manuscript for submission

Title: A systematic review of systematic reviews on the non-surgical, non-pharmaceutical management of postpartum haemorrhage for primary care midwives

Tweet for journal Twitter profile: "Check out latest evidence based recommendations for South African midwives in managing postpartum haemorrhage."

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Author contributions: HBB wrote the protocol for this review. JC reviewed protocol and addressed comments. HBB completed literature search. JC checked literature search. HBB and JC reviewed titles and abstracts for inclusion in the review. HBB and JC performed quality assessment on the full-text articles. HBB and JC extracted data for analysis. HBB wrote the article and JC checked for accuracy and provided in-depth insight and comments through-out the process.

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APPENDIX A: Papers excluded after abstract review

APPENDIX B: Reviews excluded after AMSTAR2 Quality Assessment

Title: A systematic review of systematic reviews on the non-surgical, non-pharmaceutical management of postpartum haemorrhage for primary care midwives

ABSTRACT

Background: Postpartum haemorrhage (PPH) is one of the main conditions responsible for maternal mortality. Midwives provide most of the maternity care at primary health care level and the quality of management of PPH is poor. Although many systematic reviews for the management of postpartum haemorrhage exist, they mainly focus on surgical and pharmaceutical interventions for medical practitioners. There is a paucity of research on clinical nursing interventions for acute PPH for midwives at the primary care level.

Aim: The aim of this study was to systematically review and synthesise current evidence on the acute management of PPH in order to make recommendations on non-surgical, non-pharmaceutical management of PPH by midwives at the primary health care level.

Methods: A systematic review of reviews of available published evidence was conducted using standard PRISMA guidelines. All included reviews were subjected to the AMSTAR-2 quality assessment tool and a qualitative synthesis of evidence was conducted

Results: A total of sixteen reviews were found of which four (4) reviews were included. Interventions for midwives at the primary health care level in these reviews included nipple stimulation and uterine massage, both with non-significant results. Non-pneumatic anti-shock garments significantly reduced maternal mortality, but self-administered oxytocin was not significant. Small study sizes of the primary studies limited the generalizability of the findings for this review.

Conclusion: There is some evidence for the use of pneumatic anti-shock garments, though study limitations of existing studies should be taken into consideration.

Recommendations: Further high-quality research should be done to establish accurate methods for the management of PPH for midwives, at the primary care level.

Keywords: Postpartum haemorrhage; midwives; systematic review

INTRODUCTION

Postpartum haemorrhage (PPH) is one of the most preventable causes of maternal death, yet it still ranks as one of the main conditions responsible for maternal mortality (Ajenifuja et al. 2010, 72). PPH can be defined as more that 500ml of blood lost from the vagina within 24 hours of delivery (WHO, 2012). Severe PPH is defined as a blood loss of more than 1000ml in the same time period (WHO, 2012). It has serious adverse effects on maternal health. Apart from death, PPH can cause adult respiratory distress syndrome, coagulation disorders, shock, hysterectomy and subsequent loss of fertility (ACOG 2017, 169). As bleeding after delivery is expected, women often do not realise the seriousness of their condition until it is too late (Valdes et al. 2018, 203). Mothers often do not survive to be referred to a more specialised level of care (Fawcus and Moodley 2011, 306).

In South Africa, primary health care is administered at midwife obstetric units, by midwives, and referral to a higher level of care is through emergency services (Boltman-Binkowski 2015, 551). In 2015, the 2011 -2013 Saving Mothers Report on maternal deaths in South Africa, reported that deaths due to obstetric haemorrhage was one of the top three causes of maternal mortality in that tri-ennium (Saving Mothers Report 2015), and has remained unchanged since the 2017 Saving Mothers Report(Saving Mothers Report 2017). Nearly a third (30.4%) of all maternal deaths during this period was due to obstetric haemorrhage, which was preventable in 89% of all cases (Saving Mothers Report 2015, Saving Mothers Report 2017). This report highlighted that poor clinical assessment was amongst the top health provider related errors, and a contributing factor to maternal deaths (Saving Mothers Report 2015, Saving Mothers Report 2017).

The diagnosis and management of PPH is complex, with the primary challenge being with the visual assessment of blood loss (Natrella, et al. 2017). As women are not able to warn healthcare providers timeously about their condition, the situation is compounded by poor clinical assessments, a lack of accuracy in diagnosis, lack of resources, and differing methods of treatment (Lombaard and Pattinson 2006, Natrella et al., 2017). Most of the primary maternity care in South Africa is provided by midwives, and the overall quality of care during the management of PPH is poor (Boltman-Binkowski 2015, 552). And additionally the scope of practice of midwives is limited. Unless a registered midwife has a prescribing license, they may not administer any medications, with the exception of oxytocin (South African Nursing

Council Regulation 2488, 1990). Midwives may also not perform any surgical interventions (South African Nursing Council Regulation 2488, 1990).

A number of systematic reviews have been published on the management of PPH, however, most of these are focused on the evidence for surgical and pharmaceutical interventions for medical practitioners. Midwives are required to manage this complex clinical syndrome using mainly non-pharmaceutical and non-surgical methods and may find the pharmacology or surgeries to be unusable, and not applicable to their scope of practice or to the resources available to them.

The aim of this study was therefore to systematically review all available published evidence for the acute non-pharmaceutical, non-surgical, management of PPH for use by midwives at a primary maternity care setting. On initial searches, a number of systematic reviews were identified and the aim was revised to conduct a systematic review of systematic reviews to address the review question: *What are the most effective non-pharmaceutical, non-surgical acute management strategies (I) to decrease negative health outcomes (O) for women with PPH (P)?*

RESEARCH METHODS AND DESIGN

The systematic review of systematic reviews was conducted using standard systematic review methodology using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher Liberati Tetzlaff and Altman 2009) (Figure 1)

Search strategy

A comprehensive electronic search was conducted using the major electronic biomedical databases, namely PubMed, EBSCO, Medline, Google Scholar, Science Direct, Academic Search Premier, CINAHL, Global Library of Women's Medicine, Science Direct, SAGE, Joanna Briggs Institute, British Nursing Index, EMBASE, SCOPUS, Allied and Complementary Medicine database and the Cochrane Controlled Trials register were searched. The bibliographies of reviews were consulted to ensure that all the relevant reviews were included in the review.

PRISMA reporting guidelines require a well-defined PICOS for every systematic review, namely.(P): participant (women with primary PPH), (I): intervention (non-pharmaceutical non-surgical acute midwifery interventions), (C): control/comparison (n/a), (O): outcome (outcomes related to PPH), (S): study type (systematic review), defining the inclusion and exclusion criteria (Table 1). Key terms for the search included synonyms of (*postpartum haemorrhage* Or *bleeding after delivery)* And (*management* Or *assessment* Or *medication* Or *pharmaceuticals* Or *diagnosis* Or *prediction test)* And (*Systematic Review)* AND *>2007*. Key words and terms were used in isolation but also in combination with each other. On completion of the search, the same terms were entered in the Epistomonikos database in order to confirm whether there were any outstanding systematic reviews.

Table 1: Inclusion/Exclusion - (P): participant, (I): intervention, (C): control/comparison, (O): outcome, (S): study type.

	Inclusion	Exclusion
Participants	Women with primary PPH post normal vaginal delivery	Women with secondary PPH, women with antepartum bleeding, women with vaginal bleeding of non-pregnancy causes, women with PPH post caesarean section delivery
Intervention	Non pharmaceutical management steps on the management of PPH, initial assessment steps (general physical assessment, visual assessment of the diagnostic tract, further diagnostic steps) of PPH, Oxytocic related interventions for PPH, only	Pharmaceutical management (tranexamic acid, prostaglandins, carbetocin), surgical management (uterine compression sutures, hysterectomy, uterine artery embolization, caesarean section, anaesthetic management practices), management of third stage of labour
Outcomes	Decreased risk of death Decreased adverse effects from blood loss such as adult respiratory distress syndrome, coagulation disorders, shock, hysterectomy and subsequent loss of fertility.	Adverse outcomes post-surgical intervention for postpartum haemorrhage (bleeding, necrosis, shock, coagulation disorders).
Types of study	Systematic reviews: reviews with a quantitative review process, English language	Reviews without a systematic review process, Primary studies, non-english language

Study selection

All reviews identified during the search were downloaded in to a reference manager (Endnote 7). Firstly, all duplicates and irrelevant papers from the initial search were deleted using the duplicate function and an initial title review. This was followed by a review of all abstracts based on the PI[C]OS (Table 1). Lastly full texts were extracted for all selected abstracts and abstracts that were unclear and after application of the PI[C]OS, a final set of reviews were

selected for quality assessment. Review of abstracts and full texts were conducted by two reviewers and disagreements were discussed and resolved (Figure 1). Only reviews already in the public sphere was utilised, and authors of reviews were not contacted for further details.

Quality Assessment

The selected reviews were assessed for quality using the latest version of the AMSTAR-2 (A MeaSurement Tool to Assess systematic Reviews) Reviews were excluded from the analysis if they were identified as having a low or critically low level of quality, according to the AMSTAR-2 user guide (Shea et al. 2017) (Appendix B).

Data extraction and analysis

Data were extracted from the reviews and entered into Excel. Due to the heterogeneity of the reviews, no quantitative synthesis of the outcome data could be conducted and a qualitative synthesis, using a summary table format, was used. Each intervention was also graded according to the Oxford Centre for Evidence-Based Medicine Level 1-5 (Table 3) (OCEBM Working Group 2011). The Oxford Centre has set out five levels of evidence, with level one (1) being the strongest and level five (5) the weakest. Level 1 evidence includes systematic reviews and randomised controlled trials with narrow confidence intervals, level two evidence includes cohort studies and low-quality randomised controlled trials, while level five evidence are expert opinion papers.

Ethical considerations

Ethics clearance for the study was sought from the University of the Western Cape Faculty of Community and Health Sciences Higher Degrees Committee and Senate. Patient consent is not required in a systematic review of literature. As only documents available online were reviewed, informed consent and protection of data are not required. The ethical guidelines for a review were maintained. Authors were not contacted for study data, only data in the public sphere were used.

RESULTS

Search and selection

The initial search revealed 443 papers, of which 150 were systematic reviews. After the examination of the titles, 22 duplicates and 394 irrelevant titles were removed (Figure 1) resulting in 27 abstracts to be reviewed by both reviewers against the PI[C]OS criteria (Table

1), after which a further 11 were excluded (Figure 1) (Supplementary Material: Appendix A). The remaining 16 reviews were examined for eligibility against the AMSTAR 2 criteria and 12 were excluded due to low quality (Supplementary Material: Appendix B), resulting in four (4) reviews which were found to be eligible to be included in the study.

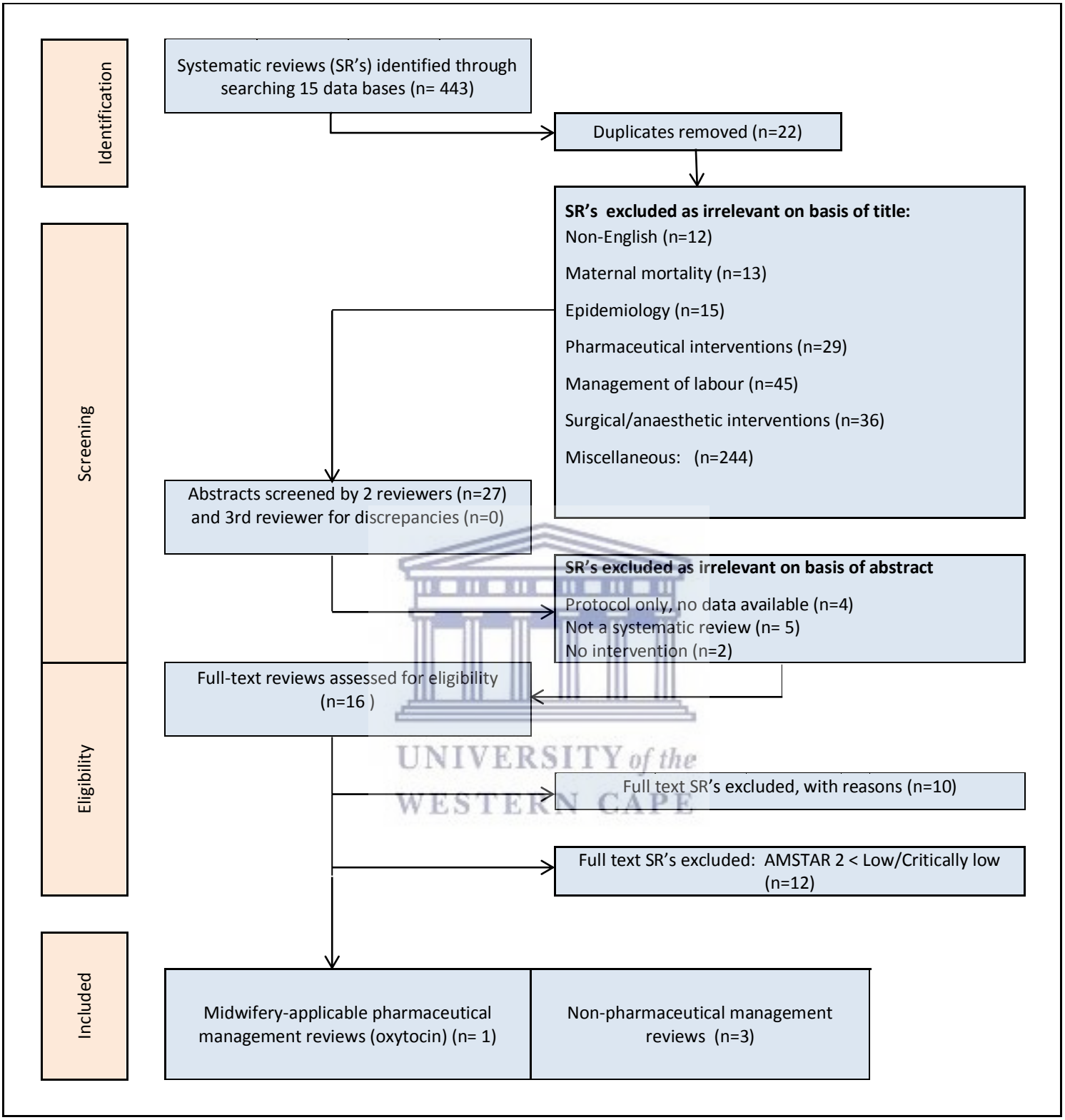

Figure 1: PRISMA flow diagram for identification of studies

Characteristics of included studies

Four (4) reviews were eligible for inclusion in this review, three (3) non-pharmaceutical (Abedi et al. 2016, Hofmeyer Abdel Aleem and Abdel Aleem 2013, and Pileggi-Castro et al. 2015) and one (1) midwifery-applicable pharmaceutical intervention to manage PPH (Pantoja et al. 2016). The non-pharmaceutical interventions were nipple stimulation (Abedi et al. 2016) and uterine massage to prevent PPH (Hofmeyer Abdel Aleem and Abdel Aleem 2013), and the use of non- pneumatic anti shock garments as part of the management of PPH (Pileggi-Castro et al. 2015). The quality of four included reviews was high, with either one or no non-critical weakness as described in the AMSTAR-2 quality assessment tool (Table 2), with high levels of evidence for the reported outcomes (Table 3).

Two out of the four systematic reviews contained pooled data, with only one study containing meta-analysis of randomised controlled trials and the other containing pooled data of randomised controlled trials and observational studies (Table 2). The remaining two reviews did not contain enough data to justify a meta-analysis (Table 2). Levels of evidence for included studies were high with two studies being at level one and two studies evaluated at level two (Table 3).

Two reviews were published in 2016 (Abedi et al. 2016, Pantoja et al. 2016), one in 2015 (Pileggi-Castro et al. 2015) and the earliest was published in 2013 (Hofmeyer Abdel Aleem Abdel Aleem 2013). Three out of the four reviews were Cochrane reviews (Abedi et al. 2016, Hofmeyer Abdel Aleem and Abdel Aleem 2013, and Pantoja et al. 2016). Pileggi-Castro et al. 2016 was published in BioMed Central. The birth settings for the primary studies within the reviews range from high income settings in the United Kingdom (Abedi et al. 2016), to primary non-facility birth settings in Ghana (Pantoja et al. 2016). Three reviews (Abedi et al. 2016 Pileggi-Castro et al. 2015 and Pantoja et al. 2016) noted poor quality primary studies as a serious limitation while Hofmeyer Abdel Aleem and Abdel Aleem 2013 concluded a low risk of bias for primary studies included in the review.

Table 2: Characteristics of included systematic reviews

SR Characteristics	Inclusion/exclusion criteria	Participants	Intervention	Outcome Measurement
Author: Abedi et al. (2016) **Period**: July 2015 **Setting**: Hospital (India, US & UK) Community (Malawi) **Studies**: Two RCT's **Quality Assessment**: GRADE **Bias:** high in two studies, unclear in two studies **AMSTAR 2:** High, no critical or non-critical weakness (no meta-analysis) Limitations: poor quality primary studies	**Definition of PPH**: Mild to moderate vaginal bleeding in excess of 500 ml within 24 hours after birth, severe is 1000ml vaginal blood loss within 24 hours of birth **Incl**: RCT, vaginal birth, with nipple stimulation vs no treatment OR uterotonic OR uterine massage (before or after placental birth) **Exc**: not reported	#N:4608 (4472 in analysis) **Age**: unclear median age **Gravidity**: primigravidas (1) **Gestation**:38wks– term, singleton **Mode of birth**: Vaginal **Baseline:** • BMI: not stated • HB: not stated	**Nipple Stimulation** Nipple stimulation via breastfeeding or breast pump or digital stimulation immediately after birth **Duration of treatment**: range from 20 min on breast pump, 15 min of digital stimulation, early suckling I: Nipple stimulation; C: none I: Nipple stimulation; C:oxytocin	**Blood loss measurement**: • Transparent plastic jugs in units of 100ml • Physician estimation and hematocrit on day 2 post birth postpartum
Author: Hofmeyr, Abdel-Aleem H, Abdel-Aleem MA (2013) **Period:** 30 April 2013 **Setting**: University hospitals - Egypt and South Africa **Studies**: Two RCT's **Quality Assessment**: Cochrane –GRADE **Bias:** risk of bias was generally low for both included studies, except for blinding (performance and detection bias), which would be impossible in this study **AMSTAR-2**: High, no non-critical weakness **Limitations:** Insufficient evidence due to uterotonic administration	**Definition of PPH**: heavy bleeding within 24 hours of birth **Incl**: RCT, vaginal birth OR c/section, uterine massage commencing after birth of baby **Exc**: not reported	#N: 1491 (652 in analysis) **Age**:18 years and older **Gravidity/parity:** not reported **Gestation:** not reported, singleton **Mode of birth:** Vaginal **Baseline:** • BMI: not stated • HB: not stated	**Uterine massage** Uterine massage before or after placental delivery WITH standard treatment VS no uterine massage with standard treatment **Duration of treatment:** every 10 minutes for 60 minutes after birth I: Uterine massage; C: No massage	**Blood loss measurement**: Plastic drape under participant
Author: Pantoja et al. (2016) **Period:** 12 November 2015 **Setting**: Non-facility, Ghana **Studies:** One Cluster randomised controlled trial **Quality Assessment**: Cochrane -GRADE **Bias:** Detailed assessments of bias done, and quality of included studied downgraded as a result of risk of attrition and recruitment bias **AMSTAR-2:** High, no non-critical weakness **Limitations:** risk of attrition and recruitment bias and very serious imprecision	**Definition of PPH:** Blood loss greater than 500 ml after vaginal birth **Incl:** RCT, Vaginal birth in non-facility birth settings, PPH and administration of oxytocin by non-skilled attendants or birthing mother **Excl:** Not Reported	#N: 1570 (888 in analysis) **Age:** Not reported **Gravidity/parity:** Not reported **Gestation:** Not reported, **Mode of birth**: Vaginal birth **Baseline:** • BMI: not stated • HB: not stated	**Self-administration of oxytocin** Intramuscular injection of oxytocin (10IU) in the thigh after birth, using a special syringe (Uniject) which enables self-administration VS no injection **Duration of treatment**: 1 minute, immediately after birth I: oxytocin, C: no treatment	**Blood loss measurement**: Calibrated drape under participant

SR Characteristics	Inclusion/exclusion criteria	Participants	Intervention	Outcome Measurement
Author:Pileggi-Castro et al. (2015) **Period**: March 2014 **Setting**: Low-income **Studies**: Four pre and post design and one cluster randomised controlled trial **Quality Assessment:** various - dependent on study design **Bias:** Low for the included studies **Limitations:** Insufficient evidence **AMSTAR-2:** High, one non-critical weakness	**Definition of PPH:** Abnormal bleeding of 1000ml or more, or any bleeding with hypotension or blood transfusion **Incl**: Not Reported **Excl:** Not Reported	#1274 (1056 in analysis) **Age:** not reported **Gravidity/parity:** Pregnant **Gestation**: not reported **Mode of birth:** not reported **Baseline:** • BMI: not stated • HB: not stated	**Non-pneumatic anti shock garment (NASG)** Non-pneumatic anti shock garment PLUS standard care vs standard care only Duration of treatment: not reported I: NASG, C: Standard care only	**Blood loss measurement**: Not reported

Table 3: Outcomes and level of evidence per review

Identifier	Outcomes	Treatment	Control	Outcome
Author: Abedi et al. (2016)		**Nipple Stimulation**	**No Treatment**	
LOE 1 SR of RCT's: 2 RCT's included in analysis	Estimated blood loss: PPH>500ml.	167/2104 (7.9%)	178/2123 (8.4%)	z=0.53, p=0.60 (NS)
	ICU Admission	2/2104 (0.09%)	2/2123 (0.9%)	z=0.01 p=0.99 (NS)
	Other maternal morbidities:			
	Retained placenta	2/2104 (0.09%)	2/2123 (0.9%)	p=0.99, z=0.01 (NS)
	Maternal mortality	1/2104 (0.04%)	0/2123 (0%)	z=0.68, p=0.50 (NS)
	Neonatal mortality	20/2129 (0.9%)	19/2142 (0.88%)	z=0.18, p=0.86 (NS)
		Nipple Stimulation	**Oxytocin**	
	Anaemia	N=32, mean(SD)= 34(4)	N= 53, mean (SD)= 34.4 (4.4)	z= 0.43, p=067 (NS)
Author: Hofmeyr, Abdel-Aleem H, Abdel-Aleem MA (2013)		**Uterine Massage**	**No Massage**	
LOE: 1 **SR of RCT's: 2** **RCT's included in analysis**	Estimated blood loss: 500 ml or more after trial entry	45/750 (6.2%)	30/741 (4.0%)	z=0.23, p=0.81 (NS)
	Transfusion	4/735 (11.4%)	4/722 (0.55%)	z=0.04, p=0.97 (NS)
	Anaemia	5/191 (2.6%)	8/191 (4.2%)	z=0.84, p=0.40 (NS)
	Other maternal morbidities:			
	Placenta delivered more than 30 min after birth	9/753 (1.2%)	11/736 (1.49%)	z=0.54, p=0.59 (NS)
Author: Pantoja et al. (2016)		**Oxytocin**	**No treatment**	
LOE: 2 **SR of RCT's: 1** **RCT's included in analysis, no meta-analysis**	Estimated blood loss:			
	PPH>500ml	18/682 (2.63%)	49/887 (5.5%)	z=2.731, p=0.0064 (S, favours oxytocin)
	Transfer to a healthcare facility	10/682 (1.46%)	18/888 (2.02%)	z=0.83, p=0.41(NS)
	Other maternal morbidities:			
	Severe maternal morbidity	0/682 (0%)	0/888 (0%)	not estimable
	Maternal mortality	0/888 (0%)	0/888 (0%)	not estimable
	Neonatal mortality: Stillbirth	19/682 (2.8%)	18/888 (2.02%)	z=0.73, p=0.47 (NS)
Author: Pileggi-Castro et al. (2015)		**Non-pneumatic anti shock garment**	**Standard Care**	
LOE: 2 **SR of combined studies - one RCT and 5 pre/post design included.**	**Pre-Post Design Studies**			
	Preventing Transfusion	803/1069 (75%)	623/898 (69%)	z=0.47, p=0.64 (NS)
	Other maternal morbidities:			
	Preventing severe maternal outcomes	13/764 (1.7%)	32/590 (5.4%)	z=3.57, p=0.0004 (S, favours NASG)
	Preventing maternal mortality	46/1274 (3.6%)	72/1056 (6.8%)	z=3.29, p=0.001(S, favours NASG)
	Cluster Randomised Trials			
	Preventing Transfusion	167/398 (42%)	168/435 (38.6%)	z=0.98, p=0.33 (NS)
	Other maternal morbidities:			
	Preventing severe maternal outcomes	4/403 (0.99%)	12/465 (2.58%)	z=1.67, p=0.10 (NS)
	Preventing maternal mortality	4/405 (0.98%)	11/475 (2.31%)	z=1.47, p=0.14 (NS)

LOE: Level of evidence, SR: Systematic Review, RCT: Randomised Controlled Trial, PPH: Postpartum Haemorrhage, ICU: Intensive Care Unit, NASG: Non-pneumatic anti shock garment, NS: Not significant, S: Significant

Non-pharmaceutical intervention outcomes

Nipple Stimulation

One review (Abedi et al. 2016) provided information on nipple stimulation compared with no treatment and compared with oxytocin (Table 3). Though the nipple stimulation compared to no treatment resulted in a smaller percentage of cases with PPH > 500ml (.8% vs 8.4%), this result was not significant (p=0.60). The results on nipple stimulation show that there is insufficient evidence to support the use of nipple stimulation as an intervention to reduce the incidence of PPH.

Uterine Massage

One included review (Hofmeyer Abdel Aleem and Abdel Aleem 2013) compared uterine massage and standard treatment with no uterine massage. The results of the meta-analysis revealed that there was no significant difference (p= 0.81) in blood loss between groups who had received uterine massage before or after the delivery of the placenta (6.2% vs 4%.), with both groups receiving standard treatment. No statistically significant trends can be reported for this review, although positive non-significant trends were shown to favour the massage group for the outcome: mean blood loss at 30 minutes (z=2.43, p= 0.015).

Non-pneumatic anti shock garments (NASG)

One review (Pileggi-Castro et al. 2015) reported on the use of non-pneumatic anti shock garments to manage PPH. There were three outcomes reported on in the study: prevention of maternal mortality, prevention of severe maternal outcomes and prevention of blood transfusion. Statistically significant trends were shown in the metal-analysis of the pre-post design studies, but not in the cluster randomised studies. The reduction in severe maternal outcomes (1.7% vs 5.4%) was shown to favour NASG when using NASG as compared to standard care (z=3.57, p=0.0004). For prevention of maternal mortality, similar significant outcomes were shown in the same group (z=3.29, p=0.001). In the cluster randomised trial group, no significant outcomes could be reported (Table 3).

Midwifery-applicable Pharmaceutical Interventions

One systematic review (Pantoja et al. 2016) reported on the use of self-administered oxytocin vs no treatment in non-facility birth settings. Only one randomised controlled trial was included in the analysis and due to lack of primary studies, a meta-analysis could not be performed. This was the only review who showed a significant trend in the reduction of PPH (bleeding above 500ml) (Relative Risk 0.49%, 95% Confidence Interval 0.27- 0.90; 1174 women) in the oxytocin group, although the quality of the included trial was poor (Table 3).

DISCUSSION

Midwives are also often the first line of contact for women who are seeking maternal health care, which places the midwife in a unique position to be able to recognise opportunities for resuscitation early (Hamilton, 2005).The results of the review confirm the lack of evidence-based interventions for the clinical management of postpartum haemorrhage by midwives at primary care level. Nipple stimulation has no significant effect on the reduction of PPH, and while there is an indication that uterine massage may assist in the reduction of PPH, the statistical trends are also non-significant. However, the application of non-pneumatic anti-shock garments may be of value in the management of PPH at the primary health care level and self-administered oxytocin could be a valuable tool to assist women at high-risk for PPH, to reduce maternal deaths after discharge from a healthcare facility.

Initial assessment and management of the patient (both haemodynamic status and physical assessment), as well as administering drug therapy, is vital knowledge for midwives, but a factor which may affect the confidence of midwives to diagnose PPH at primary care level is that they practise within a system of medical practitioner-led care, and that the literature does not have a consistent definition of PPH, nor a reliable method of assessing blood loss (Natrella et al. 2017). This is confirmed by the findings in this study that all of the included reviews did not agree on a single definition of PPH (Table 2)

Compounding the issue of assessment and diagnosis, is the relatively narrow scope of practice of midwives in South Africa. There are not many non-pharmaceutical evidence based interventions which show a significant effect in the management of PPH. Pharmaceutical interventions other than oxytocin have been proven to have a significant effect on the reduction of PPH but midwives are not able to practice within this sphere (South

African Nursing Council R2488 1990). It does not, therefore, come as a surprise that PPH was rated as one of the top professional anxieties for midwives in clinical practice (Dahlen & Caplice, 2014).

It should be noted that the study was limited due to the restriction of reviews in the English language. Current work which was published, was of low quality and the sample sizes were small. Low sample sizes limit generalizability of the findings, and impact on the quality of reporting of the study. The review showed that there are not many high quality clinical research studies on midwifery-specific interventions for the management of PPH.

Recommendations from this study are that midwives at a primary care level could benefit from having high quality, evidence based interventions to refer to, which defines simple and accurate diagnostic criteria, outlines clinical assessment steps, and details initial management which is applicable to the setting and scope of practice of a midwife. Equipment as well as skills should be updated on a regular basis. In addition, registered nurses who have been out of practice for a period of time may find streamlined evidence-based interventions helpful for updating themselves.

CONCLUSION

It is evident from this review that the issues affecting the management of PPH by midwives in clinical practice are complex, and there are not many high quality evidence-based recommendations which assist midwives to manage postpartum haemorrhage. Studies which are published are of low quality, or are not relevant to midwifery-led care. It is a strong recommendation from this review that more high quality research is done into the assessment and management of this complex (and silent) clinical syndrome in order to lower the maternal mortality rates in this area.

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World Health Organization. 2012. *WHO recommendations for the prevention and treatment of postpartum haemorrhage.* Geneva: WHO Press. Accessed September, 2018. https://www.who.int/reproductivehealth/publications/maternal_perinatal_health/9789241548502/en/

SUPPLEMENTARY MATERIAL

APPENDIX A: EXCLUDED STUDIES AFTER ABSTRACT REVIEW

TITLE	REASON
1. Diaz, V., Abalos, E., and Carroli, G. (2014). Methods for blood loss estimation after vaginal birth. Cochrane Database of Systematic Reviews, (2). http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010980/abstract doi:10.1002/14651858.CD010980	Protocol only-no data available at time of writing up review
2. Gallos Ioannis, D., Williams Helen, M., Price Malcolm, J., Merriel, A., Gee, H., Lissauer, D., . . . Coomarasamy, A. (2015). Uterotonic agents for preventing postpartum haemorrhage: a network meta-analysis. Cochrane Database of Systematic Reviews, (5). http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD011689/abstract doi:10.1002/14651858.CD011689	Protocol only-no data available at time of writing up review
3. Jackson, K. W., Allbert, J. R., Schemmer, G. K., Elliot, M., Humphrey, A., and Taylor, J. (2001). A randomized controlled trial comparing oxytocin administration before and after placental delivery in the prevention of postpartum hemorrhage. Am J Obstet Gynecol, 185(4), 873-877. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/608/CN-00374608/frame.html doi:10.1067/mob.2001.117363	Exclusion based on type of study - this is an RCT not a systematic review
4. Kataoka, Y., Yaju, Y., Hiruta, A., Horiuchi, S., and Mori, R. (2015). Homeopathy for reducing blood loss in the third stage of labour. Cochrane Database of Systematic Reviews, (4). http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD011635/abstract doi:10.1002/14651858.CD011635	Protocol only-no data available at time of writing up review
5. Kodkany, B. S., and Derman, R. J. (2006). Evidence-based interventions to prevent postpartum hemorrhage: Translating research into practice. Int J Gynaecol Obstet, 94 Suppl 2, S114-115. doi: 10.1016/s0020-7292(06)60002-7	Keynote speech - exclude based on S: no data available for inclusion in review
6. Likis, F. E., Sathe, N. A., Morgans, A. K., Hartmann, K. E., Young, J. L., Carlson-Bremer, D., . . . Andrews, J. (2015). AHRQ Comparative Effectiveness Reviews Management of Postpartum Hemorrhage. Rockville (MD): Agency for Healthcare Research and Quality (US).	Intervention not appropriate for inclusion: pharmaceutical drugs midwives cannot administer AND surgical interventions
7. McDonald, S. J., Abbott, J. M., and Higgins, S. P. (2004). Prophylactic ergometrine-oxytocin versus oxytocin for the third stage of labour. Cochrane Database of Systematic Reviews, N.PAG-N.PAG.	Intervention: management of 3rd stage of labour excluded
8. Penn, A. W., Beam, N. K., and Azman, H. (2015). Non-pneumatic anti-shock garment (NASG) as a first aid for preventing or reversing hypovolemic shock secondary to obstetric hemorrhage. Cochrane Database of Systematic Reviews(5). doi: 10.1002/14651858.CD011700	Protocol only-no data available at time of writing up review
9. Tuncalp, O., Souza, J. P., and Gulmezoglu, M. (2013). New WHO recommendations on prevention and treatment of postpartum hemorrhage. Int J Gynaecol Obstet, 123(3), 254-256. doi: 10.1016/j.ijgo.2013.06.024	WHO Guideline - exclude based on S: no data available for inclusion in review
10. Walraven, G., Wanyonyi, S., and Stones, W. (2008). Management of post-partum hemorrhage in low-income countries. Best Practice and Research Clinical Obstetrics and Gynaecology, 22(6), 1013-1023. doi: https://doi.org/10.1016/j.bpobgyn.2008.08.002	Systems/policy recommendations - exclude based on S: no data available for inclusion in review
11. Zelop, C. M. (2011). Postpartum hemorrhage: becoming more evidence-based. Obstet Gynecol, 117(1), 3-5. doi: 10.1097/AOG.0b	Comment on another article- exclude based on S: no data available for inclusion in review

APPENDIX B: EXCLUDED STUDIES BASED ON AMSTAR2 WITH REASONS

	Study	Quality Score	Reason
1	Chelmow, 2011	CRITICALLY LOW >1 critical flaw with/without non-critical weaknesses	Five critical and five non-critical flaws were found: Critical flaws –it was not stated that the review methods were set out prior to the study , no list of excluded studies with reasons were provided, and risk of bias (RoB) assessments for individual studies not included, RoB not included in the discussion of results. Also, adequate discussion of publication bias was not found in the study. Non-critical flaws were: study selection and data extraction not performed in duplicate, sources of funding or conflict of interest, if any, were not revealed, no satisfactory discussion of heterogeneity was included in the results for the review, and potential sources of conflict of interest were not revealed.
2	Doumoutchsis, Papageorghiou and Arulkumaran, 2007	CRITICALLY LOW >1 critical flaw with/without non-critical weaknesses	Two critical and three non-critical flaws were found: Critical flaws - risk of bias (RoB) assessments for individual studies not included, RoB not included in the discussion of results. Non critical flaws were: sources of funding or conflict of interest, if any, were not revealed, and no satisfactory discussion of heterogeneity was included in the results for the review.
3	Gizzo, et al., 2013	CRITICALLY LOW >1 critical flaw with/without non-critical weaknesses	Six critical and four non-critical flaws were found: Critical flaws - it was not stated that the review methods were set out prior to the study, the authors did not use a comprehensive literature search strategy – only four databases were used, no list of excluded studies with reasons were provided, and risk of bias (RoB) assessments for individual studies not included, RoB not included in the discussion of results. Also, adequate discussion of publication bias was not found in the study. Non critical flaws were: selection of study designs for inclusion in the review were not described, study selection and data extraction not performed in duplicate, and no satisfactory discussion of heterogeneity was included in the results for the review.
4	Hancock, Weeks and Lavender, 2015	CRITICALLY LOW >1 critical flaw with/without non-critical weaknesses	Two critical and two non-critical flaws found: risk of bias (RoB) assessments for individual studies not included, RoB not included in the discussion of results. Non critical flaws were: sources of funding, if any, were not revealed, and no satisfactory discussion of heterogeneity was included in the results for the review.
5	McCormick, Sanghvi, Kinzie, McIntosh, 2002	CRITICALLY LOW >1 critical flaw with/without non-critical weaknesses	Six critical and six non-critical flaws were found: Critical flaws - it was not stated that the review methods were set out prior to the study, the authors did not use a comprehensive literature search strategy, no list of excluded studies with reasons were provided, and risk of bias (RoB) assessments for individual studies not included, RoB not included in the discussion of results. Also, adequate discussion of publication bias was not found in the study. Non-critical flaws were: research question did not include the components of the PICO, authors did not explain their selection of study designs for inclusion in the study, study selection and data extraction not performed in duplicate, included studies were not described in adequate detail, and no satisfactory discussion of heterogeneity was included in the results for the review.
6	Miller, Martinand Morris, 2008	CRITICALLY LOW >1 critical flaw with/without non-critical weaknesses	Five critical and five non critical flaws found. Critical flaws were: The report did not contain a statement which stated that the review methods were established prior to the review, and thus deviations from the protocol could not be established, a list of excluded studies and their reasons for exclusion were not found, risk of bias (RoB) assessments for individual studies not included, RoB not included in the discussion of results, publication bias not accounted for or discussed. Non critical flaws were: inclusion criteria did not include the PICO, study designs for inclusion in the review were not discussed, study selection and data extraction not performed in duplicate. No explanation of heterogeneity was provided.

7	Natrella, et al., 2016	CRITICALLY LOW >1 critical flaw with/without non-critical weaknesses	Six critical and six non critical flaws were found: Critical flaws - it was not stated that the review methods were set out prior to the study, no list of excluded studies with reasons were provided, and risk of bias (RoB) assessments for individual studies not included, sources of funding for the studies included in the review not revealed, RoB not included in the discussion of results. Also, adequate discussion of publication bias was not found in the study. Non-critical flaws were: research question did not include the components of the PICO, authors did not explain their selection of study designs for inclusion in the study, study selection and data extraction not performed in duplicate, no satisfactory discussion of heterogeneity was included in the results for the review, and potential sources of conflict of interest were not declared in this review.
8	Pacagnella, et al., 2013	CRITICALLY LOW >1 critical flaw with/without non-critical weaknesses	Four critical flaws and no none-critical flaws were found. The large number of critical flaws found, influenced the quality assessment rating. Critical flaws were: no list of excluded studies with reasons were provided, and risk of bias (RoB) assessments for individual studies not included, RoB not included in the discussion of results. Also, adequate discussion of publication bias was not found in the study.
9	Roach, Abramovici and Tita, 2012	LOW 1 critical flaw with/without non-critical weaknesses	One critical and four non-critical flaws found. The critical flaw was: a satisfactory technique for assessing risk of bias (RoB)for individual studies not included. Non critical flaws were: It was not clear whether study selection and data extraction was performed in duplicate, and sources of funding and conflicts of interest not stated.
10	Sathe et al., 2016	CRITICALLY LOW >1 critical flaw with/without non-critical weaknesses	Three critical flaws were found. They were: a list of the excluded studies with justifications for exlusion were not found, a satisfactory technique for assessing risk of bias (RoB)for individual studies not included, and the authos did not account for RoB in the discussion of the review.
11	Sentilhes, et al., 2016	CRITICALLY LOW >1 critical flaw with/without non-critical weaknesses	Five critical and four non-critical flaws were found. Critical flaws - it was not stated that the review methods were set out prior to the study, no list of excluded studies with reasons were provided, and risk of bias (RoB) assessments for individual studies not included, RoB not included in the discussion of results. Also, adequate discussion of publication bias was not found in the study. Non-critical flaws were: authors did not explain their selection of study designs for inclusion in the study, study selection and data extraction not performed in duplicate, and no satisfactory discussion of heterogeneity was included in the results for the review.
12	Sloan, Durocher, Alrich, Blum, Winikoff, 2010	CRITICALLY LOW >1 critical flaw with/without non-critical weaknesses	Five critical and one non-critical flaws were found. Critical flaws - it was not stated that the review methods were set out prior to the study, no list of excluded studies with reasons were provided, and risk of bias (RoB) assessments for individual studies not included, RoB not included in the discussion of results. Also, adequate discussion of publication bias was not found in the study. Non-critical flaw was: no evidence was found that the authors assessed the impact of RoB in individual studies on the results of the meta-analysis.

4.3. Conclusion

This chapter presented the results and discussion in a manuscript format. The results showed that there are very few evidence-based recommendations for midwives to apply in their practice. A detailed discussion of the results as well as recommendations can be found in Chapter 5 of this study.

CHAPTER FIVE

CONCLUSION AND RECOMMENDATIONS

5.1. Introduction

This chapter will focus on the discussion of the previous results which were presented in Chapter Four. It also concludes the thesis by looking at the key findings of the study, presenting the recommendations out of the study, the study limitations and the concluding remarks.

5.2. Key findings of the study

The results of the review conclude that very few evidence-based interventions exist for the actual clinical management of postpartum haemorrhage by midwives at primary care level. It is not surprising that the maternal mortality trends are unchanged in recent years. Nipple stimulation has no effect on the reduction of PPH, and while there is an indication that uterine massage may assist in the reduction of PPH, the statistical trends are also non-significant. In addition, the application of non-pneumatic anti-shock garments may be of value in the management of PPH at the primary maternity care level. Also, self-administered oxytocin could be a valuable tool to assist women at high-risk for PPH, to reduce maternal deaths after discharge from a healthcare facility.

5.3. Discussion

In this study, all four included systematic reviews had a different definition of PPH, and three out of four reviews did not report on the method of assessment of blood loss. Although PPH is one of the top causes of maternal mortality worldwide, knowledge of risk factors and assessment is vital to form part of an 'early warning' system of thinking for

midwives. This is to combat the perception that bleeding after delivery is part of the delivery process, and to prevent delays in the initiation of resuscitation (Nangalia & Thaddeus, 2004; Ogunjimi, Ibe & Ikorok, 2012). Midwives are also often the first line of contact for women who are seeking maternal health care, which places the midwife in a unique position to be able to recognise opportunities for resuscitation early (Hamilton, 2005; Ogunjimi, Ibe & Ikorok, 2012). All of these factors contribute to the importance of maintaining a theoretical knowledge base of etiology, causes, and risk factors of this condition.

PPH is usually painless and occurs without warning. Monitoring of the haemodynamic status of the patient through vital signs, means that the indication of shock will only manifest after at least 1000ml of blood is lost. Blood loss between 500-1000 ml usually does not produce severe symptoms in a healthy patient (National Department of Health South Africa, 2015). This means the clinical practitioner must depend on other clinical signs, most usually the visual estimation of blood loss. Although literature has documented this as notoriously inaccurate, there are assistive measures to enable midwives to more accurately estimate blood loss. These include filling up bottles of water (500ml to 1000ml) with added colouring, to bed linen in order to visualise the actual staining that would occur at differing amounts of fluid (World Health Organization, 2008).

Initial assessment and management of the patient (both haemodynamic status and physical assessment), as well as administering drug therapy, is vital knowledge for midwives, but a factor which may affect the confidence of midwives to diagnose PPH at primary care level is that they practise within a system of medical practitioner-led care, and that the literature does not have a consistent definition of PPH, nor a reliable method of assessing blood loss.

Compounding the issue of assessment and diagnosis is the relatively narrow scope of practice of midwives in South Africa. There are not many non-pharmaceutical evidence based interventions which show a significant effect in the management of PPH. Pharmaceutical interventions other than oxytocin have been proven to have a significant effect on the reduction of PPH but midwives are not able to practice within this sphere (Chelmow, 2011). It does not, therefore, come as a surprise that PPH was rated as one of the top professional anxieties for midwives in clinical practice (Dahlen & Caplice, 2014).

5.4. Recommendations

The results of this study show that there are no comprehensive, evidence based management guidelines aimed at midwives in the primary care setting, a single, simple resource for midwives may assist with clarity in management of this condition at a primary care level. This will lead to the following recommendations in the various professional areas:

- Education

The primary area that this thesis sought to address was to provide an evidence based guideline to guide the continuing education of midwives in practice. Midwives should be given the necessary support in terms of accessibility to online resources, perhaps as part of continuous professional development programmes, in order to keep their skill set current, and expose clinical practitioners to the latest level of evidence-based care.

- Practice

Clear referral guidelines for patients with PPH should be implemented and established. Regular emergency procedure drills should assist midwives at the primary care level with maintaining clinical competency to manage obstetric emergencies. Emergency kits containing management algorithms as well as basic equipment should be available in the post-natal and labour ward areas.

- Policy

It is recommended that the scope of midwives in primary maternity care be addressed in the changing healthcare climate. This is vital to ensure that we have practitioners which are enabled by both internal and professional policy to manage and stabilise mothers in critical conditions.

- Research

It is recommended that further high quality evidence-based clinical research be done to establish education and clinical practices which are scientific, for midwives. Focus areas for research may be, for example, to establish an accurate method of estimating blood loss which does not require invasive intervention and can be implemented in low-resource setting. Estimation of blood loss and accurately diagnosing the patient's condition early enough may prevent serious maternal morbidity associated with this condition.

5.5. Limitations of the study

This study was limited, in that it was only able to review clinical guidelines in the English language. There was also a lack of good quality clinical evidence published in English. There was also a lack of good quality systematic reviews on the topic.

5.6. Conclusion and concluding remarks

Midwives do not have much high quality evidence to rely on when trying to treat PPH, and their scope of practice is also not favourable to improving maternal health outcomes in the management of this condition. Due to the scanty evidence-base, it can be understood that the management of PPH is one of the primary sources of clinical anxieties for midwives.

Postpartum haemorrhage is still one of the main causes of maternal mortality. Having effective yet simple evidence-based clinical management tools accessible to midwives in practice may reduce confusion and increase response times to the management of this condition, as midwives are often the first point of contact for many South African women seeking maternal health care. Ensuring steps towards evidence-based care for midwives in South Africa is an imperative, considering the status of maternal health at present, and its implication for Millennium Development Goals.

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APPENDIX A: Reviews Excluded from analysis: Pharmacology

	Carbetocin
1	Jin, B., Du, Y., Zhang, F., Zhang, K., Wang, L., & Cui, L. (2016). Carbetocin for the prevention of postpartum hemorrhage: a systematic review and meta-analysis of randomized controlled trials. Journal of Maternal-Fetal & Neonatal Medicine, 29(3), 400-407. doi: 10.3109/14767058.2014.1002394
2	Peters, N. C. J., & Duvekot, J. J. (2009). Carbetocin for the prevention of postpartum hemorrhage: a systematic review. Obstetrical & Gynecological Survey, 64(2), 129-135. doi: 10.1097/OGX.0b013e3181932e5b
3	Su, L., Chong, Y., & Samuel, M. (2012). Carbetocin for preventing postpartum haemorrhage. Cochrane Database of Systematic Reviews(4), N.PAG-N.PAG.

	Misoprostol
1	Alfirevic, Z., & Weeks, A. (2014). Oral misoprostol for induction of labour. Cochrane Database of Systematic Reviews(6), N.PAG-N.PAG. doi: 10.1002/14651858.CD001338.pub3
2	Conde-Agudelo, A., Nieto, A., Rosas-Bermudez, A., & Romero, R. (2013). Misoprostol to reduce intraoperative and postoperative hemorrhage during cesarean delivery: a systematic review and metaanalysis. American Journal of Obstetrics & Gynecology, 209(1), 40.e41-40.e17. doi: 10.1016/j.ajog.2013.03.015
3	Langenbach, C. (2006). Misoprostol in preventing postpartum hemorrhage: A meta-analysis. International Journal of Gynecology & Obstetrics, 92(1), 10-18. doi: 10.1016/j.ijgo.2005.10.001
4	Hoefler, R., Silva, M., Galvao, T., Zaconeta, A., & Pereira, M. (2011). P1-282 Sublingual misoprostol for preventing postpartum haemorrhage: a systematic review. Journal of Epidemiology & Community Health, 65(Supplement 1), A144-A144.
5	Hofmeyr, G. J., Gülmezoglu, A. M., Novikova, N., & Lawrie Theresa, A. (2013). Postpartum misoprostol for preventing maternal mortality and morbidity. Cochrane Database of Systematic Reviews, (7). http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD008982.pub2/abstract doi:10.1002/14651858.CD008982.pub2
6	Hofmeyr, G. J., Gülmezoglu, A. M., Novikova, N., Linder, V., Ferreira, S., & Piaggio, G. (2009). Misoprostol to prevent and treat postpartum haemorrhage: a systematic review and meta-analysis of maternal deaths and dose-related effects. Bulletin of the World Health Organization, 87(9), 666-F.

7	Hofmeyr, G. J., Walraven, G., Gülmezoglu, A. M., Maholwana, B., Alfirevic, Z., & Villar, J. (2005). Misoprostol to treat postpartum haemorrhage: a systematic review. BJOG: An International Journal of Obstetrics & Gynaecology, 112(5), 547-553. doi: 10.1111/j.1471-0528.2004.00512.x
8	Hundley, V., Avan, B., Sullivan, C., & Graham, W. (2013). Should oral misoprostol be used to prevent postpartum haemorrhage in home-birth settings in low-resource countries? A systematic review of the evidence. BJOG: An International Journal of Obstetrics & Gynaecology, 120(3), 277-287. doi: 10.1111/1471-0528.12049
9	Oladapo Olufemi, T., Fawole, B., Blum, J., & Abalos, E. (2012). Advance misoprostol distribution for preventing and treating postpartum haemorrhage. Cochrane Database of Systematic Reviews, (2). http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD009336.pub2/abstract doi:10.1002/14651858.CD009336.pub2
10	Olefile, K. M., Khondowe, O., & M'Rithaa, D. (2013). Misoprostol for prevention and treatment of postpartum haemorrhage: A systematic review. Curationis, 36(1), 1-10. doi: 10.4102/curationis.v36i1.57
11	Smith, J. M., Gubin, R., Holston, M. M., Fullerton, J., & Prata, N. (2013). Misoprostol for postpartum hemorrhage prevention at home birth: an integrative review of global implementation experience to date. BMC Pregnancy Childbirth, 13, 44. doi: 10.1186/1471-2393-13-44
12	Tan, J., Cao, Q., He, G.-l., Cai, Y.-h., Yu, J.-j., Sun, X., & Li, Y.-p. (2016). Misoprostol versus ergometrine-oxytocin for preventing postpartum haemorrhage: a systematic review and meta-analysis of randomized controlled trials. Journal of Evidence-Based Medicine, 9(4), 194-204. doi: 10.1111/jebm.12201
13	Villar, J., Gulmezoglu, A. M., Hofmeyr, G. J., & Forna, F. (2002). Systematic review of randomized controlled trials of misoprostol to prevent postpartum hemorrhage. Obstet Gynecol, 100(6), 1301-1312.
14	Wei, S., & Fraser, W. D. (2008). Review: misoprostol and intramuscular prostaglandins do not prevent postpartum haemorrhage more than injectable uterotonics. Evidence Based Medicine, 13(3), 82-82.

	Tranexamic Acid
1	Alam, A., & Choi, S. (2015). Prophylactic Use of Tranexamic Acid for Postpartum Bleeding Outcomes: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Transfusion Medicine Reviews, 29(4), 231-241. doi: 10.1016/j.tmrv.2015.07.002
2	Faraoni, D., Carlier, C., Samama, C. M., Levy, J. H., & Ducloy-Bouthors, A. S. (2014). [Efficacy and safety of tranexamic acid administration for the prevention and/or the treatment of post-partum haemorrhage: a systematic review with meta-analysis]. Annales Francaises D'anesthesie Et De Reanimation, 33(11), 563-571. doi: 10.1016/j.annfar.2014.07.748

4	Heesen, M., Böhmer, J., Klöhr, S., Rossaint, R., Van De Velde, M., Dudenhausen, J. W., & Straube, S. (2014). Prophylactic tranexamic acid in parturients at low risk for post-partum haemorrhage: systematic review and meta-analysis. Acta Anaesthesiologica Scandinavica, 58(9), 1075-1085. doi: 10.1111/aas.12341
5	Ker, K., Shakur, H., & Roberts, I. (2016). Does tranexamic acid prevent postpartum haemorrhage? A systematic review of randomised controlled trials. BJOG: An International Journal of Obstetrics & Gynaecology, 123(11), 1745-1752. doi: 10.1111/1471-0528.14267
6	Li, C., Gong, Y., Dong, L., Xie, B., & Dai, Z. (2017). Is prophylactic tranexamic acid administration effective and safe for postpartum hemorrhage prevention?: A systematic review and meta-analysis. Medicine (Baltimore), 96(1), e5653. doi: 10.1097/md.0000000000005653
7	McClure, E. M., Jones, B., Rouse, D. J., Griffin, J. B., Kamath-Rayne, B. D., Downs, A., & Goldenberg, R. L. (2015). Tranexamic Acid to Reduce Postpartum Hemorrhage: A MANDATE Systematic Review and Analyses of Impact on Maternal Mortality. American Journal of Perinatology, 32(5), 469-474. doi: 10.1055/s-0034-1390347
8	Novikova, N., Hofmeyr, G. J., & Cluver, C. (2015). Tranexamic acid for preventing postpartum haemorrhage. Cochrane Database of Systematic Reviews, (6). http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD007872.pub3/abstract doi:10.1002/14651858.CD007872.pub3
9	Sentilhes, L., Brun, S., Madar, H., & Deneux-Tharaux, C. (2016). Tranexamic Acid for Prevention PPH: a Promising Drug But Today Only a Promising Drug...Alam A, Choi S. Prophylactic Use of Tranexamic Acid for Postpartum Bleeding Outcomes: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Transfus Med Rev. 2015 Oct;29(4):231-41. Transfusion Medicine Reviews, 30(2), 100-100. doi: 10.1016/j.tmrv.2016.01.003
10	Sentilhes, L., Brun, S., Madar, H., Merlot, B., Deneux-Tharaux, C., Sentilhes, L., & Brun, S. (2017). Re: Does tranexamic acid prevent postpartum haemorrhage? A systematic review of randomised controlled trials: A very welcome publication (Vol. 124, pp. 982-982). Malden, Massachusetts: Wiley-Blackwell.
11	Simonazzi, G., Bisulli, M., Saccone, G., Moro, E., Marshall, A., & Berghella, V. (2016). Tranexamic acid for preventing postpartum blood loss after cesarean delivery: a systematic review and meta-analysis of randomized controlled trials. Acta Obstetricia et Gynecologica Scandinavica, 95(1), 28-37.
12	Wang, H. Y., Hong, S. K., Duan, Y., & Yin, H. M. (2015). Tranexamic acid and blood loss during and after cesarean section: a meta-analysis. Journal of Perinatology, 35(10), 818-825. doi: 10.1038/jp.2015.93

APPENDIX B: Papers excluded from analysis: Surgical Interventions

1	Aya, A. G., Ducloy-Bouthors, A. S., Rugeri, L., & Gris, J. C. (2014). [Anesthetic management of severe or worsening postpartum hemorrhage]. J Gynecol Obstet Biol Reprod (Paris), 43(10), 1030-1062. doi: 10.1016/j.jgyn.2014.10.001
2	Baskett, T. F. (2007). Uterine Compression Sutures for Postpartum Hemorrhage. Obstetrics & Gynecology, 110(1), 68-71.
3	Boulay, G., & Hamza, J. (2004). [Anesthesic practices in patients with severe postpartum hemorrhage with persistent or worsening bleeding]. J Gynecol Obstet Biol Reprod (Paris), 33(8 Suppl), 4s80-84s88.
4	Chandraharan, E., & Arulkumaran, S. (2008). Surgical aspects of postpartum haemorrhage. Best Practice & Research Clinical Obstetrics & Gynaecology, 22(6), 1089-1102. doi: https://doi.org/10.1016/j.bpobgyn.2008.08.001
5	Conde-Agudelo, A., Nieto, A., Rosas-Bermudez, A., & Romero, R. (2013). Misoprostol to reduce intraoperative and postoperative hemorrhage during cesarean delivery: a systematic review and metaanalysis. American Journal of Obstetrics & Gynecology, 209(1), 40.e41-40.e17. doi: 10.1016/j.ajog.2013.03.015
6	Condous, G. S., & Arulkumaran, S. (2003). Medical and Conservative Surgical Management of Postpartum Hemorrhage. Journal of Obstetrics and Gynaecology Canada, 25(11), 931-936.
7	de la Cruz, C. Z., Thompson, E. L., O'Rourke, K., & Nembhard, W. N. (2015). Cesarean section and the risk of emergency peripartum hysterectomy in high-income countries: a systematic review. Archives of Gynecology and Obstetrics, 292(6), 1201-1215. doi: 10.1007/s00404-015-3790-2
8	Delotte, J., Novellas, S., Koh, C., Bongain, A., & Chevallier, P. (2009). Obstetrical prognosis and pregnancy outcome following pelvic arterial embolisation for post-partum hemorrhage. European Journal of Obstetrics & Gynecology and Reproductive Biology, 145(2), 129-132. doi: https://doi.org/10.1016/j.ejogrb.2009.03.013
9	d'Ercole, C., Shojai, R., Desbriere, R., Cravello, L., & Boubli, L. (2004). [Surgical management of primary postpartum hemorrhage]. J Gynecol Obstet Biol Reprod (Paris), 33(8 Suppl), 4s103-104s119.
10	Dhariwal, S. K., Khan, K. S., Allard, S., Wilson, M., Moore, P., Daniels, J., . . . Gardner, I. (2014). Does current evidence support the use of intraoperative cell salvage in reducing the need for blood transfusion in caesarean section? Current Opinion in Obstetrics and Gynecology, 26(6), 425-430. doi: 10.1097/GCO.0000000000000116
11	Doumouchtsis, S., Nikolopoulos, K., Talaulikar, V., Krishna, A., & Arulkumaran, S. (2014). Menstrual and fertility outcomes following the surgical management of postpartum haemorrhage: a systematic review. BJOG: An International Journal of Obstetrics & Gynaecology, 121(4), 382-388. doi: 10.1111/1471-0528.12546
12	Fotopoulou, C., & Dudenhausen, J. W. (2010). Uterine compression sutures for preserving fertility in severe postpartum haemorrhage: an overview 13 years after the first description. Journal Of Obstetrics And Gynaecology: The Journal Of The Institute Of Obstetrics And Gynaecology, 30(4), 339-349. doi: 10.3109/01443611003650233
13	Gizzo, S., Saccardi, C., Silvio Patrelli, T., Di Gangi, S., Breda, E., Fagherazzi, S., . . . Battista Nardelli, G. (2013). Fertility rate and subsequent pregnancy outcomes after conservative surgical techniques in postpartum hemorrhage: 15 years of literature. Fertility & Sterility, 99(7), 2097-2107. doi: 10.1016/j.fertnstert.2013.02.013
14	Homer, H., & Saridogan, E. (2010). Uterine artery embolization for fibroids is associated with an increased risk of miscarriage. Fertility & Sterility, 94(1), 324-330. doi: 10.1016/j.fertnstert.2009.02.069

15	Irani, M., & Deering, S. (2015). Challenges affecting access to cesarean delivery and strategies to overcome them in low-income countries. International Journal of Gynecology and Obstetrics, 131(1), 30-34. doi: 10.1016/j.ijgo.2015.04.036
16	Knight, M., Kurinczuk, J. J., Spark, P., Brocklehurst, P., Knight, M., Kurinczuk, J. J., . . . Brocklehurst, P. (2010). Emergency postpartum hysterectomy for uncontrolled postpartum bleeding: a systematic review (Vol. 115, pp. 1306-1307). Baltimore, Maryland: Lippincott Williams & Wilkins.
17	Machado, L. S. M. (2011). Emergency peripartum hysterectomy: Incidence, indications, risk factors and outcome. North American Journal of Medical Sciences, 3(8), 358-361. doi: 10.4297/najms.2011.358
18	Morrison, J. J., Galgon, R. E., Jansen, J. O., Cannon, J. W., Rasmussen, T. E., Eliason, J. L., . . . Rasmussen, T. E. (2016). A systematic review of the use of resuscitative endovascular balloon occlusion of the aorta in the management of hemorrhagic shock. Journal of Trauma & Acute Care Surgery, 80(2), 324-334. doi: 10.1097/TA.0000000000000913
19	Myers, T. T. (2016). Uterine Artery Embolization for Postpartum Hemorrhage. Journal of Radiology Nursing, 35(2), 142-145. doi: https://doi.org/10.1016/j.jradnu.2016.01.008
20	Pirard, C., Squifflet, J., Gilles, A., & Donnez, J. (2002). Uterine necrosis and sepsis after vascular embolization and surgical ligation in a patient with postpartum hemorrhage. Fertil Steril, 78(2), 412-413. doi: https://doi.org/10.1016/S0015-0282(02)03229-6
21	Poujade, O., Ceccaldi, P., Davitian, C., Amate, P., Chatel, P., Khater, C., Aflak, N., Vilgrain, V. and Luton, D. (2013). Uterine necrosis following pelvic arterial embolization for post-partum hemorrhage: review of the literature. European Journal of Obstetrics & Gynecology and Reproductive Biology, 170(2), pp. 309-314.doi: https://doi.org/10.1016/j.ejogrb.2013.07.016
22	Ruiz Labarta, F. J., Pintado Recarte, M. P., Alvarez Luque, A., Joigneau Prieto, L., Perez Martín, L., Gonzalez Leyte, M., . . . De Leon-Luis, J. (2016). Outcomes of pelvic arterial embolization in the management of postpartum haemorrhage: a case series study and systematic review. European Journal Of Obstetrics, Gynecology, And Reproductive Biology, 206, 12-21. doi: 10.1016/j.ejogrb.2016.07.510
23	Shah, M., & Wright, J. D. (2009). Surgical Intervention in the Management of Postpartum Hemorrhage. Seminars in Perinatology, 33(2), 109-115. doi: https://doi.org/10.1053/j.semperi.2008.12.006
24	Shub, A., Walker, S. P., Shub, A., & Walker, S. P. (2015). Planned early delivery versus expectant management for monoamniotic twins. Cochrane Database of Systematic Reviews(4), N.PAG-N.PAG. doi: 10.1002/14651858.CD008820.pub2
25	Soro, M.-A. P., Denys, A., Rham, M., Baud, D., & de Rham, M. (2017). Short & long term adverse outcomes after arterial embolisation for the treatment of postpartum haemorrhage: a systematic review. European Radiology, 27(2), 749-762. doi: 10.1007/s00330-016-4395-2
26	Sud, S., Maheshwari, A., & Bhattacharya, S. (2009). Obstetric outcomes after treatment of fibroids by uterine artery embolization: a systematic review. Expert Review of Obstetrics & Gynecology, 4(4), 429-441.
27	Winograd, R. H. (2008). Uterine artery embolization for postpartum hemorrhage. Best Pract Res Clin Obstet Gynaecol, 22(6), 1119-1132. doi: 10.1016/j.bpobgyn.2008.08.009

28	Xodo, S., Saccone, G., Cromi, A., Ozcan, P., Spagnolo, E., & Berghella, V. (2016). Cephalad-caudad versus transverse blunt expansion of the low transverse uterine incision during cesarean delivery. European Journal of Obstetrics & Gynecology & Reproductive Biology, 202, 75-80. doi: 10.1016/j.ejogrb.2016.04.035
29	Yue-Zhou, Y., Xu-Ping, Y., & Xiao-Xi, S. (2017). Maternal and neonatal morbidity: repeat Cesarean versus a trial of labour after previous Cesarean delivery. Clinical & Investigative Medicine, 40(3), E135-E145.
30	Uterine artery embolization for emergent management of postpartum hemorrhage associated with placenta accrete. Hye Na Jung1, Sung Wook Shin1, Suk-Joo Choi2, Sung Ki Cho1, Kwang Bo Park1, Hong Suk Park1, Minho Kang1, Sung Wook Choo1, Young Soo Do1, In-wook Choo1. Acta Radiologica, vol. 52, 6: pp. 638-642. , First Published July 1, 2011.
31	Massive postpartum hemorrhage treated with transcatheter arterial embolization: technical aspects and long-term effects on fertility and menstrual cycle. L.-G. Eriksson, A. Mulic-Lutvica, L. Jangland, R. Nyman. Acta Radiologica, vol. 48, 6: pp. 635-642. , First Published Jul 1, 2007.
32	Uterine Artery Embolization for Heavy Menstrual Bleeding. Jonathan Moss*1, Andrew Christie1. Women's Health, vol. 12, 1: pp. 71-77. , First Published January 1, 2016.

APPENDIX C: AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both

1. Did the research questions and inclusion criteria for the review include the components of PICO?

For Yes:	Optional (recommended)	
Population Intervention Comparator group Outcome	Timeframe for follow-up	Yes No

2. Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?

For Partial Yes:	For Yes:	
The authors state that they had a written protocol or guide that included ALL the following:	As for partial yes, plus the protocol should be registered and should also have specified:	
		Yes
review question(s)	a meta-analysis/synthesis plan,	Partial Yes
a search strategy	if appropriate, *and*	No
inclusion/exclusion criteria	a plan for investigating causes of heterogeneity	
a risk of bias assessment	justification for any deviations from the protocol	

3. Did the review authors explain their selection of the study designs for inclusion in the review?

For Yes, the review should satisfy ONE of the following:	
Explanation for including only RCTs	Yes
OR *Explanation for* including only NRSI	No
OR *Explanation for* including both RCTs and NRSI	

4. Did the review authors use a comprehensive literature search strategy?

For Partial Yes (all the following):	For Yes, should also have (all the following):	
searched at least 2 databases (relevant to research question)	searched the reference lists / bibliographies of included studies	Yes
provided key word and/or search strategy	searched trial/study registries	Partial Yes
justified publication restrictions (e.g. language)	included/consulted content experts in the field	No
	where relevant, searched for grey literature	
	conducted search within 24 months of completion of the review	

5. Did the review authors perform study selection in duplicate?

For Yes, either ONE of the following:	
at least two reviewers independently agreed on selection of eligible studies and achieved consensus on which studies to include	Yes
OR two reviewers selected a sample of eligible studies and achieved good agreement (at least 80 percent), with the remainder selected by one reviewer.	No

6. Did the review authors perform data extraction in duplicate?

For Yes, either ONE of the following: at least two reviewers achieved consensus on which data to extract from included studies OR two reviewers extracted data from a sample of eligible studies and achieved good agreement (at least 80 percent), with the remainder extracted by one reviewer.	Yes No

7. Did the review authors provide a list of excluded studies and justify the exclusions?

For Partial Yes: provided a list of all potentially relevant studies that were read in full-text form but excluded from the review	For Yes, must also have: Justified the exclusion from the review of each potentially relevant study	Yes Partial Yes No

8. Did the review authors describe the included studies in adequate detail?

For Partial Yes (ALL the following): described populations described interventions described comparators described outcomes described research designs	For Yes, should also have ALL the following: described population in detail described intervention in detail (including doses where relevant) described comparator in detail (including doses where relevant) described study's setting timeframe for follow-up	Yes Partial Yes No

9. Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?

RCTs For Partial Yes, must have assessed RoB from unconcealed allocation, *and* lack of blinding of patients and assessors when assessing outcomes (unnecessary for objective outcomes such as all-cause mortality)	For Yes, must also have assessed RoB from: allocation sequence that was not truly random, *and* selection of the reported result from among multiple measurements or analyses of a specified outcome	Yes Partial Yes No Includes only NRSI
NRSI For Partial Yes, must have assessed RoB: from confounding, *and* from selection bias	For Yes, must also have assessed RoB: methods used to ascertain exposures and outcomes, *and* selection of the reported result from among multiple measurements or analyses of a specified outcome	Yes Partial Yes No Includes only RCTs

10. Did the review authors report on the sources of funding for the studies included in the review?

For Yes Must have reported on the sources of funding for individual studies included in the review. Note: Reporting that the reviewers looked for this information but it was not reported by study authors also qualifies	Yes No

11. If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?

RCTs	
For Yes:	
The authors justified combining the data in a meta-analysis	Yes
AND they used an appropriate weighted technique to combine study results and adjusted for heterogeneity if present.	No
AND investigated the causes of any heterogeneity	No meta-analysis conducted
For NRSI	
For Yes:	
The authors justified combining the data in a meta-analysis	Yes
AND they used an appropriate weighted technique to combine study results, adjusting for heterogeneity if present	No
AND they statistically combined effect estimates from NRSI that were adjusted for confounding, rather than combining raw data, or justified combining raw data when adjusted effect estimates were not available	No meta-analysis conducted
AND they reported separate summary estimates for RCTs and NRSI separately when both were included in the review	

12. If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?

For Yes:	
included only low risk of bias RCTs	Yes
OR, if the pooled estimate was based on RCTs and/or NRSI at variable RoB, the authors performed analyses to investigate possible impact of RoB on summary estimates of effect.	No
	No meta-analysis conducted

13. Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?

For Yes:	
included only low risk of bias RCTs	Yes
OR, if RCTs with moderate or high RoB, or NRSI were included the review provided a discussion of the likely impact of RoB on the results	No

14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?

For Yes:	
There was no significant heterogeneity in the results	
OR if heterogeneity was present the authors performed an investigation of sources of any heterogeneity in the results and discussed the impact of this on the results of the review	Yes
	No

15. If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?

For Yes:	
performed graphical or statistical tests for publication bias and discussed the likelihood and magnitude of impact of publication bias	Yes
	No
	No meta-analysis conducted

AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both

16. Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	
For Yes:	
The authors reported no competing interests OR	Yes
The authors described their funding sources and how they managed potential conflicts of interest	No

Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, Moher D, Tugwell P, Welch V, Kristjansson E, Henry DA. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ. 2017 Sep 21;358:j4008.

APPENDIX D: PRISMA GUIDELINE CHECKLIST

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2)	

		for each meta-analysis.	

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement.
PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: **www.prisma-statement.org**.

APPENDIX E: ELECTRONIC SEARCH STRATEGY

Database	Type of Search	Search Terms	No. of articles	Date of search	Comments/Field Notes
Google Scholar		Systematic Review AND postpartum hemorrhage OR postpartum haemorrhage	5	16/08/2017	This was done right at the end to see whether any articles were missed. At page 2, duplicates kept coming up,so I was satisfied that the search had reached saturation. Five reviews were saved from the initial pages. 18 000 results were reported
Pubmed	MESH	Systematic Review AND postpartum hemorrhage OR postpartum haemorrhage	0	16/08/2017	None
Pubmed ALL TERMS - FILTER	Filtered	Filters applied: systematic reviews, meta-analysis, titiles only. Search Terms ((systematic review[Title]) AND postpartum heamorrhage[Title]) OR postpartum hemorrhage[Title]	61	16/08/2017	None
Ebsco: Academic Search Complete, CINAHL, MEDLINE, E- Journals		Systematic Review AND postpartum hemorrhage OR postpartum haemorrhage	197	16/08/2017	None
Ebsco: Academic Search Complete, CINAHL, MEDLINE, E- Journals		Systematic Review AND postpartum hemorrhage AND management	12 all included in 197	16/08/2017	None
Ebsco: Academic Search Complete, CINAHL, MEDLINE, E- Journals		Systematic Review AND postpartum hemorrhage AND assessment	all included in 197	16/08/2017	None
Ebsco: Academic Search Complete, CINAHL, MEDLINE, E- Journals		Systematic Review AND postpartum hemorrhage AND pharmaceutical	all included in 197	16/08/2017	None
Science Direct	Mixed				None
Cochrane Controlled Trials Register		postpartum heamorrhage OR postpartum hemorrhage	28	16/08/2017	None

Database	Type of Search	Search Terms	No. of articles	Date of search	Comments/Field Notes
JBI		postpartum heamorrhage OR postpartum hemorrhage	5	16/08/2017	http://journals.lww.com/jbisrir/pages/results.aspx?txtkeywords=postpartum+hemorrhage, 1 post C/S intervention, 4 non PPH (waterbirth, IOL, maternal mortality, preterm labour)
Global Library of Womens Medicine (GLOWM)		postpartum heamorrhage OR postpartum hemorrhage	23	16/08/2017	no SR's
Allied and Complementary Medicine Database		postpartum heamorrhage OR postpartum hemorrhage	13		no SRs relevant for inclusion
British Nursing Index		no access	0		None
EMBASE		no access	0		None
Sage Journals Online		postpartum hemorrhage OR postpartum heamorrhage OR obstetric haemorrhage AND systematic review	144	16/08/2017	limited search to 2007-2017, 156 not systematic reviews, not on PPH. Search is saved under login on Sage. One article for abstract review, saved in folder on laptop not able to export to endnote
SCOPUS		postpartum hemorrhage OR postpartum heamorrhage OR obstetric haemorrhage AND systematic review	62	16/08/2017	limited search to 2007-2017, review articles only,
Science Direct		postpartum hemorrhage OR postpartum heamorrhage OR obstetric haemorrhage AND systematic review	40	16/08/2017	limited search to 2007-2017, review articles only,

APPENDIX F: DATA EXTRACTION SHEETS

Characteristics of Included Studies

Identifier	Study description
	Country:
	Period of data collection/enrollment:
	Birth Setting:
	Facility characteristics:
	Funding:
	Design of included studies:
	# data bases searched:
	Gray literature searched:
	# studies included:
	# RCT's included in analysis:
	Instrument to assess scientific quality:
	Countries:
	Recognition of bias:
	Limitations:

PICOS across Studies

Identifier	Inclusion/exclusion criteria	Participants	Intervention	Outcomes
Author:	definition of PPH:	Age:	Description of intervention:	Estimated blood loss:
	Inclusion criteria:	Gravidity/parity:	Groups:	
	Exclusion criteria:	Gestation at birth:	N at treatment:	Transfusion:
	Method of blood loss measurement:	Mode of birth:	N at follow-up:	Anemia:
		BMI:	Duration of treatment:	Surgical intervention required:
		Baseline HB:	timing of treatment: delivery	Length of hospital stay:
		Singleton pregnancy:	Order of treatment:	Harms of intervention:NR
		Multiple pregnancy:	Length of follow-up:	Other maternal morbidities:
				Maternal mortality:
				Preterm birth:
				Neonatal morbidity:
				Neonatal mortality:

APPENDIX G: All excluded articles with reasons

	TABLE OF EXCLUDED STUDIES AFTER ABSTRACTS REVIEWED	Reason
1	Diaz, V., Abalos, E., & Carroli, G. (2014). Methods for blood loss estimation after vaginal birth. Cochrane Database of Systematic Reviews, (2). http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010980/abstract doi:10.1002/14651858.CD010980	Protocol only-no data available at time of writing up review
2	Gallos Ioannis, D., Williams Helen, M., Price Malcolm, J., Merriel, A., Gee, H., Lissauer, D., . . . Coomarasamy, A. (2015). Uterotonic agents for preventing postpartum haemorrhage: a network meta-analysis. Cochrane Database of Systematic Reviews, (5). http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD011689/abstract doi:10.1002/14651858.CD011689	Protocol only-no data available at time of writing up review
3	Jackson, K. W., Allbert, J. R., Schemmer, G. K., Elliot, M., Humphrey, A., & Taylor, J. (2001). A randomized controlled trial comparing oxytocin administration before and after placental delivery in the prevention of postpartum hemorrhage. Am J Obstet Gynecol, 185(4), 873-877. http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/608/CN-00374608/frame.html doi:10.1067/mob.2001.117363	Exclusion based on type of study - this is an RCT not a systematic review
4	Kataoka, Y., Yaju, Y., Hiruta, A., Horiuchi, S., & Mori, R. (2015). Homeopathy for reducing blood loss in the third stage of labour. Cochrane Database of Systematic Reviews, (4). http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD011635/abstract doi:10.1002/14651858.CD011635	Protocol only-no data available at time of writing up review
5	Kodkany, B. S., & Derman, R. J. (2006). Evidence-based interventions to prevent postpartum hemorrhage: Translating research into practice. Int J Gynaecol Obstet, 94 Suppl 2, S114-115. doi: 10.1016/s0020-7292(06)60002-7	Keynote speech - exclude based on S: no data available for inclusion in review
6	Likis, F. E., Sathe, N. A., Morgans, A. K., Hartmann, K. E., Young, J. L., Carlson-Bremer, D., . . . Andrews, J. (2015). AHRQ Comparative Effectiveness Reviews Management of Postpartum Hemorrhage. Rockville (MD): Agency for Healthcare Research and Quality (US).	Intervention not appropriate for inclusion: pharmaceutical drugs midwives cannot administer AND surgical interventions
7	McDonald, S. J., Abbott, J. M., & Higgins, S. P. (2004). Prophylactic ergometrine-oxytocin versus oxytocin for the third stage of labour. Cochrane Database of Systematic Reviews, N.PAG-N.PAG.	Intervention: management of 3rd stage of labour excluded
8	Penn, A. W., Beam, N. K., & Azman, H. (2015). Non-pneumatic anti-shock garment (NASG) as a first aid for preventing or reversing hypovolemic shock secondary to obstetric hemorrhage. Cochrane Database of Systematic Reviews(5). doi: 10.1002/14651858.CD011700	Protocol only-no data available at time of writing up review
9	Tuncalp, O., Souza, J. P., & Gulmezoglu, M. (2013). New WHO recommendations on prevention and treatment of postpartum hemorrhage. Int J Gynaecol Obstet, 123(3), 254-256. doi: 10.1016/j.ijgo.2013.06.024	WHO Guideline - exclude based on S: no data available for inclusion in review
10	Walraven, G., Wanyonyi, S., & Stones, W. (2008). Management of post-partum hemorrhage in low-income countries. Best Practice & Research Clinical Obstetrics & Gynaecology, 22(6), 1013-1023. doi: https://doi.org/10.1016/j.bpobgyn.2008.08.002	Systems/policy recommendations - exclude based on S: no data available for inclusion in review
11	Zelop, C. M. (2011). Postpartum hemorrhage: becoming more evidence-based. Obstet Gynecol, 117(1), 3-5. doi: 10.1097/AOG.0b	Comment on another article- exclude based on S: no data available for inclusion in review