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THESIS

Title of project:

The Causes and Prevention of Maternal Mortality in Low and Middle Income Countries: The Role of Ultrasound and The Role of Novel Postpartum Haemorrhage Treatments

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Statement of Originality

This is to certify that to the best of my knowledge; the content of this thesis is my own work. This thesis has not been submitted for any degree or other purposes.

I certify that the intellectual content of this thesis is the product of my own work and that all the assistance received in preparing this thesis and sources have been acknowledged.

Name: YUSIF YAKUB

Date: 16TH SEPTEMBER 2025

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‘Women are not dying because of diseases we cannot treat. They are dying because societies have yet to make the decision that their lives are worth saving’

- Professor Mahmoud Fathallah

ABBREVIATIONS

aOR	Adjusted Odd Ratio
AFI	Amniotic Fluid Index
ANC	Antenatal Clinic
APH	Antepartum haemorrhage
BPD	Biparietal Diameter
CHPS	Community Based Health Programs
CPD	Cephalopelvic Disproportion
CI	Cephalic Index
CRF	Case Report Form
DHS	Demographic Health Survey
DMC	Data Monitoring Committee
EmONC	Emergency Obstetric and Newborn Care
EPAU	Early Pregnancy Assessment Unit
FGR	Fetal Growth Restriction
GCP	Good Clinical Practice
GHS	Ghana Health Service
GMHS	Ghana Maternal Health Survey
HDP	Hypertensive Disorders of Pregnancy
ICD	International Statistical Classification of Diseases
LMIC	Low- and Middle-Income Country
MMR	Maternal Mortality Ratio
NOS	Newcastle-Ottawa Scale
OBGYN	Obstetrics and Gynaecology
OFD	Occipito-Frontal Diameter
OR	Odd Ratio

POCUS	Point-of-Care Ultrasound
PPH	Postpartum Haemorrhage
PRISMA	Preferred Reporting Items for Systematic reviews and Meta-Analyses
RCT	Randomised Controlled Trial
RR	Relative Risk
SIGN	Scottish Intercollegiate Guidelines Network
SOP	Standard Operating Procedures
SVD	Spontaneous Vaginal Delivery
TVS	Trans Vaginal Scanning
VE	Vaginal Examination
WHO	World Health Organization

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1.1 Introduction

Maternal mortality continues to pose a critical public health challenge in low- and middle-income countries (LMICs), despite considerable global initiatives aimed at reducing them (1). Severe maternal morbidity remains a major concern, especially in sub-Saharan Africa (2). Despite remarkable progress in healthcare and medical technology, the tragic occurrence of maternal deaths during pregnancy or in the postpartum period remains a crucial challenge in this specific region (3).

Sub-Saharan countries have the highest maternal mortality and morbidity ratio (MMR) in the world, with two-thirds of the world's maternal mortality (4, 5). More than half of these maternal deaths are caused by pregnancy related complications including postpartum haemorrhage (6). It is estimated that 99% of maternal deaths happen in developing countries and particularly in sub-Saharan Africa (7).

The elevated levels of maternal mortality in sub-Saharan Africa are influenced by factors such as inadequate healthcare access and infrastructure, limited, insufficient skilled healthcare providers, cultural beliefs, inadequate antenatal care, social inequalities and poverty (8).

Obstetric care for pregnant women has undergone a revolutionary transformation due to the advent of ultrasound technology, which has bestowed invaluable insights into both prenatal care and maternal health (9, 10). Initially recognized for its role in monitoring fetal growth (11) and identifying congenital abnormalities (12), the utilization of ultrasound during pregnancy has transcended its original purpose. Recent studies indicate that ultrasound holds the potential to assume a pivotal role in evaluating maternal well-being by identifying potential complications that could otherwise result in maternal mortality (13).

Ultrasound has the potential to detect quite early any anomalies associated with pregnancies such as malpresentation in multiple gestations, ectopic gestation, placenta praevia and placental abruption (14), and this enables early intervention, thus having the ability to mitigate maternal mortality and morbidity rates in the sub-Saharan region (15, 16).

This literature review critically examines the underlying causes of maternal mortality in LMICs, highlighting the preventative roles of obstetric ultrasound and novel interventions for postpartum haemorrhage (PPH). There is a focus on sub-Saharan Africa where maternal mortality is highest, and particularly on Ghana, my home country.

1. 2 Maternal mortality and morbidity: Global Burden

To understand global patterns in maternal mortality, countries are often categorized by economic status. The World Bank uses gross national income (GNI) per capita to classify economies annually, providing a consistent basis for comparing healthcare resources and development levels across countries.

Low-income countries (LICs) are defined as those with a GNI per capita of $1,135 or less; lower-middle-income countries (LMICs) range from $1,136 to $4,465; upper-middle-income countries (UMICs) fall between $4,466 and $13,845; and high-income countries (HICs) have a GNI per capita of $13,846 or more (17). Although widely adopted, this classification has faced criticism for potentially reinforcing divisions and contributing to a sense of "otherness" within global health research discourse (18).

Maternal mortality remains a pressing issue globally, encompassing women's demise during and after pregnancy, within 42 days after the pregnancy (19). In the year 2020, a staggering tally of approximately 287,000 women lost their lives under such circumstances. This figure, deemed intolerably elevated, predominantly transpired within nations classified as developing countries (20). Despite a global decline, LMICs still face high maternal mortality ratios, with sub-Saharan Africa experiencing over 450 deaths per 100,000 live births (21). Maternal deaths are a significant public health issue in Ghana, with a maternal mortality ratio of 604 per 100,000 live births (22).

Despite advances in medical technology, the data on maternal mortality continues to be unacceptably high, with several hundreds of women dying every day from pregnancy related causes which could otherwise be prevented (23). Figure 1 shows the change in MMR in various global regions over time, between 1990 and 2015.

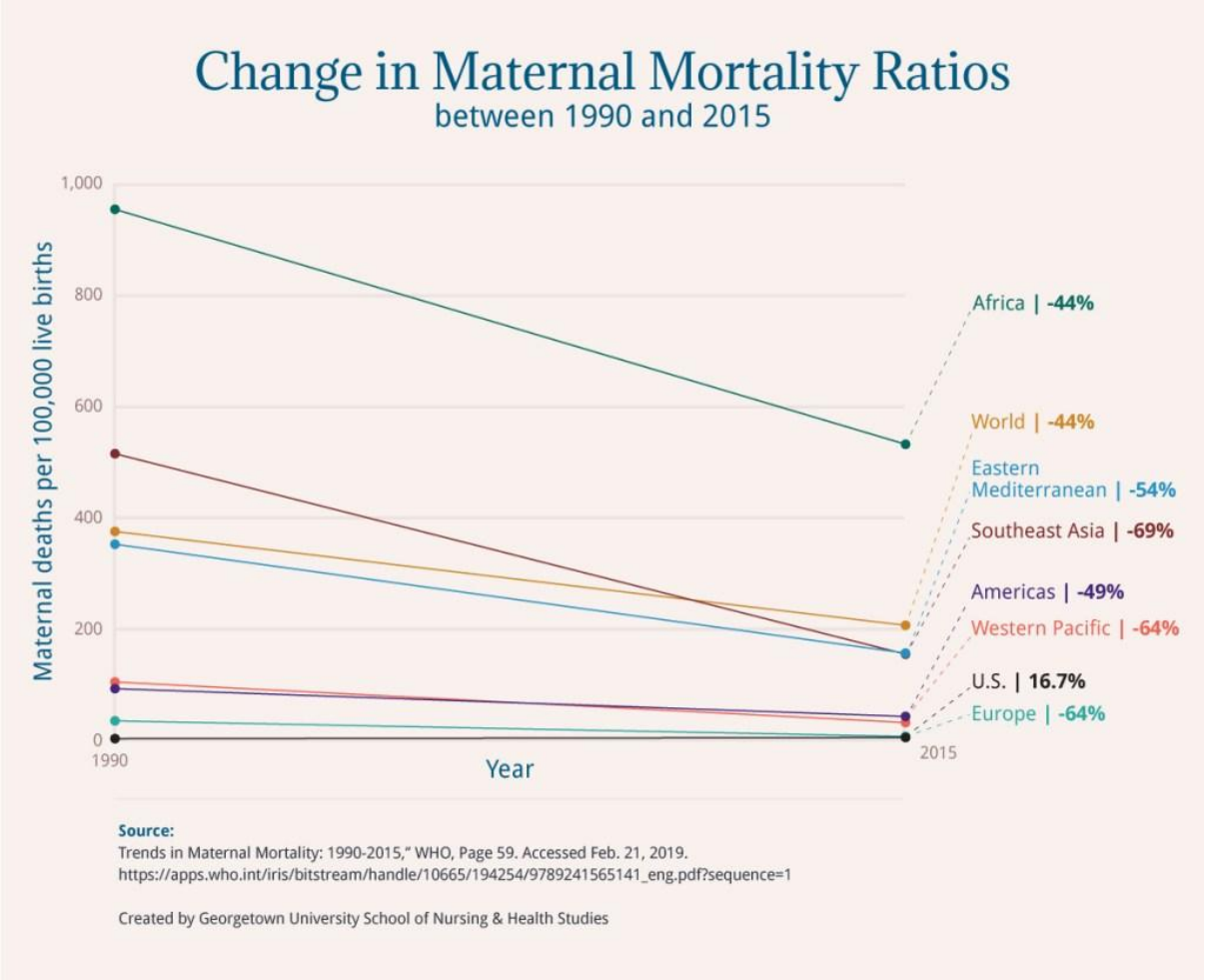

Figure 1: Changes in maternal mortality ratios between 1990 and 2015

Reporting Maternal Mortality

The quality of data on maternal mortality is critical. Within certain regions, instances of maternal mortality might evade proper reporting or be inaccurately classified, resulting in an incomplete grasp of the extent of this burden (24, 25). Accurate and comprehensive data are essential in enabling informed policy formulation and the allocation of resources that are necessary to tackle this challenge with efficacy (26, 27).

Sub-Saharan Africa carries the world's heaviest maternal mortality burden; nonetheless, obtaining precise data on maternal mortality in this region remains a challenge, hampering effective interventions. One key factor contributing to the reporting shortfall in sub-Saharan Africa is the historical utilization of inconsistent and unreliable methods for measuring maternal mortality (28). These unreliable methods include poor manual

bookkeeping records and loss of patients' data. This could be improved through electronic or digital health management record systems with cloud storage.

1.3 Disparities between high income and low income countries

Gender bias

Gender biases can have a significant impact on maternity care. In the United States, gender biases in medical establishments are reported to influence the inadequacy of maternal care (16, 29).

Gender disparities have been associated with higher maternal mortality rates. Matthew et al. 2020, investigated the long-term effects of gender inequality and maternal mortality on inclusive economic growth in Nigeria which demonstrated a positive correlation between maternal mortality rates and gender bias as measured by the Gender Inequality Index. Equal opportunities for both men and women, can play a pivotal role in mitigating gender-based disparities in maternal mortality (30). The study highlights the magnitude of issues faced by women, and it does not provide a specific count of women or births within the dataset used for the study.

While an exact quantitative figure of how much maternal mortality could have been avoided in a more gender-equal society is not provided in this study, the analysis suggests that considerable reductions in maternal mortality could be achieved through enhanced gender equality measures, including increased female education, access to healthcare, and empowerment initiatives, which collectively would save many lives (30).

In certain nations, young girls may face nutritional disparities when compared to boys. An Indian study revealed that girls received shorter breastfeeding durations than boys, particularly emphasizing the varying probabilities of discontinuing breastfeeding among female second-born children aged 12 to 36 months (31). Inadequate nutrition during infancy and early childhood can contribute to an elevated likelihood of maternal death in the future (31).

Gender biases may result in a lack of recognition and comprehension of the distinct requirements and obstacles that women encounter throughout pregnancy and childbirth, potentially leading to insufficient assistance and healthcare for expectant mothers (32).

Gender inequities profoundly shape womens' access to maternal healthcare in sub-Saharan Africa, operating through complex decision-making dynamics and entrenched social power structures. Evidence indicates that intra-familial decision-making severely restricts women's autonomy, with husbands responsible for healthcare decisions in 49.2% of cases where women were unable to access maternal services, mothers-in-law in 16.2%, and women themselves in only 2.7% of cases (33). Gender norms that condone violence against women have been shown to diminish the utilization of skilled birth attendants and antenatal care in countries such as Ghana, Uganda, and Tanzania (34).

Multi-country analyses demonstrate that multiple dimensions of gender inequity apart from decision-making autonomy, exert a significant influence on the utilization of reproductive health services (35). A comprehensive study of 35 sub-Saharan African countries found that gender relations and women empowerment components were significantly associated with adequate antenatal care and institutional delivery, with substantial between country and community variations (36). These findings underscore the importance of designing interventions that engage multiple stakeholders beyond individual women, addressing broader social and structural determinants of maternal health.

Armed conflict and humanitarian crises

Armed conflicts and humanitarian crises greatly increase maternal deaths in developing countries by disrupting healthcare services. Hospitals and clinics may be damaged, there are fewer trained health workers, and medical supplies run out (37).

Pregnant women often struggle to get care, making it harder to manage complications during pregnancy or childbirth. Living in unsafe conditions due to displacement can lead to malnutrition and infections. Violence and instability during these crises also put pregnant women at greater risk, causing more preventable deaths.

Women and children experience significant illness and death due to armed conflicts (38). Armed conflicts can lead to a considerable count of avoidable maternal and child fatalities on a global scale, with mortality rates rising during such conflicts (39).

Humanitarian crises and fragile settings have a profound impact on maternal and newborn health outcomes. In 2015, an estimated 303,000 maternal deaths occurred worldwide, with approximately 61% of these deaths taking place in countries affected by fragility and crisis (40). The attacks on educational and healthcare facilities have resulted

in the disruption of vital services, consequently increasing the levels of women and newborn deaths, and the incidence of infectious diseases (41).

In regions affected by armed conflict or humanitarian crises, access to healthcare becomes severely limited, and expectant mothers are exposed to elevated risks of maternal mortality due to disruptions in healthcare services and infrastructure (42, 43).

The civil war in Sierra Leone (1991–2002) significantly disrupted the country's health system, leading to thousands of avoidable maternal deaths. According to a World Bank study, the MMR increased by over 75% during the conflict, rising from approximately 970 to nearly 2,000 deaths per 100,000 live births by the year 2000 (44). This surge represents one of the highest maternal mortality rates globally at the time (45). Based on estimated birth rates, the total number of avoidable maternal deaths over the 11-year conflict is believed to range between 11,000 and 16,000 (44).

In Sierra Leone during the war, an estimated 75% of health facilities were destroyed, drastically reducing access to skilled birth attendants and emergency obstetric care. Empirical studies show that maternal mortality risk increased significantly during conflict, with micro-level analyses across Sub-Saharan Africa linking armed conflict exposure to elevated likelihood of maternal death (46).

Over the past two decades, protracted conflict in South Sudan, particularly the civil war from 2013 to 2021, has been strongly associated with elevated maternal mortality. During the peak conflict years, the MMR reached approximately 2,054 deaths per 100,000 live births, among the highest globally. As hostilities eased and limited health system recovery began, the MMR declined to about 1,223 deaths per 100,000 by 2020. This represents a 68% relative increase in maternal mortality during conflict periods, likely attributable to the destruction of health infrastructure, reduced access to skilled birth attendants, and large-scale displacement of pregnant women (47-49). Regional case studies have documented sharp declines in antenatal visits and facility-based deliveries during conflict, further underscoring the link between violence and preventable maternal deaths (49).

Regular and comprehensive examination of the root causes of maternal mortality in sub-Saharan Africa is imperative to inform targeted interventions (50).

Malnutrition and Anaemia

Within the sub-Saharan region, malnutrition and anaemia stand as prominent contributors to maternal mortality (41).

In sub-Saharan Africa, a region grappling with critically insufficient blood supply, severe haemorrhage emerges as a prominent contributor to maternal mortality (51). The insufficiency of blood for urgent transfusions is a substantial factor contributing to maternal mortality in the area, though it remains inadequately quantified and under-studied (51). Maternal anaemia increases susceptibility to death due to obstetric haemorrhage as there are lower reserves of haemoglobin, required to carry essential oxygen to the body.

Iron deficiency anaemia is frequently observed in pregnant women, and its influence on maternal health is extensively documented. Severe anaemia can result in circulatory issues, heightening the risk of maternal deaths (51).

Iron deficiency anaemia stands as a significant contributor to the mortality and severe illness of expectant mothers (52). An examination of 23 reports revealed that anaemia directly contributed to maternal deaths, ranging from 1 to 46 percent, with an average of 10 percent (52).

Pregnant women in sub-Saharan Africa are at heightened risk of anaemia due to a range of interrelated factors. Malaria is a major contributor, with studies showing that 63% of pregnant women in Ghana carry malaria parasites, and ecological exposure to malaria is strongly associated with increased anaemia risk (53, 54). HIV infection further heightens the risk of anaemia by contributing to bone marrow suppression and chronic systemic inflammation (54, 55).

Nutritional deficiencies contribute differently across sub-Saharan Africa. In Malawi, for instance, only 23% of anaemic pregnant women presented with isolated iron deficiency, whereas 32% had combined deficiencies involving iron, folate, vitamin B12, and vitamin A (56). Nonetheless, iron deficiency appears to be a comparatively less significant contributor to anaemia in certain populations, such as those in Ghana (53).

Inherited blood disorders make a modest contribution to the overall anaemia burden. Hemoglobinopathies are relatively common, with sickle cell trait identified in approximately 14% of Ghanaian women. However, most genetic variants exert minimal impact on anaemia risk, except for homozygous alpha-thalassemia, which is associated with a more pronounced effect (53).

Poverty and Socioeconomic disparity

Maternal mortality presents a substantial public health challenge in sub-Saharan Africa, with poverty and socioeconomic disparities serving as pivotal challenges and root causes of this pressing concern (24). Economic hardship can constrain healthcare accessibility, resulting in insufficient prenatal care and a dearth of access to emergency obstetric services (24, 25).

Persistent maternal mortality in rural areas is largely driven by economic hardship, entrenched gender disparities, and weak healthcare systems that limit access to essential maternal services (57). Maternal healthcare utilization is also shaped by social factors such as women's decision-making power, place of residence, and the availability of emotional and community support (58).

Malnutrition stands as a prominent factor impacting the well-being of expectant mothers in developing nations. Inadequate nutrition throughout pregnancy can give rise to complications such as anaemia and pre-eclampsia, increasing the risk of maternal death, as well as fetal growth restriction, preterm birth and future adult disease in the newborn influenced by the intra-uterine environment (3, 59).

Cultural Dynamics of Family and Women's Health in Sub-Saharan Africa.

Cultural factors play a critical role in shaping maternal health outcomes and patterns of family formation in sub-Saharan Africa. Women's subordinate position within many societies, reflected in limited autonomy in decision-making, early and often coerced marriages, and persistent gender-based inequities in access to food and healthcare, substantially exacerbates maternal vulnerability (60). These structural disadvantages increase the likelihood of life-threatening complications such as obstructed labour, haemorrhage, and sepsis, which remain leading causes of maternal mortality in the region. Furthermore, traditional beliefs, harmful cultural practices, and reliance on unskilled birth attendants frequently delay timely access to emergency obstetric care (60).

Traditional practices including female genital circumcision, restrictive dietary taboos during pregnancy, and harmful delivery rituals, further compound maternal health risks (61). Cultural beliefs surrounding witchcraft, stigma against caesarean sections, and

preference for traditional birth attendants over skilled medical care create barriers to maternal health service utilization (61, 62).

Research on cultural perspectives of family formation in sub-Saharan Africa reveals considerable heterogeneity across regions and ethnic groups, yet traditional belief systems consistently exert a strong influence on fertility behaviours. The region continues to record the highest fertility rates globally, averaging 6–7 children per woman, largely sustained by cultural preferences for large families and deeply rooted social expectations that link women's social value to childbearing. High fertility is often regarded as a source of economic security, social prestige, and continuity of lineage, reinforcing pressure on women to bear multiple children (63).

However, this cultural emphasis on high fertility significantly increases maternal health risks by elevating the likelihood of closely spaced pregnancies, maternal depletion, and complications during childbirth (64). Moreover, these norms may limit women's utilization of family planning services and antenatal care, thereby compounding maternal morbidity and mortality (65). Understanding the intersection between cultural norms and fertility patterns is therefore essential for developing effective, culturally responsive strategies to improve maternal health outcomes in the region.

1.4 Disparities in maternal healthcare

1.4.1 Factors contributing to maternal mortality in Low Income Countries

Teenage pregnancies

Maternal mortality poses a substantial challenge in sub-Saharan Africa, with teenage pregnancies representing one of its underlying causes. Younger mothers encounter higher risks during pregnancy and childbirth in comparison to adult women, including higher risks of anaemia, preterm delivery, malposition, preeclampsia, and eclampsia (66). If not adequately managed, these complications can result in maternal mortality.

The prevalence of teenage pregnancies as a percentage of total births in Africa is notably high, and certain countries within the continent grapple with particularly alarming rates. In South Africa, the proportion of teenage births in the Vhembe district of Limpopo was found to be above 56% (66). There was almost a 50% increase from 2017 to 2021 of birth among teenagers (66). In Ghana, a study carried out in the Upper East Region revealed that 20.5% of junior high school girls, mostly in their teen ages, had experienced early pregnancies (67).

A recent study undertaken in Bolgatanga, Ghana, unveiled that teenage pregnancy was a prevalent occurrence among young women, with a considerable number of them having faced pregnancy before reaching the age of 18 (68).

Another research conducted in the Sunyani West District between 2011 and 2015 revealed that 97.4% of the documented 2,189 pregnant adolescents fell within the age bracket of 15 to 19, underscoring a notably high incidence of teenage pregnancy within this demographic (69).

Within the Ahafo Ano South District of Ghana, a striking statistic emerges: 28 out of 59 pregnancies were unplanned and are teenagers, highlighting a prevalent occurrence of teenage pregnancies in the area (70).

Teenage mothers frequently encounter challenges in accessing specialized antenatal care and essential health education, both of which are vital for preventing complications and mitigating the likelihood of maternal death (27).

Young mothers may confront social and economic challenges that can contribute to the likelihood of maternal death including restricted educational prospects, lower income potential, and an increased susceptibility to domestic violence (42).

Teenage pregnancy is linked to physical immaturity, which can be a contributing factor to complications during labour and delivery. Due to the elevated incidence of labour dystocia and other complications, teenage pregnancy frequently necessitates a heightened demand for instrumental deliveries, such as forceps or vacuum extraction or caesarean sections (71).

Teenage mothers are less inclined to access antenatal and childbirth healthcare from medical professionals. This may result in insufficient prenatal care, consequently increasing the risk of pregnancy and childbirth complication risks. Teenage pregnancy can be a contributing factor to elevated population growth rates, exerting pressure on resources and services (71).

Revising the Ghana Education Service curriculum to include mandatory basic sex education and delivering it with increased emphasis by qualified educators have a good potential to addressing the menace of teenage pregnancies.

Antenatal care

Limited availability of antenatal care has also been a key global barrier to preventing maternal mortality (72). Regular antenatal care is crucial for identifying and managing potential pregnancy-related complications (73).

Complications arising during pregnancy and childbirth, including bleeding, high blood pressure-related conditions, infections, and obstructed labour, are among the prevalent factors that can result in maternal mortality (38, 39). These complications can often be effectively managed with timely medical interventions, but limited availability of emergency obstetric care continues to pose a substantial challenge in many regions (41).

However, in many parts of the world, women do not receive adequate antenatal care due to various barriers, including distance to healthcare facilities, cultural beliefs, and socioeconomic factors (25). Other potential barriers that could impede the utilization of antenatal care include prolonged waiting times, inadequate equipment, disjointed care, a lack of privacy, and insufficient health education (74).

Antenatal care is an essential element of maternal healthcare, holding the potential to reduce both maternal and infant mortality. The World Health Organisation (WHO) defines adequate antenatal care as a requirement for expectant mothers to engage in a minimum of four prenatal care visits, all conducted by trained healthcare professionals, and with the initial visit taking place during the first trimester of pregnancy (75).

The WHO also advocates for comprehensive antenatal care, encompassing a spectrum of interventions, including the screening and management of infections, nutritional guidance, and providing guidance on preparing for childbirth and readiness to address possible complications (76).

A 2016 study conducted at the Tamale Teaching Hospital in Ghana revealed and supported the notion that there are substantial gaps in ANC provision, including ultrasound services, in sub-Saharan Africa, which impact the early detection and management of congenital anomalies (77). Another analytical cross-sectional study that assessed socioeconomic inequalities in ANC service utilization across 36 sub-Saharan African countries between 2008 and 2018, highlighted that poorer women often have fewer than the recommended four ANC visits, while richer women tend to have more. On average, women with fewer visits lack about two visits to meet the recommendation, and those with more visits exceed it by about two. The study revealed between 13% and 71% of women in the 36 sub-Saharan African countries had fewer than four ANC visits,

while 2% to 76% had more than four. Wealth, education, and where someone lives play major roles in these gaps, suggesting that improving education, especially for women, could help close these disparities (78).

Similarly, another population-based, cross- sectional investigation conducted in 36 sub-Saharan African countries from 2006 to 2018 examined a total participant of 300,575 women from recent demographic and health surveys. The study found out that only about 6.8% of women in the 36 countries met the WHO guideline of recommended ANC visits. Factors like where they live, education levels, media access, and family planning use really make a difference. Higher birth order seems to decrease the likelihood of attending these visits (79).

In another study with a total of 89,489 mothers, looked at how many of these mothers from 14 sub-Saharan African countries had eight or more ANC visits, based on recent survey data from 2018 to 2023. The survey revealed only about 9% of mothers met the eight-visit mark, varying widely by country. Factors like mother's age, education, wealth, and urban living increased the chances of more visits. Things like having many kids already or not using contraception decreased the chances (80).

In another study that looked at how antenatal care visits vary across different regions of Nigeria and what factors influence women's use of these services based on the 2018 Nigeria Demographic and Health Survey, revealed factors associated with incomplete ANC attendance included maternal age, education, partner's education, working status, ethnicity, parity, religion, media exposure, residence, wealth index, region, and community literacy (81). This study with a total of 20,003 women aged 15-49 found out high levels of incomplete ANC visits were observed in the northern regions of Nigeria, potentially due to developmental disparities, rural-urban differences, and limited access to maternal health services (81).

In another recent study that used data from demographic and health surveys of eight sub-Saharan African countries including 63,266 pregnant women, examined noncompliance with the WHO's recommended eight ANC visits in the region. The pooled analysis showed that 92.3% of pregnant women did not attend the WHO recommended minimum of eight ANC visits. Zambia had the highest prevalence of noncompliance (98.7%), while Libya had the lowest (73.4%). Factors such as women's age, education, economic status, media exposure, parity, health insurance, religion, and place of residence were significantly associated with noncompliance (82).

In a Sri Lanka study over the decades, specifically indicates that by 1958, about 58% of births were attended by skilled personnel, and by 2001, the percentage of institutional

deliveries had risen sharply to 92% of all births. The study indicates a significant increase in the utilization of antenatal and delivery services in Sri Lanka over the decades. The data primarily reflect national trends derived from surveys such as the DHS of 2000 and other national records, rather than a specific cohort study. While exact numbers of women or a defined cohort are not explicitly provided in the study, the data point to a population-wide increase in service utilization over time, covering all childbirths nationally. For instance, in 2001, nearly all (92%) of deliveries occurred in institutions, representing broad population coverage rather than a sample of specific women (83).

This suggests that implementing strategies to enhance antenatal care has effectively lowered maternal mortality rates. The extension of both community-based and healthcare facility services, along with the offering of cost-free services and the incorporation of family planning and other elements into maternal healthcare programs, has led to increased utilization of antenatal and delivery services provided by skilled midwives and healthcare practitioners in Sri Lanka. Consequently, this has resulted in improved access to specialized care and emergency obstetric services (83).

Demographic factors

Advanced Maternal age

Maternal age constitutes a risk factor for maternal mortality, particularly for women aged 35 and above, and those aged more than 45 but less than 50 (84). In addition to adolescent pregnancies, pregnancies in older women also pose higher risks of maternal mortality due to socio-physiological factors (28, 85).

The Lancet Global Health conveyed that, women aged 50 years or more faced a significantly increased risk of maternal mortality when contrasted with those aged between 40 and 45 years (86). In Canada, a comprehensive study conducted on a national scale with a population-based cohort, encompassing over three million pregnancies, revealed that extreme maternal ages, particularly those 45 years or older, were linked to severe maternal illness and death (87).

With the ongoing trend of rising maternal age in many high-income nations, gaining insight into the consequences of maternal age on maternal mortality and morbidity has become significant for public health and educational deliberations (87).

Educational Status

Evidence indicates that maternal mortality is linked to maternal educational attainment, yet this relationship is complex and influenced by various social and healthcare factors (85, 88).

In a case–control study that aimed to assess maternal mortality inequality and its main contributors based on the level of education amongst mothers living in Isfahan, Iran, 171 maternal deaths from 2001–2016 were examined versus 523 living mothers as controls. The study revealed medical causes and number of pregnancies were key healthcare contributors to inequality. Maternal mortality disproportionately affected less educated women, signalling the need for better health education (89).

Similarly, a cohort study which looked at maternal mortality in LMICs using a huge dataset from 2010 to 2013, tracked over 277,000 pregnancies and found that no formal education, primary education only, secondary education only, lack of antenatal care, caesarean section delivery, haemorrhage, and hypertensive disorders were associated with a higher risk of maternal death. The study revealed mortality was higher in women with non-formal education, and lower in women with university education (90).

The association is also observed in high income countries. In the United States, a study that investigated maternal deaths from indirect obstetric causes between 1999 and 2017, exploring differences by race, income, immigrant status, marital status, and geography, unveiled a stark contrast in maternal mortality rates based on education levels, with women having <12 years of education facing 4.4 times higher mortality than those with a college degree (91).

Women with limited educational opportunities may lack the information and means needed to make informed choices regarding their health, including the significance of prenatal care (28).

1.5 Barriers to reducing maternal mortality and morbidity in low-income countries including Ghana.

Several interrelated factors contribute to high rates of maternal mortality and morbidity, which are summarised in Table 1.1 and expanded further below:

Barrier	Summary
Access to Quality Healthcare	Shortages of skilled health professionals, essential medicines, and emergency obstetric services limit maternal care.
Infrastructure and Transport	Poor road networks, lack of reliable ambulances, and long distances lead to delay in timely intervention.
Socioeconomic Factors	Poverty, low income, and healthcare costs reduce access to skilled birth attendance.
Delayed Referrals and Emergency Care	Weak referral systems, inadequate triage, and slow emergency response contribute to preventable maternal deaths.
Urban–Rural Disparities	Urban facilities are typically better staffed and equipped, creating inequities in service availability and outcomes.
Cultural, Religious, and Traditional Birth Practices	Preference for home births, reliance on traditional birth attendants, and certain religious norms can deter facility-based care.

Table 1. Barriers to Reducing Maternal Mortality and Morbidity in Low-Income Countries including Ghana.

Access to Quality healthcare

Access to high-quality healthcare services plays a pivotal role in lowering maternal mortality rates. Scarce healthcare access and a deficit of adequately trained medical professionals are contributing factors to the elevated maternal mortality rates, particularly in developing nations (92). Women who encounter substandard care or mistreatment during childbirth may be disinclined to seek future care, thereby contributing to unfavourable maternal health outcomes (92).

Priority to enhancing accessibility to high-quality healthcare services, bolstering healthcare systems, and resolving the social and economic determinants that exacerbate health disparities, could mitigate maternal mortalities (65).

Adequate maternal healthcare requires a team of healthcare providers who are trained and equipped to provide quality care to expectant mothers. These providers include perinatal care providers, culturally competent healthcare providers, primary healthcare providers, and mental health providers (93, 94).

In certain regions, where healthcare systems are fragile or underdeveloped, the provision of proper maternal health services faces significant challenges. These include skilled assistance during childbirth, emergency obstetric care, and postnatal support (51). The scarcity of medical resources, and well-trained healthcare personnel all play a role in yielding unfavourable maternal health outcomes (52).

Midwives play an instrumental role in delivering high-quality healthcare and effectively curbing maternal mortality rates. Extensive research has consistently demonstrated that increasing the availability of trained and licensed midwifery roles can affect a substantial decline in maternal mortality rates (95).

However, midwives encounter numerous obstacles when delivering quality care, including issues like understaffing, inadequate infrastructure, and the pervasive effects of poverty. Hence, providing more midwives and the necessary supplies and equipment for both antenatal and postnatal care could potentially mitigate the difficulties they encounter in delivering quality healthcare (96).

Inadequate access to quality healthcare is also a key contributing factor to maternal mortality, particularly in restricted resource settings (97). Maternity care is an important aspect of healthcare, but there is a global deficit in its provision (98). In resource-constrained environments, there exists a worldwide shortage of maternity care, stemming from a range of impediments. These include direct and indirect expenses associated with maternal healthcare, encompassing medical fees and transportation costs, the variability of which is contingent upon the specific regulations and policies of each country (99, 100).

Lack of access to skilled healthcare providers, well-equipped medical facilities, and essential maternal health services are important factors that can have detrimental effects on the health and well-being of mothers and their newborns during pregnancy, childbirth, and the postnatal period (101).

The WHO (102) asserted, there is a significant global deficit in maternity healthcare workers. However, specific information on the extent of the deficit or the regions most affected is not provided. Additional research is warranted to fully understand the scope of the issue and develop effective solutions. The WHO however reports a significant

global deficit in healthcare workers, predicting a shortage of 18 million healthcare professionals which include obstetricians and midwives by the year 2030. This shortfall is especially pronounced in economically challenged nations or regions, where the lack of access to qualified healthcare providers is most severe. For instance, in sub-Saharan Africa alone, there is an alarming, estimated shortage of 4.3 million healthcare workers (102).

The shortage of accessible skilled healthcare providers exhibits regional disparities. Within low resourced countries, it is predominantly the rural areas that bear the brunt of this deficit. To illustrate, in sub-Saharan Africa, rural regions host merely 23% of the healthcare workforce, despite accommodating a substantial 62% of the population (103). Furthermore, notable imbalances persist in the distribution of healthcare workers even within individual countries (102).

Limited access to quality maternal care substantially elevates the risk of maternal morbidity in addition to maternal mortality. In Ghana, women with secondary education had a 34% greater likelihood of receiving skilled antenatal care compared to those without formal education (aOR = 1.34; 95% CI: 1.07–1.88), while those in rural locations experienced 45% lower odds of skilled care at birth (aOR = 0.55; 95% CI: 0.41–0.74), as reported by Dickson et al. in 2017 when they looked into what influences women in Ghana to choose skilled antenatal care providers (104). Wealth also played a strong role; women in the richest quintile were over five times more likely to access skilled ANC (aOR = 5.19; 95% CI: 2.28–11.85) (104). Moreover, possession of national health insurance increased optimal ANC uptake by 64% (aOR = 1.64; 95% CI: 1.14–2.38), a cross-sectional study at three sites in Ghana revealed (105).

Economic barriers had tangible consequence, and women citing cost as a barrier for ANC were more than twice as likely to face adverse pregnancy outcomes (aOR = 2.15; 95% CI: 1.16–3.99), in a quantitative cross-sectional study that was conducted of 643 women aged 19–48 years who presented for delivery at selected public hospitals and private traditional birth revealed (106).

Collectively, these utilization metrics validate how scarce access and staffing deficits, shaped by factors such as education, geography, insurance, and cost, translate into heightened maternal risk.

Research consistently indicates that expanding the availability of trained midwives is strongly associated with significant reductions in maternal mortality. Historical analyses from 19th-century Sweden demonstrate that a twofold increase in the number of trained midwives led to 20–40% decline in maternal mortality rates (95). Homer et. al,

2014, estimated that universal access to midwifery interventions could avert 61% of maternal, fetal, and neonatal deaths in countries with a low Human Development Index. When integrated with family planning services, the impact rises to 83% (107)

Nove et al. in 2020, projected that substantial increases in midwife-delivered interventions could significantly reduce maternal and neonatal mortality and stillbirths in LMICs by 2035. However, these studies emphasize that to achieve maximum impact, midwives must be skilled, work in adequately staffed teams, and operate in enabling environments (108).

Infrastructure and transport

Inadequate road infrastructure, elevated transportation expenses, and a scarcity of transportation options are recognized as substantial obstacles to reaching maternal healthcare services. (109). This lack of access hinders timely and appropriate medical interventions during pregnancy and childbirth, leading to increased maternal mortality rates. The worldwide shortfall in infrastructure and transportation presents a substantial impediment to the reduction of maternal mortality (110).

A Focused Group Discussion study conducted in the Upper West region communities of Ghana revealed that inadequate infrastructure and transportation remain critical obstacles to reducing maternal mortality, and poor road networks and limited vehicle availability restrict timely access to healthcare facilities, often compelling pregnant women to depend on unsafe transport options or seek care from traditional birth attendants (111). Reliable transportation and well-developed road infrastructure are essential for transforming potential access into the actual use of maternal health services (109).

The lack of reliable transportation undermines the effectiveness of community-based health programs (CHPS), limiting their potential to improve maternal and child health outcomes (111). Financial constraints further exacerbate the challenge by restricting both access to and utilization of maternal and child health services in rural Ghana (112). Overcoming these challenges necessitates the strengthening of primary healthcare systems, the development of reliable rural transport infrastructure, and the long-term sustainability of national health insurance schemes to improve equitable access to care in remote communities (111, 112).

Research in Uganda found that the introduction of free 24-hour ambulance services more than doubled caesarean section rates (from 0.57% to 1.21%) and increased

hospital deliveries by over 50% annually (113). Similarly, in Kenya, the adoption of an Uber-style transport system combined with personalized text reminders improved maternal healthcare utilization, raising odds of women attending four or more antenatal care visits (aOR = 4.7) and postnatal care visits (aOR = 4.10), while reducing travel time to health facilities (114). In South Africa's Free State Province, the introduction of dedicated maternity care vehicles contributed to a decline in maternal mortality from 279 to 152 per 100,000 live births and shortened emergency dispatch times from 32 to 22 minutes (115). These interventions target critical delays in accessing care, recognizing that timely emergency services could avert up to 75% of maternal deaths (116).

Socioeconomic factors

Socioeconomic disparities among nations and within nations have been highlighted as a social determinant of quality health (117). Women hailing from economically disadvantaged backgrounds frequently experience elevated maternal mortality rates. (91). Elevated maternal mortality rates among disadvantaged populations can be linked to a multifaceted combination of factors, including poverty, low literacy levels, and restricted access to essential resources. (118, 119). These challenges lead to a delay or insufficiency in seeking proper healthcare during pregnancy.

A large population-based study in South Korea comprising 3,334,663 nulliparous women enrolled in the Korean National Health Insurance Service database between 2003 and 2018 revealed that women with lower incomes faced an elevated likelihood of maternal mortality within the first six weeks and one year after giving birth. The study found that women with lower income levels had a significantly elevated risk of maternal death. Specifically, the risk ratio (RR) within six weeks after childbirth was 2.42 (95% CI = 1.65–3.53), meaning these women were more than twice as likely to die compared to women with higher incomes. For maternal death within one year, the RR was 1.83 (95% CI = 1.47–2.28), indicating nearly double the risk compared to higher-income women (120). This extensive sample provides robust evidence of the association between socioeconomic status and maternal mortality in South Korea (120).

Maternal mortality in Ghana is influenced by a spectrum of socioeconomic factors. Disparities in the utilization of trained childbirth attendants during childbirth persist among women from diverse economic and social backgrounds in Ghana (71). Women residing in rural areas face reduced access to trained birth attendants and emergency obstetrical care, heightening the vulnerability to maternal deaths (71). In Ghana, 60% of deliveries without skilled birth attendants occurred in rural regions, in contrast to 40% in

urban areas (71). Wealth, educational attainment, and residential location were primary drivers of socioeconomic disparities in the use of trained birth attendants by women during childbirth in Ghana. (71).

Delayed referrals and emergency care

Several factors could contribute to undue delay in receiving emergency care, thus raising the incidence of maternal mortality. A commonly cited barrier to accessing timely and appropriate obstetric care at healthcare facilities is the deficiency of necessary equipment. (22). These include medical instruments like forceps or vacuum extractors, which are employed to aid in the delivery of a baby in situation involving prolonged labour or fetal distress. The tools may also consist of a blood pressure monitor, a blood glucose monitor, and a urine dipstick. These tools are employed to assess the health status of both the mother and the newborn throughout the delivery stages and labour (42).

Challenges within the supply chain related to the procurement of vital medications, equipment, supplies, and blood can lead to disruptions and subsequently result in late access to surgical care. The presence of a inefficient system of referral can exacerbate substantial delays in obtaining surgical care (42).

In certain situations, emergency obstetric care may necessitate the utilization of ambulances or alternative transportation methods to transfer women requiring specialized care to a healthcare facility at a higher level and that may be lacking (43).

In rural regions of Ghana, difficulties in transportation can serve as a hindrance to women's access to crucial maternal and child healthcare services (43). Insufficient road networks and the inadequate maintenance of roads compound the transportation challenges in rural areas. These increase the difficulties faced by pregnant women in reaching healthcare facilities. With limited access to vehicular transport, certain pregnant women resort to utilizing risky modes of transportation like bicycles, tricycles, or motorbikes to reach obstetric healthcare services (43). As the duration of travel from a woman's residence to the healthcare facility increases, there is a significant decrease in the utilization rate of birthing services (121).

Research conducted in Accra, Ghana uncovered that, for 280 labouring patients referred to the Greater Accra Regional Hospital, the average duration between referral and arrival was 307 minutes. In instances where midwives accompanied the patients, the median referral time was reduced to 73 minutes (121).

Difference in timings may be because midwives frequently possess a deeper understanding of the healthcare system and the processes of patient referrals. They may have established professional connections with healthcare providers, facilitating a smoother and more efficient referral process.

Midwives also serve as strong advocates for their patients, playing a pivotal role in prioritizing their needs throughout the referral process. This advocacy can involve ensuring timely transportation, suitable medical interventions, and effective communication among healthcare providers.

Midwives typically receive training in emergency preparedness, equipping them with a heightened awareness of the urgency in certain situations. This expertise enables them to effectively convey the necessity for prompt care and facilitates the allocation of appropriate resources to the patient. This urgency is missing, and patients choose to go to referral centres at their own pace.

Financial barriers can contribute to delayed referrals and emergency maternal care in Ghana. Women residing in rural areas of Ghana often face the challenge of traveling extended distances to access maternal healthcare services. The associated transportation costs can pose a substantial financial barrier, impeding women from seeking timely emergency maternal care (43).

Women may also find themselves responsible for covering the costs of medications and supplies required for emergency maternal care, often having to do so out-of-pocket. This financial burden can be substantial, resulting in delayed referrals and access to critical emergency maternal care (122).

A considerable number of women in Ghana lack health insurance coverage, posing challenges to their ability to reach emergency maternal care services. The absence of health insurance often necessitates women to personally bear the costs of emergency maternal care (122).

To mitigate these financial burdens, in 2008, Ghana implemented a policy providing free maternal care services to pregnant women at public and accredited private healthcare facilities. Nevertheless, the influence of this policy on indicators related to maternal and child health in Ghana has produced uncertain results (123), due to dearth of data and this calls for further studies to investigate.

Urban-rural disparities

The allocation of healthcare resources, including skilled healthcare professionals and medical supplies, frequently exhibits an imbalance favouring urban regions in Ghana (124). The unequal distribution of resources intensifies the discrepancies in maternal healthcare between urban and rural areas, ultimately leading to elevated maternal mortality rates in rural regions.

The least developed regions of Ghana recorded elevated maternal mortality rates, with the northern region reporting the highest incidence of maternal deaths (125). Stakeholders must recognize the importance of developing a strategy for incentivizing healthcare workers to accept assignments in rural areas and to establish well-equipped healthcare facilities as a means to combat this challenge effectively (85).

In the rural areas of Ghana, the presence of skilled birth attendance is less common, standing at 43%, in contrast to urban areas where it is higher at 74%. The presence of skilled birth attendants is indispensable in guaranteeing safe deliveries and mitigating maternal mortality. Further, women residing in rural areas of Ghana frequently experience lower levels of education and income in comparison to their urban counterparts (124).

The reason for paucity of health care workers in Ghana's rural areas is that healthcare professionals in rural regions typically receive reduced salaries and fewer benefits in comparison to their urban counterparts. This discrepancy can pose challenges in both attracting and retaining qualified staff in rural healthcare settings (91).

Again, rural areas frequently face deficits in essential infrastructure, such as adequate roads and transportation systems, which can hinder healthcare workers from delivering quality care (126). Healthcare professionals working in rural regions may encounter restricted access to training and professional development opportunities and that demotivates health care workers to take up roles in rural areas of Ghana (127).

Healthcare workers stationed in rural areas often experience limited access to technology, including mobile phones and computers. This constraint can impede their ability to communicate with colleagues and access vital medical information (127).

If these challenges are tackled, there is potential to draw in and retain a greater number of healthcare professionals in Ghana's rural areas, consequently enhancing access to high-quality healthcare for rural communities.

Cultural, religious and traditional birth practices

The risk of maternal mortality is often exacerbated by entrenched cultural norms and longstanding traditions (65, 92). These elements can hinder women from pursuing suitable healthcare or exercising decision-making authority throughout pregnancy and childbirth. Consequently, there can be significant delays in seeking necessary medical attention or even the adoption of harmful practices that intensify the threat to maternal health (128, 129).

Traditional customs, cultural beliefs, and social taboos frequently play a role in shaping antenatal care of women in Ghana and are a significant determinant of maternal deaths (130). As an illustration, expectant mothers are often prohibited from consuming healthy and nourishing food like okra, snails among others, due to concerns about potential complications during pregnancy and childbirth.

Despite endeavours to reduce geographical and financial impediments to skilled deliveries, approximately 30% of births in Ghana continue to take place either at home or traditional maternity care givers (69). Traditional birth attendants, often lacking formal training and essential skills to manage delivery complications, can inadvertently contribute to maternal mortality (131).

Additionally, natural remedies such as herbal plants are commonly employed by expectant mothers and traditional birth attendants use them to encourage labour and manage haemorrhage during childbirth (130), which may sometimes have detrimental effects, though the other benefits cannot be ruled out.

Many communities lack sufficient health education regarding traditional practices that pose risks to maternal health. Many traditional birth attendants are elderly, illiterate individuals involved in farming, and they often do not possess the essential knowledge and skills required to offer safe delivery services (132).

An additional article proposes that women who opt for unconventional herbal uterotonics during pregnancy and labour may encounter unfavourable consequences (5). There is an urgent need for education targeting pregnant women and their families to raise awareness about the potential adverse effects associated with the usage of unapproved traditional or herbal remedies during pregnancy (21).

1.6 Primary causes of maternal mortality and morbidity in low income countries including Ghana.

Maternal mortality and morbidity are influenced by various factors, and Table 2 summarises the primary causes in low income countries including Ghana.

Cause	Summary
Indirect Causes	Pre-existing health conditions such as anaemia, malaria, and HIV/AIDS that worsen during pregnancy and childbirth.
Obstructed Labour	Labour that fails to progress due to fetal position or pelvic issues, leading to complications like uterine rupture.
Haemorrhage	Heavy bleeding after childbirth, often due to uterine atony, retained placenta, or trauma.
Infection	Severe infection during or after delivery, often due to unsterile conditions or prolonged labour.
Hypertensive Disorders	High blood pressure conditions in pregnancy such as pre-eclampsia that can lead to seizures (eclampsia), organ failure, or death.

Table 2: Primary causes of maternal mortality and morbidity in low-income countries including Ghana.

Indirect Causes

Indirect causes make a substantial contribution to maternal mortality in Ghana, representing approximately 15.2% to 22.4% of all maternal deaths (133). Frequent indirect contributors to maternal mortality include infections, sickle cell disease, anaemia, and chronic liver disorders (133, 134). Socioeconomic and cultural determinants are recognized as fundamental drivers of maternal complications (135).

Factors associated with elevated maternal mortality encompass limited or no formal education, fewer than four antenatal visits, and the need for emergency caesarean sections (134). Ghana's maternal mortality ratio remains high, with estimates ranging between 604 and 1,004 deaths per 100,000 live births (134, 136).

In order of frequency, haemorrhage has emerged the lead common cause of maternal mortality in several studies (137), and other causes include low levels of haemoglobin, hypertensive disorders, dystocia and infections (138).

Other common causes include ectopic pregnancy, embolism, cardiovascular diseases, anaemia and other indirect causes that include conditions like diabetes, malaria, and HIV/AIDS, which can complicate pregnancy and contribute to maternal mortality (139).

Maternal mortality and morbidity risks are heightened in cases of teenage pregnancy. This arises from the fact that teenage mothers face a higher likelihood of encountering complications during pregnancy and childbirth, including hypertensive disorders, anaemia, and preterm labour (28, 70).

Within the demographic of teenage pregnant women in Ghana, labour dystocia can emerge as a significant concern. Labor dystocia, often referred to as obstructed labour, is a medical condition wherein the baby's head or shoulders encounter obstruction in the birth canal, resulting in an extended and challenging childbirth process (71).

Recommended strategies to address this challenge include expanding access to high-risk obstetric care, strengthening contraceptive uptake, promoting early initiation of antenatal care, and enhancing health education initiatives (135, 136).

Obstructed labour

Obstructed labour stands as a significant factor in maternal mortality rates in Ghana (137, 138). In a quantitative survey carried out within a community in Ghana, it was found that obstructed labour contributed to 6.8% of maternal deaths in the district (138). In a separate study carried out at the Wa Regional Hospital in Ghana, it was revealed that obstructed labour was as a prominent factor in maternal mortality, constituting 7% of maternal fatalities (137).

Obstructed labour could lead to a range of fetal and maternal complications, and it is categorized as abnormal when the foetus’s presenting part cannot advance through the vagina irrespective of robust contractions of the uterus and ranks among the foremost contributors to perinatal mortality (139).

Preventable maternal deaths attributed to obstructed labour can be significantly reduced with timely access to high-quality delivery care, encompassing emergency obstetric interventions and caesarean sections (93).

Numerous studies have been undertaken to identify the factors and variables that predict and determine obstructed labour, along with its associated risks. Nulliparous women have a higher chance of obstructed labour compared with parous (or multiparous) women. Conversely, higher odds of obstructed labour were associated with factors such as failure to use partograph, prolong labour exceeding 24 hours, and birthing roughly up to 50 kilometers away from the healthcare facility (94).

Factors identified as determinants for obstructed labour encompass maternal illiteracy, maternal primary education, gestational age in third trimester at the first antenatal care visit, admission during the 37–42-week gestation range, admission beyond 42 weeks, having a spouse engaged in merchant activities, and a history of prior caesarean section (95).

Ultrasound is used to estimate the cephalic index (CI), which is a measurement used to assess the shape of a fetal head. It is the ratio of the biparietal diameter (BPD) to the occipitofrontal diameter (OFD) of the fetal head, multiply by 100. Typically, the normal range for the fetal cephalic index is approximately 78, with an accepted range falling between 74 and 83 (140).

A cephalic index above the normal value signifies a case of megalencephalic fetus (one with bigger head than normal), potentially leading to a cephalopelvic disproportion (CPD) and this could inform the right mode of delivery by averting spontaneous vaginal delivery (SVD), which however would put mother and baby into a higher risk of mortality.

Haemorrhage

Haemorrhage, characterized by excessive bleeding, remains a key cause or challenge to maternal mortality in Ghana (5, 96). As per a five-year retrospective study carried out in southern Ghana, haemorrhage emerges as one of the chief elements leading to maternal deaths, representing 21.8% of pregnancy-related deaths (98, 99).

In another study, it was identified that haemorrhage stood as the highest single cause of maternal deaths in Ghana (100). Additionally, research at the Korle-Bu Teaching Hospital revealed, haemorrhage was underlying cause for a fifth of all maternal deaths (141). In a study carried out in the Ejisu District of Ghana, PPH emerged as the primary cause, and responsible for 45.5% of all maternal deaths (138).

PPH represents a grave concern and emerges as the most common cause of maternal mortality in Ghana, responsible for about a fifth of maternal fatalities (102). Nonetheless, the maternal haemorrhage case rate witnessed a decline in the late 1980's. This decrease

could potentially be attributed to a rise in the caesarean section rate (103). The maternal haemorrhage case fatality rate in Ghana declined from 1.34% in 1981 to 0.7% in 1989, with haemorrhage responsible for 27% of maternal deaths during this period (142). At Korle Bu Teaching Hospital, haemorrhage was the second leading cause of maternal mortality, accounting for 20.6% of deaths between 2015 and 2019 (134). A 13-year study in rural Ghana reported that the overall maternal mortality ratio remained largely unchanged between 1987 and 2000, although the proportion of deaths attributable to haemorrhage declined over this period (143). Recent studies in Ghana highlight the persistent challenge of maternal mortality due to haemorrhage. Haemorrhage remains a leading cause of maternal deaths, accounting for 21.8-22.8% of cases (144).

To mitigate maternal mortality resulting from haemorrhage, recommended interventions include enhancing the quality of delivery care across a wide coverage and establishing surgical facilities at local health centres (30). The EMOTIVE trial by Gallos et al. in 2023 is also a way of reducing severe PPH.

Furthermore, maternal mortality resulting from haemorrhage can be reduced by preventing PPH through access to skilled birth delivery care and uterotonics, which are medications designed to prevent and treat PPH (31).

Infection

Infectious diseases play a substantial role in maternal illness and death (65, 128). Infections can lead to severe organ dysfunction or even fatalities, and obstetric infections resulting in sepsis rank as the third most prevalent cause of maternal deaths (128). A study carried out in Mozambique revealed that infectious diseases were responsible for no less than half of all maternal fatalities at a tertiary hospital (129).

Key infectious aetiologies associated with maternal deaths include HIV/AIDS, pneumonia, malaria, meningitis, and tuberculosis (145, 146). Infections directly associated with pregnancy, including metritis and septic abortion, remain important contributors to maternal morbidity and mortality (146). Other clinically significant infections in pregnancy include viral hepatitis, rubella, cytomegalovirus, and toxoplasmosis, all of which are associated with adverse maternal outcomes and potential congenital complications (147).

Pregnant women exhibit increased susceptibility to certain infections, such as malaria, HIV, and listeriosis, and may also experience heightened disease severity with conditions like influenza, malaria, hepatitis E, and herpes simplex virus, particularly during late

pregnancy (148). Effective prevention and management of these infections are essential to reducing maternal mortality and enhancing perinatal outcomes.

Infections arising from inadequate sterile conditions during childbirth continue to pose a major challenge in sub-Saharan Africa. Post-surgical site infections are particularly prevalent, with incidence rates reported between 7.3% and 15.6%. These infections contribute substantially to maternal morbidity and are frequently associated with extended durations of hospitalization (149, 150). A large proportion of caesarean sections in sub-Saharan Africa are performed under emergency circumstances, and many women do not receive perioperative antibiotic prophylaxis. This gap in preventive care significantly heightens the risk of postoperative infections (150),

In community-based settings, suboptimal hygiene practices such as limited use of clean delivery surfaces and inadequate hand hygiene following latrine use play a critical role in the occurrence of neonatal infections. These practices are strongly associated with respiratory and ophthalmic infections in newborns, whereas diarrhoeal infections appear to be less prevalent than anticipated (151). Additionally, antimicrobial resistance among pathogens causing sterile site infections is high and variable, complicating treatment and highlighting the need for standardized surveillance and improved infection control (152).

Hypertensive Disorders

In Ghana, hypertensive disorders of pregnancy (HDP) have emerged as the leading cause of maternal mortality, surpassing obstetric haemorrhage (153). A retrospective descriptive study conducted at the Korle Bu Teaching Hospital in Accra, Ghana, which involved a comprehensive review of all maternal deaths attributable to hypertensive disorders, revealed HDP accounted for 31.7% of maternal deaths, with eclampsia being the primary immediate cause (153).

A multicentred study reported elevated rates of maternal near-miss events and mortality linked to hypertensive disorders of pregnancy occurring remote from term, with a maternal mortality ratio of 3,100 per 100,000 live births (154). A hospital-based review identified hypertensive disorders of pregnancy as the leading cause of maternal mortality in Ghana, accounting for 26.4% of deaths (136).

Addressing this issue requires interventions aimed at minimizing delays in emergency obstetric care, promoting contraceptive use, encouraging early antenatal attendance, and enhancing multidisciplinary management of women experiencing hypertensive emergencies (136, 154).

African populations experience disproportionately elevated risks of hypertension and preeclampsia relative to other ethnic groups (155). In sub-Saharan Africa, hypertensive disorders of pregnancy contribute to an estimated 16% of maternal deaths, making them the second leading cause of maternal mortality after obstetric haemorrhage (156).

The increased susceptibility is partly attributed to genetic variations prevalent among African populations, particularly those influencing the renin–angiotensin–aldosterone system, sodium regulation pathways, and salt sensitivity (157). However, these genetic predispositions operate in conjunction with environmental influences such as dietary practices, urbanization, and socioeconomic conditions (158).

Although some theories propose that hypertension presents as a 'distinct disease' among African populations, no unique genetic variants have been conclusively identified. Instead, observed disparities appear to reflect differential distributions of established risk factors (158).

1.7 How can maternal mortality be reduced?

Maternal mortality remains a pressing global health challenge, particularly in LMICs. Effective reduction requires a multidimensional approach that addresses systemic, individual, geographic, and societal determinants of maternal health. The framework presented integrates these factors to highlight key interventions necessary for reducing maternal deaths.

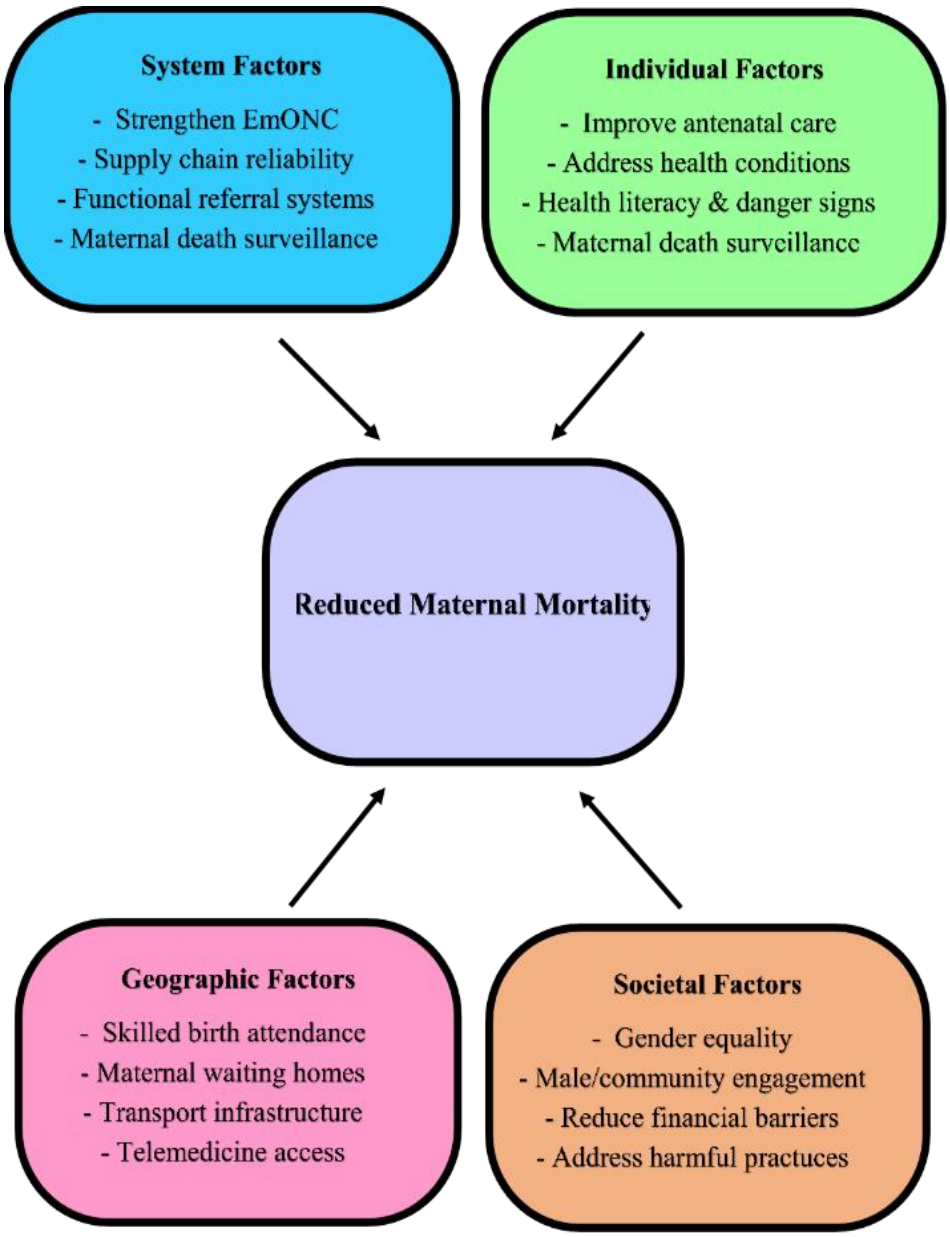

Figure 2: Framework for Reducing Maternal Mortality by Author

Footnote: EmONC is Emergency Obstetric and Newborn Care.

Systemic Factors

Emergency obstetric and newborn care (EmONC) is essential in addressing life-threatening complications that arise during pregnancy and childbirth, conditions estimated to affect about 15% of all deliveries globally (159). Strengthening the capacity of EmONC services is critical for countries experiencing elevated maternal and neonatal mortality rates (160). Key strategies encompass strengthening health facilities, implementing competency-based training for healthcare providers, and ensuring effective government coordination (159). Community-based interventions, including the distribution of maternal and neonatal health packs and the training of healthcare providers, play a significant role in enhancing access to EmONC services (161).

However, significant barriers to the utilization of EmONC services remain, such as limited awareness, prevailing misconceptions, entrenched traditional practices, and financial constraints (162). To improve the uptake of EmONC services, policymakers should prioritize enhancing women's awareness, dispelling misconceptions, ensuring the delivery of quality care, addressing the inequitable distribution of EmONC facilities, and mitigating financial barriers (162).

Reliable supply chain systems are fundamental to guaranteeing the consistent availability of essential medical commodities and thereby improving maternal health outcomes. Evidence indicates that weak procurement and distribution mechanisms, particularly in rural health facilities, often result in inadequate emergency obstetric care services (163). Centralized procurement and tendering mechanisms have the potential to generate cost efficiencies, while well-structured supply chain management programs can minimize stock-outs and enhance the consistent availability of essential medicines (164).

Haemorrhage remains the leading cause of maternal deaths worldwide, emphasizing the importance of ensuring a safe and available blood supply (165). Achieving the Sustainable Development Goal targets for maternal mortality reduction requires countries to invest in strengthening collaborations between maternal health programs and blood transfusion services, while also implementing interventions consistent with regional strategic frameworks on blood safety and availability (165). These efforts are essential for improving maternal health outcomes in LMICs.

Maternal Death Surveillance and Response (MDSR) systems play a pivotal role in improving maternal health outcomes and ensuring accountability. These systems involve identifying, reporting, reviewing, and responding to maternal deaths (166). MDSR systems enable real-time monitoring of maternal mortality patterns and underlying

causes, thereby facilitating the assessment of progress in reducing maternal deaths (166). Integration with existing disease surveillance systems can be both beneficial and challenging (167). Effective implementation requires strong political commitment, clearly defined roles and responsibilities, and sufficient supervisory mechanisms (167).

Although many countries have established policies for maternal death notification and review, deficiencies persist in aggregate reporting, dissemination of findings, and engagement with communities.

Individual Factors

Individual factors significantly influence maternal and fetal outcomes, contributing to maternal mortality reduction efforts. Education level, wealth status, and health insurance coverage are key determinants of maternal health service utilization (168). Women's decision-making autonomy, gestational age at presentation, and household income are additional factors that significantly influence maternal and fetal health outcomes (169).

Beyond individual-level determinants, macrostructural factors such as education, private sector development, governance quality, and broader economic policies exert a critical influence on maternal mortality reduction (170). Addressing these distal determinants, in conjunction with expanding access to family planning, safe abortion services, and quality delivery care, is essential for achieving sustainable reductions in maternal mortality (170).

Research indicates that strengthening maternal health literacy, particularly in relation to the recognition of pregnancy danger signs, enhances women's capacity to seek timely care. Studies conducted in Indonesia, India, and Tanzania demonstrate that structured educational interventions substantially improve pregnant women's knowledge of obstetric danger signs (171-173). Although many women take appropriate action upon recognizing obstetric danger signs, overall awareness remains limited, with most able to identify only a small number of such signs (174).

Birth preparedness and complication readiness constitutes a crucial intervention aimed at minimizing delays in accessing skilled care during childbirth and obstetric emergencies (175). This involves identifying an appropriate health facility, arranging reliable transportation, setting aside financial resources, and undertaking other preparatory measures (176). A systematic review of Ethiopian studies found limited data on birth preparedness and complication readiness at the national level, highlighting the need for more comprehensive research (177).

Geographic Factors

Geographic factors are particularly significant in rural and underserved areas. Ensuring access to skilled birth attendants is essential for lowering maternal and neonatal mortality, particularly in rural and underserved regions. Despite global initiatives, numerous developing countries continue to encounter substantial obstacles in delivering skilled childbirth care (178). Globally, only 51% of women receive skilled care during childbirth, with disparities between high and low-income nations (178).

Maternity waiting homes, where women in their late pregnancy wait so they are closer to a hospital that can provide good care, are recommended as an effective strategy to minimize delays in accessing obstetric care, especially for women residing far from health facilities (179). Studies in Rwanda and Zambia indicates that maternity waiting homes offer a supportive environment and facilitate timely obstetric care, contributing to improved maternal and neonatal outcomes (179, 180).

Strengthening access to emergency care in rural and remote settings requires multifaceted strategies. Improving transport infrastructure is particularly vital, as many patients must travel long distances to referral hospitals, frequently without reliable motorized transportation (181). Telemedicine has emerged as an innovative approach to broaden access to specialist consultations and enhance healthcare delivery in underserved areas (182, 183). It can reduce costs, increase efficiency, and enhance both emergency and diagnostic care in rural areas (182).

Innovations in health service delivery such as telehealth, e-health, and enhanced medical transportation, hold substantial potential to improve the quality of care and health outcomes in remote settings (184). Effective implementation of these solutions necessitates multisectoral collaboration and an enabling regulatory environment to achieve their full impact (183).

Societal Factors

Societal factors also contribute substantially to maternal health outcomes. Advancing gender equality is fundamental to enabling women to make informed reproductive health choices. Empowerment through education, financial autonomy, and decision-making authority is strongly associated with greater utilization of reproductive health services (185).

Gender inequality, deeply embedded in cultural norms and discriminatory practices, constrains women's access to resources, education, and healthcare throughout their lives (186). Addressing these disparities is essential to advancing reproductive health and rights, which are internationally recognized as fundamental human rights (187).

Research shows that men's involvement in maternal and newborn health enhances care-seeking behaviours, strengthens home care practices, and improves couple communication (188). Paternal engagement has been linked to higher rates of antenatal care utilization, skilled birth attendance, and postpartum care (188, 189).

Partner support is influenced by sociodemographic factors, with greater involvement reported among partners of primiparous white women residing in less deprived settings (189). In certain contexts, men perceive pregnancy and childbirth as primarily a women's responsibility, restricting their participation to traditional roles such as financial support (190).

Harmful cultural practices remain a major threat to maternal health in several African contexts, including early marriage, preference for home births, and engagement in unsafe sexual practices (191). In rural areas of Nigeria and South Africa, limited awareness of the health risks linked to certain cultural practices persists, partly due to inadequate targeted mass media campaigns (191, 192).

A study in Southern Ethiopia reported that 71.4% of women practiced harmful cultural traditions during the perinatal period, with low maternal education, rural residence, limited antenatal care, and absence of skilled birth attendants identified as significant risk factors (193). To mitigate these challenges, scholars advocate for comprehensive awareness campaigns, policies that enhance women's social and economic status, and the promotion of girl child education. Additionally, culturally sensitive interventions and improved access to skilled care are critical to reducing maternal mortality (191, 193).

1.8. Role of ultrasound in maternal healthcare

Below is a summarized table elaborating the potential lifesaving uses of ultrasound in maternal healthcare:

Major Use of Ultrasound	**Key Lifesaving Benefits**
Early Pregnancy Assessment	Detects ectopic pregnancy, confirms intrauterine pregnancy, and estimates gestational age to guide timely care.
Detection of Multiple Pregnancies	Identifies twins or higher-order multiple pregnancies early, enabling closer monitoring and prevention of complications.

Placental Assessment	Diagnoses placenta praevia, abruption, or abnormal placental attachment (accreta), reducing risk of haemorrhage and maternal death.
Fetal Well-being and Growth Monitoring	Detects fetal growth restriction (FGR) and oligohydramnios, allowing interventions to prevent stillbirth and neonatal complications.
Diagnosis of Congenital Anomalies	Identifies severe fetal abnormalities early, guiding referral, birth planning, and management decisions.
Assessment of Amniotic Fluid	Helps diagnose oligohydramnios or polyhydramnios, both associated with poor maternal and fetal outcomes.
Guidance During Obstetric Procedures	Assists in safe performance of procedures such as amniocentesis, external cephalic version, and management of postpartum complications.
Monitoring High-Risk Pregnancies	Essential in hypertensive disorders, diabetes in pregnancy, and maternal infections to prevent morbidity and mortality.

Table 3: Potential Lifesaving Uses of Ultrasound in Maternal Healthcare

Early Pregnancy Assessment

Ultrasound assessment during the first trimester constitutes a critical diagnostic tool, as it enables the accurate differentiation between viable intrauterine pregnancies, failed intrauterine pregnancies, and ectopic pregnancies (194, 195). Transvaginal ultrasound provides superior image resolution, making it especially valuable for evaluating early embryonic development and detecting signs of potential pregnancy failure (196). When combined with quantitative human chorionic gonadotropin testing, it can effectively diagnose ectopic pregnancies (196). Prompt identification of ectopic pregnancies is critical, as it substantially mitigates the risk of maternal morbidity and mortality (196).

Additionally, first-trimester ultrasound not only confirms the presence of an intrauterine pregnancy and provides precise gestational dating but also increasingly facilitates the early screening of chromosomal and structural fetal abnormalities (195, 197).

In acute clinical scenarios, transvaginal ultrasound is the modality of choice for assessing first-trimester pregnancy viability, determining gestational age, identifying multiple gestations, and evaluating pregnancy-related complications (197).

Detection of Multiple Pregnancies

Multiple gestations are associated with substantially elevated maternal and fetal risks relative to singleton pregnancies. Women carrying multiples are at increased risk of complications such as preeclampsia, gestational diabetes, preterm labour, and postpartum haemorrhage (198, 199).

Multiple gestations further increase the risk of fetal complications, including prematurity, intrauterine growth restriction, and perinatal mortality (200). Early detection and provision of specialized care are essential for the management of high-risk pregnancies. Ultrasound serves a pivotal role in monitoring fetal development and identifying complications (200).

Ultrasound plays a crucial role in assessing chorionicity and amnionicity in multiple gestations, which is essential for determining pregnancy risks and management (201). Early determination of chorionicity and amnionicity is crucial, as monochorionic twin pregnancies carry an increased risk of complications, including twin-twin transfusion syndrome and fetal growth restriction (202). Timely and accurate determination facilitates appropriate referral to specialized fetal medicine centers and enables tailored management of complications unique to monochorionic and monoamniotic twin pregnancies (202).

Placental Assessment

Placental anomalies, such as placenta praevia and placenta accreta, represent major contributors to obstetric haemorrhage and remain significant causes of maternal morbidity and mortality (203). The incidence of these conditions has increased, a trend attributed to rising caesarean delivery rates, advanced maternal age, and the growing use of assisted reproductive technologies (203, 204).

Ultrasound plays a crucial role in antenatal diagnosis, enabling the timely detection and appropriate management of placental abnormalities (205, 206). Early detection facilitates accurate counselling, planned delivery in appropriately equipped multidisciplinary centers, and the consideration of conservative management strategies (205). For persistent placenta praevia, a planned caesarean delivery is recommended (206).

Referral to tertiary care centers equipped with multidisciplinary teams is recommended to optimize maternal and perinatal outcomes (204). Advances in prenatal diagnosis and management have markedly improved outcomes for conditions that previously represented major contributors to maternal mortality (206).

Fetal Well-being and Growth Monitoring

Fetal growth restriction (FGR) complicates approximately 5–8% of pregnancies and is strongly associated with elevated risks of perinatal morbidity and mortality (207). Ultrasound imaging is central to the detection and surveillance of fetal growth restriction, offering essential information that guides timely intervention and management (208).

A standardized approach to the management of fetal growth restriction enhances outcomes, reduces the risk of stillbirth, and supports the optimization of delivery timing (209). Early-onset FGR (before 32 weeks) differs from late-onset FGR (at or beyond 32 weeks) in both clinical presentation and surveillance requirements (207). In early-onset FGR, deterioration is often heralded by abnormal ductus venosus Doppler findings necessitating preterm delivery, whereas late-onset FGR is predominantly characterized by abnormal cerebral Doppler parameters (207, 209).

When ultrasound indicates fetal growth restriction, prenatal care encompasses confirmation of the diagnosis, assessment of severity, close monitoring of fetal well-being, and determination of the optimal timing for delivery (210). From 38 weeks of gestation onward, the overall risk-benefit profile favours proceeding with delivery (209).

Diagnosis of Congenital Anomalies

The prenatal detection of severe fetal anomalies through ultrasound plays a pivotal role in guiding clinical decision-making and shaping care management strategies (211). Although prenatal diagnosis of congenital anomalies can elevate maternal anxiety and depressive symptoms, it significantly reduces neonatal morbidity and mortality by enabling clinicians to optimize prenatal care and plan deliveries in settings equipped with the necessary personnel for immediate postnatal stabilization (211).

Early detection allows for the preparation of neonatal care teams to optimize outcomes and facilitates counselling on appropriate management options (212). However, the shift from postnatal to prenatal diagnosis elicits complex emotional responses in parents, who must make challenging decisions while often feeling unprepared to confront abnormal findings (213).

Successful completion of referrals depends on effective communication among sonographers, patients, and healthcare facilities; however, significant barriers such as cost, transportation, and navigating hospital systems persist (214).

Assessment of Amniotic Fluid

Ultrasound assessment of amniotic fluid abnormalities provides a critical indicator of underlying maternal and fetal pathology. Oligohydramnios is linked to placental insufficiency, fetal compromise, and a higher likelihood of obstetric interventions (215). Severe oligohydramnios occurring before 22 weeks of gestation impairs pulmonary development and may result in limb deformities (216).

Polyhydramnios is often indicative of maternal diabetes or underlying fetal anomalies (217). In cases of polyhydramnios, approximately 66% are linked to fetal conditions, including structural anomalies and chromosomal disorders, whereas around 12% are associated with maternal diabetes (218). Both oligohydramnios and polyhydramnios are associated with substantially higher risks of perinatal mortality and congenital anomalies compared with normal amniotic fluid volumes (217). Early detection through ultrasound facilitates appropriate diagnostic evaluation and the formulation of effective management strategies (215, 216).

Guidance During Obstetric Procedures

In clinical practice, ultrasound substantially improves obstetric interventions by providing objective measurements for labour management. It aids in pre-induction cervical length assessment and accurately determines fetal head position during instrumental deliveries, a task that is frequently challenging with digital examination alone (219).

Ultrasound guidance is essential for prenatal interventions, with real-time three-dimensional imaging enhancing safety by visualizing needle tips in three orthogonal planes, thereby minimizing the risk of injury to fetal structures (220). The proficiency and experience of the operator remain critical factors in minimizing procedure-related morbidity during these interventions (220).

Monitoring High-Risk Pregnancies

Ultrasound imaging is an essential tool for monitoring pregnancies complicated by diverse conditions, facilitating early detection and management of complications. In malaria-endemic regions, ultrasound effectively evaluates the impact of maternal infection on fetal growth, with second-trimester malaria linked to reduced fetal head growth; however, timely treatment mitigates these adverse effects (221).

In pregnancies complicated by diabetes, sonography provides essential management support throughout all trimesters, delivering critical information on gestational age, fetal growth patterns, anatomical development, and overall fetal well-being (222).

A comprehensive study involving 350 pregnant women demonstrated the high sensitivity of ultrasound in detecting pregnancy complications, including among women with gestational diabetes (85%), preeclampsia (79%), and intrauterine growth restriction (82%), underscoring its continued importance in antenatal care (223).

Ectopic Pregnancy

Ectopic pregnancy is a medical condition where the embryo implants outside the uterine cavity and has the potential to become life-threatening if not diagnosed and treated promptly (224). Ultrasound stands as the cornerstone of ectopic pregnancy diagnosis, offering the potential for earlier detection, which in turn can facilitate timelier treatment and reduce the occurrence of ectopic pregnancy ruptures and their associated severe haemorrhage (225, 226).

Transvaginal scanning (TVS) is the preferred imaging method for diagnosing ectopic pregnancy. This technique entails inserting a probe into the vagina to capture high-resolution images of the pelvic organs. TVS has demonstrated a sensitivity ranging from 88.5% to 93.1% and a specificity between 95.7% and 96.5% in detecting ectopic pregnancies (227, 228).

An additional study by Pape et al. in 2021 validated the strong accuracy of transvaginal ultrasound (TVS) in diagnosing ectopic pregnancies, emphasizing its reliability across five distinct morphological types, regardless of their location (229). TVS aids in the identification of different types of ectopic pregnancies, including tubal, interstitial, and cervical ectopic pregnancies (230). In the case of caesarean scar ectopic pregnancies, increasingly common with the more widespread use of caesarean section, transvaginal ultrasonography played a critical role in diagnosing the condition, potentially saving the patient's life (231, 232).

A research study by Rodgerson et al. in 2001 showed that performing right upper quadrant ultrasound in the emergency department is linked to a shortened time frame for diagnosing and treating ruptured ectopic pregnancies (233). TVS is instrumental in evaluating the existence of free fluid and blood within the pelvic cavity, which can serve as indicators of a leaking ectopic pregnancy (229). The observation of moderate to complex free fluid along with a heterogeneous structure in the adnexa region can also provide indications of haemorrhage linked to an ectopic pregnancy (234, 235).

Placenta Praevia

Placenta praevia is a medical condition during pregnancy where the placenta partially or completely covers the cervix, which can cause bleeding and other complications. This condition can lead to profuse bleeding per vaginum before the birth of the baby. Early in pregnancy, ultrasound can identify placenta praevia, enabling timely and suitable management and ongoing monitoring (236).

Ultrasound assumes a pivotal role in the diagnosis of placenta praevia (237). TVS is regarded as the definitive method or gold standard, while transabdominal ultrasound scanning technique is employed for the initial screening. The accuracy of ultrasound in assessing praevia placentation has been high between 93% to 98% (238). The timely identification of placenta praevia by ultrasound empowers healthcare providers to strategize a safe delivery, by scheduling a caesarean section and avoiding the profuse bleeding that can occur during an attempted spontaneous vaginal delivery (239). Complications such as postpartum haemorrhage, the need for hysterectomy, and neonatal mortality can thus be avoided (236).

Ultrasound's Role in Maternal Mortality

Ultrasound imaging is a critical tool in efforts to reduce maternal mortality, as it facilitates the early detection and diagnosis of life-threatening pregnancy complications. According to the WHO, the principal causes of maternal mortality include haemorrhage, sepsis, complications of abortion, eclampsia, and obstructed labour conditions in which timely ultrasound assessment can play a role in improving maternal outcomes (240).

Ultrasound proves particularly valuable in the diagnosis of high-risk conditions such as ectopic pregnancy, placenta praevia, placental abruption, and postpartum haemorrhage (241). Although the WHO recognizes ultrasound as a low-cost and portable diagnostic technology, evidence of its impact remains limited in low-income countries, where 99% of preventable maternal deaths occur. These complications are commonly associated with severe obstetric bleeding, which poses an immediate threat to maternal survival (242).

Telemedicine initiatives have demonstrated considerable potential in expanding access to ultrasound services, with studies reporting successful remote consultations for high-risk obstetric conditions such as breech presentation, placenta praevia, and multiple gestations (243).

1.9 Regional trends in the use of obstetrics ultrasound-Global, Africa and Ghana

Global disparity

Global patterns of obstetric ultrasound utilization highlight pronounced inequities across geographic, socioeconomic, and demographic contexts. A population-based study by Adams et. al, analysed 80,536 pregnancies involving 57,881 women in Saskatchewan, Canada, between 2014 and 2018. It found that approximately 87.7% of pregnancies carried beyond 23 weeks received a second trimester ultrasound. Significant disparities were observed: women in rural areas had a 30% lower odds (adjusted odds ratio [aOR], 0.70; 95% CI, 0.63-0.77), those in remote areas had a 65% lower odds (aOR, 0.35; 95% CI, 0.32-0.39), and First Nations women had a 50% lower odds (aOR, 0.50; 95% CI, 0.46-0.53) of receiving the second trimester ultrasound. Conversely, women in higher income neighbourhoods were nearly twice as likely (aOR, 1.86; 95% CI, 1.62-2.13) to undergo the ultrasound. Overall, higher socioeconomic status and proximity to healthcare services significantly increased ultrasound utilization, indicating substantial sociodemographic disparities in prenatal imaging access (244).

Access to obstetric ultrasound remains poor in many developing countries, particularly in rural settings, despite its proven potential to improve maternal and neonatal outcomes (245). Obstetrics ultrasound imaging in developing countries, has been limited, with outdated or broken equipment being a common issue. This indicates a lack of resources and infrastructure in these regions (246).

Sippel et al (2011) summarized multiple research studies, demonstrating the impact and feasibility of clinician-performed ultrasound in developing countries. For example, in Rwanda, ultrasound changed patient management in 43% of cases, influencing procedures, medications, and referrals. In Liberia, ultrasound altered management in 62% of cases, with notable effects in obstetrics and abdominal assessments. Additionally, a Ghanaian study performed 67 ultrasounds with 81% abnormal findings, which contributed significantly to diagnosis and treatment. Overall, the literature indicates that ultrasound influences clinical decisions in approximately 28% to 62% of cases in these settings, supporting its utility as a diagnostic tool in resource-limited environments (247).

According to this review article by Sippel et al. published in 2011, point-of-care ultrasound is increasingly used in rural and resource limited parts of the world (247)

However, there are still many challenges and barriers, such as lack of sonography education, inadequate trained sonographers, and limited access to equipment and maintenance (248, 249).

Cost-effectiveness

Investment in both equipment and human resources for ultrasound in obstetrics has been shown to be cost-effective and should be prioritized for the improvement of healthcare. It can enhance maternal and fetal health outcomes (250, 251). Several studies found that ultrasound screening can detect fetal abnormalities early (252, 253), allowing for timely interventions and reducing the need for costly and invasive procedures.

Recent studies have evaluated the cost-effectiveness of obstetric ultrasound across different clinical settings. Findings suggest that a presentation-only scan in late pregnancy offers the most cost-effective approach, whereas universal screening for fetal size is unlikely to provide good value for resources invested (254). In emergency care settings, ultrasound has been shown to improve cost-effectiveness, especially in the assessment of paediatric appendicitis and abdominal trauma (255).

However, in LMICs, the introduction of antenatal screening ultrasound is unlikely to be economically efficient, primarily due to the substantial costs associated with training and equipment maintenance, despite minimal impact on overall healthcare expenditures (256). The cost-effectiveness of ultrasound is highly dependent on its specific clinical application and the healthcare context, highlighting the need for context-specific evaluations when planning the implementation of obstetric ultrasound screening programs.

Innovative uses of obstetrics and gynaecology ultrasound

Deep learning techniques have demonstrated considerable potential in the analysis of ultrasound images for pregnancy-related conditions. These methods offer the capacity to address limitations inherent in conventional diagnostic approaches (257).

Point-of-care ultrasound (POCUS) is transforming obstetric and gynaecological practice by facilitating immediate bedside imaging, thereby supporting timely and potentially life-saving clinical decision-making (258). It is especially valuable in emergency contexts,

resource-constrained settings, and in the evaluation of a wide range of pregnancy-related conditions (259, 260).

POCUS has been shown to enhance diagnostic accuracy, reduce the incidence of undiagnosed breech presentations, while also providing essential obstetric information including fetal status, gestational age, and placental location and support the identification of various gynaecological conditions (258). Its broad adoption is encouraged given its cost-effectiveness, portability, and demonstrated potential to improve patient care and clinical outcomes (261).

However, effective implementation requires comprehensive training to ensure accurate image acquisition and reliable interpretation (258, 259). Integrating POCUS training into educational programs for midwives, medical students, and healthcare practitioners is essential (261). Overall, POCUS signifies a paradigm shift in obstetrics and gynaecology, providing numerous potential benefits in both well-resourced and resource-limited healthcare v settings (258, 260).

Ultrasound is used to follow up on ovarian follicles in infertility cases and in intraoperative ultrasound, it is used during fertility-sparing surgery (262). 3D/4D ultrasound can be used in the prenatal diagnosis of structural fetal anomalies (263). 3D ultrasound can be used in the prenatal diagnosis of other fetal anomalies, such as microcephaly, ventriculomegaly, holoprosencephaly and anencephaly (264).

Ultrasound training and education

In developing regions, healthcare practitioners frequently highlight the absence of adequate training as a fundamental obstacle to the consistent utilization of ultrasound within their medical practice (248, 265). A systematic review study found that training programs to date pregnancies using ultrasound have been successful in LMICs, with 96% of trainees passing criteria to do so (266).

However, most programs fell short of the minimum standards recommended by international organizations. The use of ultrasound in LMICs has been expanding, with most studies originating from Southeast Asia and sub-Saharan Africa (267). Emergency medicine training programs, including those focused on ultrasound, have been established through collaborations between high- and low-resource settings; however, they often encounter challenges related to local adaptation, contextual relevance, and long-term sustainability (268).

Health facilities that conduct obstetrics and gynaecological ultrasound.

Generally, the level of health facilities that conduct obstetrics and gynaecological ultrasound can vary depending on the region and resources available. These facilities play a crucial role in providing comprehensive women's health care and prenatal services.

At the basic level, primary health centres and small clinics often provide routine obstetric and gynaecological ultrasound services. These facilities are essential for early pregnancy confirmation, basic fetal monitoring, and assessing common gynaecological issues (269, 270).

In a qualitative study that explored the facilitators and barriers to introducing obstetric ultrasound in primary health care facilities in Ethiopia, where obstetric ultrasound coverage is low, it was concluded that the health system provides an enabling environment to introduce limited obstetric ultrasound services at the primary health care level. The study also found out that trained and supervised mid-level maternal and neonatal care providers can deliver routine limited obstetric ultrasound scans as part of ANC services (270).

Similarly, another study from South Africa that looked at training advanced midwives to use limited obstetric ultrasound during prenatal care in primary healthcare settings, found that, ultrasound performed by trained midwife at the primary health centre will trigger an appropriate referral (269).

Secondary and tertiary hospitals and clinics contribute greatly to giving obstetric and gynaecological ultrasound services to facilitate swift and accurate identification and treatment of diverse range of conditions across nearby medical facilities. They typically have more advanced ultrasound capabilities. They offer a wider range of obstetric and gynaecological ultrasound services, including detailed fetal anatomy scans, assessment of uterine abnormalities, and initial evaluation of gynaecological conditions (271).

Academic medical centres and research institutions play a role in pushing the boundaries of obstetrics and gynaecological ultrasound. They are involved in advanced research, innovation, and training of medical professionals in the latest ultrasound techniques and applications (272). Private diagnostic centres, often affiliated with hospitals or independently operated, provide obstetrics and gynaecology services. These centres may offer convenience and expedited appointments for routine scans and specialized assessments (273).

The level of health facility conducting obstetrics and gynaecological ultrasound varies from basic primary care centres to advanced tertiary care hospitals and specialized clinics. The availability of ultrasound services at different levels contributes to comprehensive women's health care and ensures that women receive appropriate diagnostics and treatment throughout their reproductive journey.

Telemedicine and ultrasound services?

Telemedicine and ultrasound services are progressively being integrated to offer remote healthcare delivery and diagnostic imaging.

With technological advancements, telemedicine platforms and mobile health services are incorporating ultrasound as well in industrialised nations (274). L consultations and point-of-care ultrasound are becoming increasingly common, allowing healthcare providers to offer guidance and assessments even in underserved or remote areas (275, 276). In such instances, there is a human operator with the woman or patient, and a more skilled person or specialist would be giving instructions in real-time usually via video conferencing.

In a remote Canadian community, a study implemented a telerobotic ultrasound system for conducting obstetrical ultrasound examinations amidst a COVID-19 outbreak. In this setup, a sonographer remotely controlled the ultrasound probe and its settings from a location situated 605 kilometres away, with radiologists interpreting the results of the exams (277).

A 5G field test framework was employed to facilitate preclinical diagnostics using mobile ultrasound for emergency patients. This test demonstrated exceptional capabilities, including high-quality bi-directional audio-video data transmission, minimal latency, and robust throughput for both ultrasound image data and video streams (278).

In a refugee camp located in Tanzania, local staff received training in basic ultrasound imaging techniques. Subsequently, telemedicine consultations were carried out by uploading the ultrasound images to a telemedicine portal. This method enabled specialist interpretation and guidance in patient care, even in remote settings (279).

In a phantom experiment, panoramic ultrasound reconstruction was employed to transmit a single image encompassing all the acquisition data. This innovative technique proved effective, particularly for acquiring images at greater depths and with higher

contrast, rendering it well-suited for teleultrasound monitoring in rural regions where internet bandwidth is constrained (280).

Low obstetric ultrasound coverage by health facilities in developing countries is a significant issue that affects maternal and infant mortality rates (281). While there is almost a universal access to obstetric ultrasound in developed countries, access in developing countries is poor, particularly in rural areas (282), and introduction of telemedicine resources would greatly improve maternal health outcome.

Evidence from several case studies highlights the feasibility and clinical value of implementing ultrasound in combination with telemedicine in low-resource settings. A systematic review documented a wide range of applications across Africa, particularly in cardiology and obstetrics, demonstrating that ultrasound images transmitted through telemedicine platforms to expert interpreters were of sufficient quality to support accurate clinical diagnosis and management (283).

In South Africa, an asynchronous telemedicine model allowed specialists to remotely guide a midwife in performing obstetric ultrasounds. Through this system, 25 high-risk conditions including breech presentations and fetal malformations were successfully identified among 91 pregnant women (243).

In Peru, the application of a telediagnostic system utilizing volume sweep imaging enabled operators with no prior ultrasound training to acquire diagnostic quality scans in 96% of cases (284). Similarly, in rural Uganda, the integration of point-of-care ultrasound with telemedicine support altered clinical management in 87% of patients with positive findings, demonstrating effectiveness across a range of conditions including trauma, shock, and cardiorespiratory disorders (285).

Availability and procurement of ultrasound equipment

When procuring an ultrasound machine, it is important to consider factors such as cost, availability of spare parts and accessories, technical support, and whether to opt for a new or refurbished machine. It is also important to ensure that machines are readily available for use when required (111).

A new machine will come with a warranty, but a refurbished machine can be a more cost-effective option (286). Availability of spare parts and accessories is an important consideration when purchasing an ultrasound machine. Ideally, you want a machine with

readily available parts such as monitors, keyboards power suppliers, upper control panels, panels, buttons, and keys (287).

Point-of-care ultrasound (POCUS) is increasingly acknowledged as a valuable and cost-effective diagnostic tool in LMICs, including Ghana, owing to its portability and its capacity to enhance clinical decision-making in resource-limited settings (288, 289). POCUS systems are cheaper but have more limited diagnostic ability.

However, in rural Ghana, POCUS has been shown to substantially influence patient management, with nearly half of examinations confirming clinical diagnoses and more than a quarter leading to referrals for higher-level care (289). Limited access to ultrasound equipment remains a significant barrier, with cost and availability frequently cited as major challenges, although most healthcare providers acknowledge its role in improving quality of care (249).

While the cost of POCUS systems is lower than full diagnostic ultrasound machines, affordability remains a concern relative to health budgets in LMICs (249, 288). Even in higher-resource settings, deficiencies in equipment availability and shortages of adequately trained personnel persist, underscoring the need for sustained and targeted investment (290).

Community perspectives of ultrasound use during pregnancy in the sub-Saharan African region.

A study conducted in Northern Nigeria found that about a fifth of the sampled pregnant mothers had not utilized obstetric ultrasound, and the main reason for accessing ultrasound was to know fetal viability (291). Another study in the same area found at least 60% of respondents had a positive view of ultrasound use during pregnancy'. These studies suggest that while there are challenges to ultrasound utilization in developing countries, there is also a willingness among pregnant women to use the technology when it is available (292).

Many women have reported a higher level of tolerance for ultrasound during labour in the stead of digital vaginal examination (293). In situations where feasible, it is recommended to offer trans perineal ultrasound as a substitute for digital vaginal examination throughout the labour process (294).

Studies across diverse African populations indicate that expectant mothers generally perceive prenatal ultrasound as both essential and trustworthy. For instance, research in

Nigeria found that 84.6% of pregnant women considered prenatal sonography necessary, 66.7% perceived the results as reliable, and 88.7% expressed satisfaction with the services received (295). Similarly, a study conducted in Lagos reported that 94% of respondents expressed positive psychological responses to ultrasonography, while 84% believed it posed no risk to their babies (296).

In northern Nigeria, 93.8% of women regarded ultrasound as necessary during pregnancy, with 97% perceiving it as safe and essential for assessing fetal viability and well-being (297). In Ghana, women similarly perceived antenatal ultrasound as beneficial; however, notable communication gaps were identified in the explanation of procedures and interpretation of results (298). Collectively, these studies demonstrate consistently high levels of acceptance and trust in prenatal ultrasound across diverse African healthcare settings, despite persistent variations in women's understanding of the procedures.

In a systematic review to sample women's view on pregnancy ultrasound, they and their families found ultrasound to be attractive (299). While physicians also widely value pregnancy ultrasounds, there is a growing sense of concern regarding deficiencies in ultrasound equipment quality and the insufficient number of proficient physicians capable of conducting and independently interpreting ultrasound scans (300).

1.10 Interventions for Postpartum Haemorrhage in Low-Income Settings

Postpartum haemorrhage remains the leading direct cause of maternal mortality globally, with its burden disproportionately affecting LMICs (1). In recent years, the exploration and implementation of novel haemostatic agents have gained attention as strategies to improve the management of PPH, particularly in settings with limited access to surgical interventions or blood transfusion services (301).

The WHO recommends that 10 units of intravenous or intramuscular oxytocin is given for the prevention of PPH, or if not available, alternatives such as parenteral ergometrine or oral misoprostol (302). In a systematic review and network meta-analysis, prophylactic oxytocin was associated with a relative risk reduction of 42%, for post-partum haemorrhage > 500mL, with even greater benefits observed for ergometrine plus oxytocin or misoprostol plus oxytocin (303).

In a recent large multicentre cluster trial in Kenya, Nigeria, South Africa and Tanzania, a bundle of care including the use of a calibrated blood-collection drape for early detection of PPH, and a series of rapid-response treatments (uterine massage, oxytocics,

intravenous fluid resuscitation, examination and escalation) was shown to reduce severe PPH from 4.3% to 1.6% (relative risk 0.40; 95%CI 0.32 to 0.50) compared with usual care (304). The WHO has subsequently recommended quantitative measurement of blood loss and a treatment bundle supported by a treatment strategy for all women who have a vaginal birth (305).

1.11 Chitosan Gauze as a Novel Intervention for Postpartum

Chitosan-based gauze has emerged as a particularly promising intervention for the treatment of PPH (306, 307). It has a potential advantage over alternative compression treatments such as balloon or condom tamponade because chitosan has additional haemostatic properties.

Chitosan, initially developed for use in military medicine, has demonstrated considerable potential as a haemostatic agent in the management of severe obstetric haemorrhage (307, 308). Multiple case studies have reported its effectiveness across a range of obstetric situations, including atonic postpartum haemorrhage, vaginal lacerations, and at caesarean deliveries (309, 310). A comparative study of chitosan tamponade, balloon tamponade, and medical therapy demonstrated that chitosan tamponade significantly reduced the incidence of hysterectomy, without an associated increase in adverse effects (307).

Chitosan is available in both powder and gauze forms, offering a versatile and cost-effective alternative to conventional interventions such as uterine balloon tamponade (309). Its application requires minimal training and has demonstrated success in cases where conventional treatment approaches have proven ineffective (308, 310). Chitosan-based biomaterials possess a range of other beneficial properties, including antibacterial, antifungal, and analgesic activities, along with high biocompatibility and biodegradability (311). The positively charged surface of chitosan facilitates the adsorption of red blood cells and platelets, promoting the formation of platelet-rich thrombi at the site of bleeding (312). However, the limited water solubility and relatively weak adsorption capacity of chitosan constrain its effectiveness as a local haemostatic agent, highlighting the need for further modifications and optimization (312). Despite these limitations, chitosan-based materials remain promising for achieving haemostasis in surgical and postoperative contexts, especially in resource-limited settings where access to advanced interventions is restricted (308).

A recent case report from a hospital in Mexico further highlights the efficacy of chitosan in the management of acute postpartum haemorrhage, suggesting its potential utility as a standard intervention in high-risk obstetric cases (313). The incorporation of chitosan gauze into emergency obstetric care offers a novel and practical strategy for managing postpartum haemorrhage in LMICs. Although promising, additional large-scale clinical trials are needed to establish its role within standard PPH management protocols.

1.11 Summary and Aims

Maternal mortality remains a critical global health concern, disproportionately affecting LMICs, especially in sub-Saharan Africa. Despite global declines, sub-Saharan Africa still bears two-thirds of global maternal deaths, with over 450 deaths per 100,000 live births. Contributing factors include inadequate healthcare infrastructure, limited antenatal services, poverty, gender bias, and weak health systems. Specific causes such as haemorrhage, hypertensive disorders, infections, obstructed labour, and teenage pregnancies are compounded by social determinants like poor education, low socioeconomic status, and cultural practices.

In Ghana, similar barriers including delayed referrals, insufficient emergency care, lack of skilled birth attendants, and uneven resource distribution sustain high maternal mortality rates. Many women in rural areas face transportation challenges and financial constraints, causing delays in receiving life-saving interventions. Traditional birth practices can also increase risks when unregulated.

PPH remains a predominant contributor to maternal mortality in Ghana, with its burden consistently documented across successive decades of research. National surveillance data attribute 22.8% of maternal deaths to haemorrhage, while more recent epidemiological studies report an increased contribution of approximately 24%, underscoring its persistent role as a critical driver of maternal mortality (314, 315).

The impact of PPH extends beyond maternal mortality to considerable economic consequences. Substandard uterotonics alone are estimated to impose an annual economic burden of $18.8 million, of which $6 million arises from productivity losses attributable to maternal deaths (316). Better-quality uterotonics could prevent around 100 PPH deaths annually, reducing mortality by about 11% (316).

Amid these challenges, ultrasound emerges as a key tool that may potentially improve maternal outcomes. It enables early detection of high-risk conditions such as placenta praevia, ectopic pregnancy, fetal growth abnormalities, and preeclampsia, facilitating

timely and appropriate care. Research underscores that ultrasound-based assessments may reduce perinatal and maternal morbidity and mortality by identifying complications before they become life-threatening.

However, there is paucity of evidence on the importance of quality research on efficacy of ultrasound use in LMICs. On this background, the thesis aimed to investigate two specific main areas: the use of ultrasound and to the treatment of PPH.

The specific aims are:

1. To comprehensively evaluate the literature regarding routine use of prenatal ultrasound for improving maternal and perinatal outcomes, particularly in low-resource settings.
2. To develop a systematic review protocol to assess the impact of routine prenatal ultrasound on pregnancy and perinatal outcomes in low-resource settings.
3. To conduct a systematic review using the protocol developed in Aim (2).
4. To review the Ghana Demographic Health Survey on maternal mortality in Ghana and determine causes, trends, and the potential role of obstetric ultrasound (2012–2017).
5. To develop a protocol to assess the efficacy of chitosan-covered gauze in the management of postpartum haemorrhage in low-resource settings in a cluster RCT in Ghana.

CHAPTER 2: Assessing the Impact of Routine Prenatal Ultrasound on Pregnancy and Perinatal Outcomes in Low-Resource Settings: A Systematic Review Protocol.

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Amendments
Any deviations from the protocol will be described in the final report of the review.

Support: Sources: Self-funded **Sponsor:** Yusif Yakub

Role of sponsor or funder: Principal investigator. Stores and helps in management of the research data. There would not be any restrictions on disseminating the final report of the review.

2.1 Abstract

Background

Obstetric ultrasound is an important part of pregnancy care around the world. However, limited access to this technology in low resource settings, poses a significant challenge in lowering the rates of complications and deaths during pregnancy and childbirth in these regions. We plan to conduct a systematic review to synthesize research on the impact of routine prenatal ultrasound on pregnancy and perinatal outcomes.

Method

We will include all experimental and observational studies that compare the use of routine ultrasound during pregnancy with no routine ultrasound use in pregnancy care and were conducted within low-resource settings. We will search Medline (OvidSP), CINAHL, Cochrane Library/CENTRAL, Embase (OvidSP), Scopus, Maternity and Infant Care, and Global Index Medicus. Studies published between 1st January 1980 and 30th May 2024 in any languages will be included and reference lists of relevant publications. Two authors will independently select studies and extract data from included studies. Where meta-analysis is not feasible, a narrative synthesis will be used to summarize the findings descriptively.

The primary outcome will be maternal mortality, and other outcomes will include adverse maternal and perinatal events. Subgroup analyses will include timing of gestational age at ultrasound for less than 28 weeks gestational age versus 28 or more weeks, rural/regional location versus metropolitan, maternal high socioeconomic status versus low socioeconomic status, fully trained sonographers versus sonographers with less training, and randomised controlled trials versus observational studies will be carried out as these factors may modify the relationship between routine prenatal ultrasound and outcomes.

The methodological quality of individual studies, size of effect, precision of effect estimates, the consistency of findings across studies, and the relevance and applicability of the evidence to low-resource settings will be evaluated to determine the strength of evidence.

Ethics and dissemination:

Ethics approval is not required for this systematic review, as it entails the analysis of data from previously conducted published studies

A report of this review will be shared through publication in peer-reviewed journals and presentations at conferences.

Trial registration: International prospective register of systematic reviews (PROSPERO) registration number CRD42023474088

Keywords:
Ultrasound, prenatal, maternal mortality, low-resourced setting, pregnancy

2.2 Introduction

The impact of obstetric ultrasound in enhancing outcomes for mothers and their newborns is a growing area of focus and an important element in global antenatal care (317, 318). Access to ultrasound services may play a crucial role in reducing maternal mortality rates and improving neonatal health outcomes, particularly in resource-limited settings (319).

The main goals of a first trimester routine ultrasound are to confirm intrauterine pregnancy and establish gestational age (320). It also helps detect any abnormalities in the uterus or ovaries and checks for chorionicity and amnionicity in multiple gestations (321). Routine ultrasounds in the second and third trimesters confirm the number of fetuses and placenta location (322), as well as identify any fetal abnormalities (323). These ultrasounds also help to detect placental anomalies, which significantly affects fetal and perinatal outcomes (324).

Obstructed labour, unsafe abortion, and haemorrhage collectively constitute a significant portion of maternal fatalities (325) (see Section 1.6 of this thesis), and ultrasound emerges as a promising strategy for effectively managing these risks (326, 327). The WHO's global guidelines for pregnancy care in 2016 and 2022 incorporated a recommendation for at least one obstetric ultrasound scan before 24 weeks of gestation (328, 329).

An estimated 99% of maternal deaths occur in low-resource countries (7), with sub-Saharan Africa bearing the weight of approximately two-thirds of the world's maternal mortality (4). The region also experiences the highest rates of newborn mortality (5). In much of the sub-Saharan African region, only 6% of pregnant women in rural areas are estimated to have access to obstetric ultrasound, while those in urban settings have a slightly higher coverage of around 30% (330). Lack of access of antenatal ultrasound in sub-Saharan Africa is a significant challenge in addressing the enormous burden of perinatal morbidity and mortality (330).

The objective of this systematic review is to address how the use of routine prenatal ultrasound impact on pregnancy and perinatal outcomes for women giving birth in low-resource settings and their babies, compared with no ultrasound or only using ultrasound when specifically indicated.

2.3 Methods

Protocol design and registration

This systematic review is not an update of a previous systematic review, and the protocol has been prepared consistent with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols 2015 checklist (331).

Our systematic review protocol is registered with the International Prospective Register of Systematic Reviews (http://www. crd.york.ac.uk/PROSPERO) on 29 October 2023 with registration number CRD42023474088.

Eligibility criteria

Study designs

The review will include studies that compare routine ultrasound utilization in antenatal care with no routine ultrasound utilization in antenatal care. It will include randomised controlled trials with randomisation at the individual and cluster level. The review will also include prospective and retrospective comparative observational studies including cohort studies and case-controlled studies. Studies that reported routine prenatal ultrasound utilization in low-resource settings will be included. Non-comparative studies and studies that do not assess ultrasound in pregnancy will be excluded. The screening process will exclude commentaries, letters, and editorials.

Participants and settings

The participants will be pregnant women in low resource countries defined as gross national income per capita than US$1045 as estimated by the World Bank, signifying their economic constraints in meeting essential societal needs (332).

Intervention and Comparison Groups

The intervention is utilization of routine antenatal ultrasound on at least one occasion during the pregnancy, and the comparator is no routine antenatal ultrasound utilization. The comparator will include settings where ultrasound is available sporadically or on demand but is not done routinely.

Other eligibility criteria

Studies will be included if maternal mortality or any of the outcomes listed in the additional outcomes section below are reported. Publications from 1st January 1980 to 31st July 2024 reported in any language will be included. Studies in other languages apart from English will be initially translated using Google Translate, and key data will be confirmed by bilingual colleagues fluent in the respective languages.

Information sources:

We will search Medline (OvidSP), CINAHL, Cochrane Library/CENTRAL, Embase (OvidSP), Scopus, Maternity and Infant Care, and Global Index Medicus. To thoroughly cover the existing literature, we will examine the reference lists of the studies included and pertinent reviews that have been identified through our search for other relevant papers for possible inclusion.

2.4 Search Strategy

Searches will include terms such as ultrasound, ultrasonography, maternal, prenatal, antenatal, sub-Saharan Africa and other related terms. The planned search strategies are below:

Search Strategy for Ovid MEDLINE(R) ALL <1946 to May 30, 2024

1. ((ultraso*) adj3 (pregnan* or gestation or cyesis or antenatal or prenatal or obstetric*)).mp or Ultrasonography, Prenatal/

2. developing countries/
3. (developing countr* or low* income countr* or low* resource countr* or low* middle income countr* or LMIC or Ghana or Ethiopia or Afghanistan or Benin or Rwanda or Zimbabwe or Niger or Somalia or South Sudan or Sierra Leone or Tanzania or Togo or Uganda or Zambia or Guinea or Guinea-Bissau or Haiti or Democratic People's Republic of Korea or North Korea or Liberia or Madagascar or Malawi or Mali or Mozambique or Eritrea or Democratic republic of Congo or Burundi or Burkina Faso or Chad or Comoros or Central African Republic).mp
4. 2 or 3
5. 1 and 4

The search technique/strategy for Cochrane Library/CENTRAL database will be as follows:

1. ((ultraso*) adj3 (pregnan* or gestation or cyesis or antenatal or prenatal or obstetric*)).mp or Ultrasonography, Prenatal/

2. developing countries/
3. (developing countr* or low* income countr* or low* resource countr* or low* middle income countr* or LMIC or Ghana or Ethiopia or Afghanistan or Benin or Rwanda or Zimbabwe or Niger or Somalia or South Sudan or Sierra Leone or Tanzania or Togo or Uganda or Zambia or Guinea or Guinea-Bissau or Haiti or Democratic People's Republic of Korea or North Korea or Liberia or Madagascar or Malawi or Mali or Mozambique or Eritrea or Democratic republic of Congo or Burundi or Burkina Faso or Chad or Comoros or Central African Republic).mp.
4. 2 or 3
5. 1 and 4

Search Strategy for Global Index Medicus

(((ultraso*) AND (obstetric* OR antenatal OR prenatal OR pregnancy OR gestation OR cyesis)))

AND (("low middle income countr*" OR Ghana OR Ethiopia OR Afghanistan OR Benin OR Rwanda OR Zimbabwe OR Niger OR Somalia OR "South Sudan" OR "Sierra Leone" OR Tanzania OR Togo OR Uganda OR Zambia OR Guinea OR "Guinea-Bissau" OR Haiti OR "Democratic People's Republic of Korea" OR "North Korea" OR "Liberia" OR Madagascar OR Malawi OR Mali OR Mozambique OR Eritrea OR "Democratic Republic of Congo" OR Burundi OR "Burkina Faso" OR Chad OR Comoros OR "Central African Republic"))

Search Strategy for Embase (Ovid)

1. ((ultraso*) adj3 (pregnan* or gestation or cyesis or antenatal or prenatal or obstetric*)).mp or fetus echography/

2. developing countries/ or exp western Africa/
3. (developing countr* or low* income countr* or low* resource countr* or low* middle income countr* or LMIC or Ghana or Ethiopia or Afghanistan or Benin or Rwanda or

Zimbabwe or Niger or Somalia or South Sudan or Sierra Leone or Tanzania or Togo or Uganda or Zambia or Guinea or Guinea-Bissau or Haiti or Democratic People's Republic of Korea or North Korea or Liberia or Madagascar or Malawi or Mali or Mozambique or Eritrea or Democratic republic of Congo or Burundi or Burkina Faso or Chad or Comoros or Central African Republic).mp.

4. 2 or 3
5. 1 and 4

Search Strategy for CINAHL via EBSCO

1. "((ultraso*) N3 (pregnan* OR gestation OR cyesis OR antenatal OR prenatal OR obstetric*))"

2. "low-resource settings" OR "resource-limited settings" OR "developing countries" OR LMICs OR "Ghana" OR " Ethiopia" OR "Afghanistan" OR "Benin" OR "Rwanda" OR "Zimbabwe" OR "Niger" OR "Somalia" OR "South Sudan" OR "Sierra Leone" OR "Tanzania" OR "Togo" OR "Uganda" OR "Zambia" OR "Guinea" OR "Guinea-Bissau" OR "Haiti" OR "Democratic People's Republic of Korea" OR "North Korea" OR "Liberia" OR "Madagascar" OR "Malawi" OR "Mali" OR "Mozambique" OR "Eritrea" OR "Democratic republic of Congo" OR "Burundi" OR "Burkina Faso" OR "Chad" OR "Comoros" OR "Central African Republic"

3. 1 AND 2

SCOPUS Search Strategy

(ultraso*) W/3 (obstetric* OR antenatal OR prenatal OR pregnancy OR gestation OR cyesis)

AND

"low middle income countr*" OR Ghana OR Ethiopia OR Afghanistan OR Benin OR Rwanda OR Zimbabwe OR Niger OR Somalia OR "South Sudan" OR "Sierra Leone" OR Tanzania OR Togo OR Uganda OR Zambia OR Guinea OR "Guinea-Bissau" OR Haiti OR "Democratic People's Republic of Korea" OR "North Korea" OR "Liberia" OR Madagascar OR Malawi OR Mali OR Mozambique OR Eritrea OR "Democratic republic of Congo" OR Burundi OR "Burkina Faso" OR Chad OR Comoros OR "Central African Republic"

Maternity and Infant Care Search Strategy

1. (ultraso* adj3 (pregnan* or gestation or cyesis or antenatal or prenatal or obstetric*)).mp
2. (developing countr* or low* income countr* or low* resource countr* or low* middle income countr* or LMIC or Ghana or Ethiopia or Afghanistan or Benin or Rwanda or Zimbabwe or Niger or Somalia or South Sudan or Sierra Leone or Tanzania or Togo or Uganda or Zambia or Guinea or Guinea-Bissau or Haiti or Democratic People's Republic of Korea or North Korea or Liberia or Madagascar or Malawi or Mali or Mozambique or Eritrea or Democratic republic of Congo or Burundi or Burkina Faso or Chad or Comoros or Central African Republic).mp
3. 1 AND 2

2.5 Study Records

Data management:

The search outcomes will be transferred into Eppi-Reviewer literature review management software that allows importation of citations and PDFs to be screened for inclusion. Additional reference management software will be employed throughout the review process to eliminate duplicate references.

Study Selection:

One investigator (YY) will conduct an initial search after which all duplicates will be removed. Then, two investigators (YY and MA) will screen article titles and abstracts to exclude studies that do not meet the predetermined eligibility criteria. The full text of all potentially eligible papers will be examined independently by two investigators (YY and MA) for inclusion. Disagreements will be resolved by consensus among a panel of four investigators (RM, NN, HP and BdV). Reference lists of selected articles and pertinent reviews will be examined by two investigators (YY and MA) for other relevant papers for possible inclusion.

Data collection process:

Two authors (YY and MA) will independently extract relevant information using a piloted data collection form. The extracted data will encompass demographic details, study type, study setting, intervention specifics, and all documented patient-relevant outcomes.

Disagreement among reviewers will be addressed through discussions involving four arbitrators (RM, NN, HP, BdV). Study authors will be contacted to resolve any uncertainties

Data items:

We will extract the intervention, comparator, participant characteristics (such as pregnant women in low-resource settings), outcomes listed under 'additional outcomes' below, number of routine ultrasounds, timing of routine ultrasounds, country(s), availability of ultrasounds to women in the comparison group, mortality rate across maternal age, the geographic distance from ultrasound care and socio-economic status of the mothers.

2.6 Outcomes and Prioritization

The primary outcome is maternal mortality.

Additional outcome(s)

Other outcomes include:

Perinatal mortality: This includes stillbirths at 28 weeks' pregnancy or more and neonatal deaths up to 28 days after birth (333).

Stillbirth: This is defined as a lifeless infant weighing at least 500g at birth or, if weight is unknown, born after at least 22 weeks' gestation (334, 335)

Neonatal death: This is defined as death occurring within 28 days of birth in an infant whose birth weight was at least 500g or, if weight is unknown, born after at least 22 weeks' gestation (334).

Post-partum haemorrhage: This is excessive bleeding after childbirth.

Antepartum haemorrhage: This is genital bleeding during pregnancy after the 24th week of pregnancy up to delivery.

Maternal blood transfusion: This is the treatment with intravenous blood products to restore haemoglobin level.

Caesarean section: This is a surgical procedure by which one or more babies are delivered through an incision in the mother's abdomen.

Obstructed labour (as defined by the authors): This is when the baby is not exiting the pelvis because it is physically blocked during childbirth although the uterus contracts normally.

Maternal admission to ICU: Maternal admission to the adult intensive care unit.

Low 5-minute Apgar score (< 7 or < 4): Apgar score < 7 will be reported if available. Apgar score < 4 will be reported if available. If the paper does not report on a cut-off for low Apgar score or an alternative cut-off is reported, then results may be pooled using the author's definition.

Abnormal umbilical arterial cord gases (as defined by the authors): Authors' definitions will be used.

Gestational age at birth: This is the measure of the age of a pregnancy taken from the beginning of the woman's last menstrual period, or the corresponding age of the pregnancy as estimated by a more accurate method, if available.

Preterm birth < 37 weeks: This is a birth that occurs before the 37th week of pregnancy.

Risk of bias in individual studies

The Scottish Intercollegiate Guidelines Network (SIGN)(336) will be used to critically appraise RCTs for selection bias, randomisation and concealment bias, baseline comparability bias, blinding or masking bias, interventions and outcome biases, attrition, analysis and generalisability biases. Newcastle-Ottawa Scale (NOS)(337) will be used for observational studies to assess selection bias, comparability bias and outcome bias.

2.7 Data Synthesis

Adjusted risk measures will be extracted where available if included studies report odds ratios, risk ratios or hazard ratios, for the impact of routine prenatal ultrasound on pregnancy and perinatal outcomes.

If meta-analyses are feasible, they will be conducted using fixed effects models and reported using risk ratios. If meta-analysis is not feasible due to inadequate data, or it is not appropriate due to heterogeneity in results between studies, a narrative synthesis will be used to summarize the findings descriptively. Heterogeneity may also be explored through sensitivity and subgroup analyses.

Analyses will be conducted using Python 13.0. Subgroup analyses will be conducted by assessing whether the timing of gestational age at ultrasound, early (less than 28 weeks) versus late (greater than or equal to 28weeks), influences pregnancy and perinatal outcomes.

Subgroup analyses will be performed for the following groups:

(1) Less than 28 weeks gestational age versus 28 or more weeks

(2) Rural/regional location versus metropolitan

(3) High socioeconomic status versus low socioeconomic status

(4) Fully trained sonographers versus sonographers with less training

(5) Randomised controlled trials versus observational studies

Metropolitan areas will be defined as locations within major capital cities or urban centres with populations over 100,000, based on national census classifications. Rural/regional areas will include very remote zones, typically characterised by reduced access to tertiary hospitals and specialist health services.

High socioeconomic status will refer to participants or study areas in the top quintile of the socio-economic distribution. Low socioeconomic status will include those in the bottom quintile often linked with limited healthcare access and increased risk of poor health outcomes. If categorisation by quintiles is not possible, then the author's definitions of SES will be used.

Fully trained sonographers will be defined as individuals who had completed a certified diagnostic medical sonography program, accredited by an allied health professional body, for example Australasian Sonographer Accreditation Registry or equivalent and had two or more years of clinical experience in obstetric ultrasound. Non-specialist or partially trained personnel will include midwives, nurses, or doctors who received short-term ultrasound training, for example ≤3 months or fewer than 100 supervised scans.

Meta-bias(es):

Funnel plots will be constructed to assess publication bias where six or more trials contribute data to the meta-analyses.

Confidence in cumulative evidence:

The methodological quality of individual studies will be evaluated using appropriate tools, (SIGN for RCTs and NOS for observational studies). The consistency/heterogeneity of findings across studies will be evaluated. The strength of evidence will be assessed for

each outcome using Grading of Recommendations Assessment, Development and Evaluation (GRADE) (338).

Acknowledgements

Not applicable

Conflicts of Interests

None

Author Contribution

YY and MA conceived this chapter. YY, MA and BdV conceptualized the primary research goals and objectives for this systematic review protocol. YY, BdV, NN, and RM designed the methodological framework and developed the protocol. YY in collaboration with BdV and NN, formulated the search terms. YY incorporated extensive methodological and intellectual input from BdV, NN and RM. YY prepared the manuscript and drafted the initial version. BdV, NN, RM and HP critically reviewed and provided feedback on the initial and subsequent drafts. All authors provided feedback on the final draft and have approved the final version of the manuscript.

CHAPTER 3: Assessing the Impact of Routine Prenatal Ultrasound on Pregnancy and Perinatal Outcomes in Low-Resource Settings: A Systematic Review.

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This Chapter is formatted for publication but has not yet been submitted.

3.1 Abstract

Background:
Maternal and newborn mortality remain major health problems worldwide, with sub-Saharan Africa bearing a disproportionate burden. The use of obstetric ultrasound is increasingly recognized as crucial in improving outcomes for mothers and newborns, especially in regions with high maternal mortality rates. This systematic review aimed to evaluate the impact of routine prenatal ultrasound on maternal and perinatal outcomes in low-resource settings where the gross national income per capita was less than US$1,045.

Data Sources:

A comprehensive search was conducted across the following databases: Medline (OvidSP), CINAHL, Cochrane Library/CENTRAL, Embase (OvidSP), Scopus, Maternity and Infant Care, and Global Index Medicus from inception to July 31, 2024.

Methods:
The review was conducted in accordance with the PRISMA guidelines and included randomised controlled trials and observational studies that compared the use of routine ultrasound in antenatal care with its absence. The primary outcome was maternal mortality, and secondary outcomes were perinatal mortality, stillbirth, neonatal death, antepartum haemorrhage, postpartum haemorrhage, maternal blood transfusion, caesarean section, obstructed labour, maternal admission to intensive care unit, low 5-minute Apgar score, abnormal umbilical arterial cord gases, gestational age at birth and preterm birth. A post-hoc decision was made to include antenatal clinic attendance as a secondary outcome.

Results:
A total of 2,270 publications were identified and two met the inclusion criteria. One study, a cluster RCT, showed no significant difference between the routine prenatal ultrasound group and the control group for most outcomes. The relative risk (RR) was 0.92 (95% CI 0.43, 1.99) for maternal mortality, 0.96 (95% CI 0.81, 1.14) for neonatal mortality, 0.99 (95% CI 0.93, 1.06) for Caesarean section, 1.08 (95% CI 0.96, 1.22) for prolonged or obstructed labour and 1.03 (95% CI 0.88, 1.19) for stillbirth. Postpartum haemorrhage and antenatal clinic attendance for more than four visits were statistically significantly increased in the routine prenatal ultrasound group compared to the control group with RR of 1.28 (95% CI 1.02, 1.62) and RR of 1.06 (95% CI 1.03, 1.08) respectively. The other study included in our review, was an observational study. It reported a larger increase in antenatal clinic visits in the routine ultrasound sites compared to the control sites but did not report on any other outcomes.

Conclusion:
This systematic review highlights paucity of evidence to support the use of routine prenatal ultrasounds in low-income settings. Further studies need to be replicated to increase statistical power to detect effects in important maternal and perinatal outcomes.

Keywords:

Ultrasound, prenatal, maternal mortality, low-resourced setting, pregnancy.

3.2 Introduction

Sub-Saharan Africa bears an outsized burden of global maternal mortality with nearly half of all maternal deaths in the world occurring in this region (339). In 2020, the region accounted for 70% of all maternal deaths worldwide (340). In low- and middle-income countries (LMICs), a large percentage of births occur outside hospital settings, which heightens the risk of complications and mortality (341). In certain regions, up to 23% of childbirths occur outside of hospital settings (342). Traditional birth attendants provide care at roughly 22% of deliveries in LMICs, particularly in rural communities (343). Seventy-eight percent of hospitals are equipped to perform surgical deliveries, limiting access to critical, life-saving interventions in LMICs (344).

Key causes of maternal deaths include obstructed labour, unsafe abortion, and obstetric haemorrhage (345, 346). Postpartum haemorrhage (PPH) contributes to 30-50% of all maternal deaths in the region (347). Placenta praevia, a significant risk factor for PPH, is associated with increased maternal haemorrhagic morbidity (348). Ectopic pregnancy can also result in life-threatening haemorrhage and is a major challenge in low-resource settings (349). Ultrasound, especially transvaginal scanning (TVS), has emerged as the leading diagnostic method for detecting ectopic pregnancy and placenta praevia, surpassing laparoscopy as the gold standard (350-352).

The primary goals of routine prenatal ultrasound are to confirm pregnancy, establish gestational age, identify any uterine or adnexal anomalies, diagnose multiple pregnancies (353, 354), and detect fetal and placental anomalies that could impact fetal and perinatal outcomes (355). The WHO's global pregnancy care guidelines, updated in 2022, recommend at least one obstetric ultrasound scan before 24 weeks of gestation, emphasizing the increasingly acknowledged importance of ultrasound in improving outcomes for mothers and newborns, particularly in global antenatal care (328, 329, 356, 357).

This systematic review aimed to evaluate the impact of routine prenatal ultrasound on pregnancy and perinatal outcomes for women and their babies in low-resource settings, compared to those who receive no ultrasound or only indicated prenatal ultrasound.

3.3 Methods

Study design and eligibility criteria

This systematic literature review was conducted and reported using the PRISMA checklist for reporting systematic reviews of healthcare interventions (358) and conducted as described in Chapter 2.

The review included studies that compared the use of routine ultrasound in antenatal care with the absence of such routine use. It included randomised controlled trials with individual and cluster-level randomization, as well as prospective and retrospective comparative observational studies. Non-comparative studies and those unrelated to ultrasound in pregnancy were excluded. Commentaries, letters, and editorials were also excluded.

The review included studies that reported outcomes for pregnant women in low income resource countries, where the gross national income per capita is less than US$1,045, as estimated by the World Bank, reflecting the economic challenges in meeting basic societal needs (359).
We evaluated the quality of all included studies, using the Scottish Intercollegiate Guidelines Network (SIGN) (360), for randomised controlled trials (RCT) and Newcastle-Ottawa Scale (NOS) (337), for observational studies.

The review included studies that reported at least one of the following outcomes and published from January 1, 1980, to July 31, 2024, in any language. For studies reported in languages other than English, we planned to ask a colleague fluent in the language or translator to assist in extracting data. The primary outcome was maternal mortality, and additional outcomes included perinatal mortality, stillbirth, neonatal death, antepartum haemorrhage, postpartum haemorrhage, maternal blood transfusion, caesarean section, obstructed labour (as defined by authors), maternal admission to intensive care unit, low 5-minute Apgar score (< 7 or < 4), abnormal umbilical arterial cord gases (as defined by the authors), gestational age at birth and preterm birth < 37 weeks. A post-hoc decision was made to include antenatal clinic attendance as a secondary outcome, because clinic attendance was identified in the medical literature as a potentially important marker of improved pregnancy outcomes. The authors' definitions of this outcome were used.

Adjusted risk measures, whenever available, were extracted in studies that reported odds and risk ratios, for the impact of routine prenatal ultrasound on pregnancy and perinatal outcomes. Where meta-analysis was not feasible, a narrative synthesis was

used to summarize the findings descriptively. Analyses were conducted using Python 3.10.

3.4 Search Strategy

Searches included terms such as ultrasound, ultrasonography, maternal, prenatal, antenatal, sub-Saharan Africa and other related terms. The search strategies used are attached in Appendix 1.
We conducted a search in Medline (OvidSP), CINAHL, Cochrane Library/CENTRAL, Embase (OvidSP), Scopus, Maternity and Infant Care, and Global Index Medicus. We also reviewed the reference lists of the included studies and relevant reviews identified during our search to find additional papers for possible inclusion.

The search outcomes were imported into Covidence, a literature review management software that allows importation of citations and PDFs to be screened based on defined set inclusion criteria (361, 362). It was also used to eliminate duplicate references and facilitating collaborative work among research team members (361). Duplicates not identified by Covidence were removed manually.

Study selection

One investigator (YY) performed the initial search using the specified strategies (Appendix 1) across the respective databases. Two investigators (YY and MA) independently screened the titles and abstracts to exclude studies that did not meet the predetermined eligibility criteria, with any conflicts resolved through discussion with additional researchers (BdV, HP).

The full texts of all potentially eligible papers were reviewed independently by two investigators (YY, MA) to determine inclusion. Disagreements were resolved through consensus among the two-member panel (BdV, HP). Additionally, the reference lists of selected articles and relevant reviews were examined by two investigators (YY, MA) to identify other papers for potential inclusion.

3.5 Results

Results of the search

After exclusion of duplicate articles, 1556 publications were identified (Figure 2). Of these,1459 were excluded on reviewing the abstracts and titles, leaving 97 potentially eligible studies. On full text review, two eligible studies were identified including one cluster RCT (363) and one observational study (364), that met the inclusion criteria. The two studies compared prenatal ultrasound with no prenatal ultrasound and were included in the review as shown in the PRISMA flow diagram in Figure 3.

The Goldenberg et al 2018 (71) study was a cluster randomised trial designed to involve 58 clusters across five countries to assess the impact of routine antenatal ultrasound on maternal and neonatal outcomes in LMICs. Kawooya et al 2015 (364) was a pragmatic comparative study conducted in two constituencies to assess the impact of integrating limited obstetric ultrasound services into routine antenatal care in Mpigi District, Central Uganda.

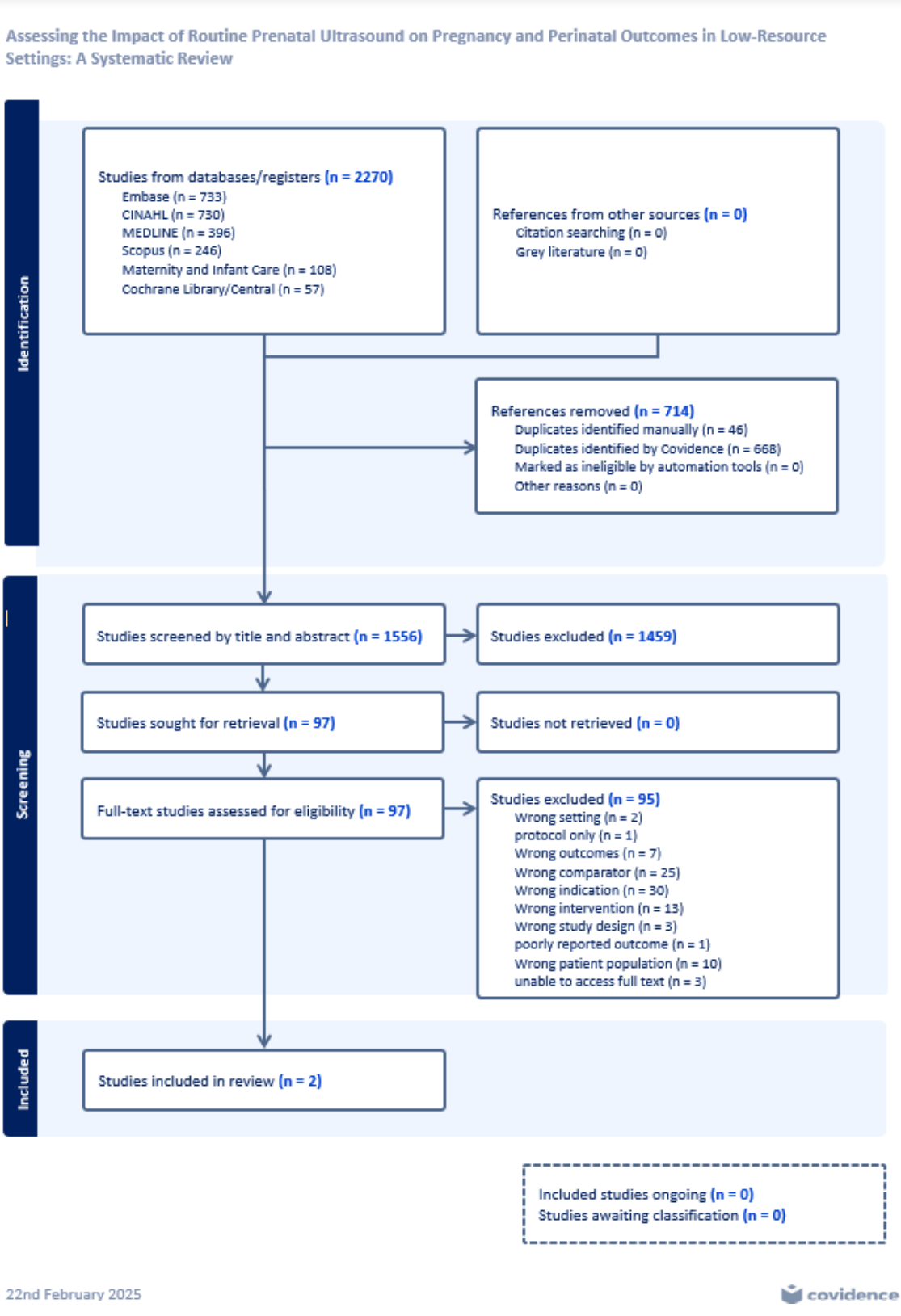

Figure 3: PRISMA, Preferred Reporting Items for Systematic Review and Meta-analysis flow chart.

Risk of Bias of included studies

Using SIGN, the study by Goldenberg et al., 2018, was assessed as have a low risk of bias across all domains, except for the blinding of participants and personnel as it was not possible to blind them due to the nature of the intervention. Despite this limitation, the overall risk of bias is considered low, and the results to be robust within the constraints imposed by the lack of blinding (Figure 4).

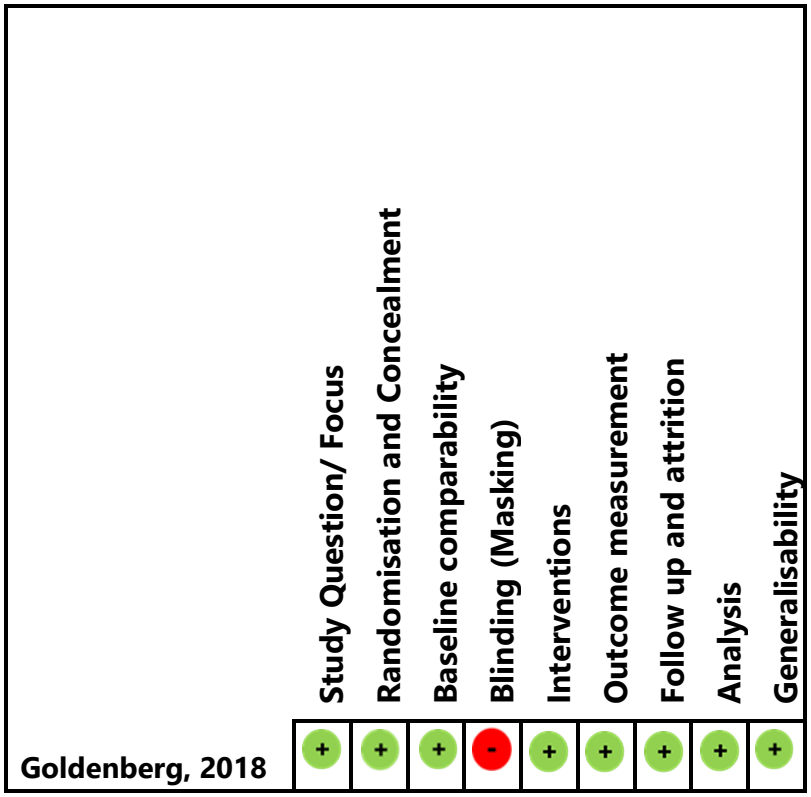

Figure 4: Risk of bias assessment for Goldenberg et al., 2018 cluster RCT using the SIGN scale.

Colour codes used in risk-of-bias table:
Green + = Method adequately addressed, low risk of bias; **Red –** = Method not addressed or high risk of bias

Kawooya et al., (2015) demonstrated strengths in drawing a comparable non-exposed group, measuring exposure and outcomes reliably, and ensuring that participants were free of the outcome at baseline. However, unclear details on how confounders were handled-both in the design and the analysis, as well as incomplete follow-up information introduce some uncertainty about the study's internal validity (Figure 5).

Figure 5: Risk of bias assessment for Kawooya et al., 2015 observational study using the NOS scale.

Colour codes used in risk-of-bias table:
Green + = Method adequately addressed, low risk of bias, **Yellow?** = Unclear methods, insufficient information

Study characteristics of the included studies

Study ID	Study Location	Study Design	Inclusion Criteria	Method of recruitment	Intervention and control	Time of prenatal Ultrasound	Primary Outcome
Goldenberg et al, 2018	(Democratic Republic of Congo, Guatemala, Kenya, Pakistan, and Zambia)	Cluster randomisedcontrolled trial	Pregnant women attending antenatal clinics in a government health centre that did not routinely provide antenatal ultrasounds. All pregnant women residing within the defined study clusters were eligible for participation. A cluster was defined as a geographic area generally served by a single health centre and its catchment area, typically with about 500 births per year.	Clusters were randomised to standard ANC or standard ANC plus two ultrasounds and referral for complications. The study trained providers in intervention clusters to perform basic obstetric ultrasounds.	(Intervention group) received prenatal ultrasound. (Control group) no routine prenatal ultrasound.	First at 16–22 weeks, second at 32–36 weeks	a). Maternal mortality b). Stillbirth c). Neonatal dealth d). Near-miss maternal mortality.
Kawooya et al, 2015	Mpigi District, Central Uganda (10 rural centres in two constituencies)	Pragmatic comparative study	Pregnant women attending antenatal care	A baseline survey was undertaken in the 10 study health facilities. The performance indicators were measured in the baseline survey and monitored during the implementation period	Prenatal ultrasound (intervention), no prenatal ultrasound (control)	Integrated into routine ANC visits	a)Numbers of pregnant mothers attending 1st & 4th ANC visits b) Facility deliveries c)Number of pregnant mothers referred from low to high level health facilities because of identified risk factors.

Footnotes*: ANC- Antenatal Clinic*

Table:4: Study characteristics of the included studies

Note that the information in table has been extracted from the corresponding publications and reworded to suit this table

Synthesis of results

In our systematic review, we identified only two studies that compared routine prenatal ultrasound with no routine prenatal ultrasound including a cluster RCT study (363) and an observational study (364).

In the cluster RCT by Goldenberg et al (363), key maternal and neonatal health outcomes were compared (Table 2). The relative risk (RR) for maternal mortality outcome was 0.92 (95% CI 0.43, 1.99). This indicates no significant difference between the routine prenatal ultrasound group and the control group.

Neonatal mortality also did not show statistically significant differences between the intervention and control group with RR of 0.96 (95% CI 0.81, 1.14).

Caesarean section and the rate of prolonged or obstructed labour did not differ significantly between the intervention and control groups, with an RR of 0.99 (95% CI 0.93, 1.06) and RR of 1.08 (95% CI 0.96, 1.22) respectively. The rates of stillbirth also did not differ significantly between the two groups, with an RR of 1.03 (95% CI 0.88, 1.19).

Postpartum haemorrhage and antenatal clinic attendance for more than four visits were statistically significantly higher in the routine prenatal ultrasound group compared to the control group (no prenatal ultrasound) with RR of 1.28 (95% CI 1.02, 1.62) and RR of 1.06 (95% CI 1.03, 1.08) respectively.

The Kawooya et al. 2015 study compared changes in antenatal clinic visits over time in sites where routine ultrasound was introduced compared with sites where routine ultrasound was not introduced. It is not possible to determine relative risks because the overall numbers of pregnant women eligible to attend antenatal visits is not known. The first antenatal clinic visits increased from 2,943 to 3,886 in the routine prenatal ultrasound group and 2,508 to 2,694 in the control group. Also, the fourth antenatal clinic visits increased from 562 to 1,388 in the intervention group (prenatal ultrasound) and decreased from 723 to 719 in the control group (no prenatal ultrasound) (Table 3).

Table 5: Maternal and Neonatal Health Outcomes Comparing Intervention and Control Groups (86).

Author, Year	Outcomes	Relative Risk	RR CI Lower	RR CI Upper	Events in Intervention Group	Sample Size in Intervention Group	Events in Control Group	Sample Size in Control Group
Goldenberg et al., 2018	Postpartum Mortality	0.92	0.43	1.99	28	23923	29	22845
	Neonatal Death	0.96	0.81	1.14	546	23495	543	22479
	Caesarean Section	0.99	0.93	1.06	2919	24008	2808	22896
	Obstructed Labour	1.08	0.96	1.22	1054	23998	931	22885
	Postpartum Haemorrhage	1.28	1.02	1.62	327	21143	250	20671
	Stillbirth	1.03	0.88	1.19	675	24254	628	23149
	≥ 4 ANC Visits	1.06	1.03	1.08	12021	24008	10866	22896

Footnote: ANC- Antenatal Clinic Visits, RR – Relative Risks, CI – Confidence Interval
The data in this table were extracted from the original publication. Relative risks and confidence intervals were calculated from the extracted data.

Table 6: Comparing changes in antenatal clinic visits between intervention and control sites (247).

Author, Year	Outcomes	Before Routine U/S	After Routine U/S	% Increase	95% CI
Kawooya et al., 2015	**First Antenatal Clinic Visit (n):** Intervention Sites (Routine U/S) Intervention Sites (No Routine U/S)	2943 2508	3886 2694	32 7.4	30 – 34 6.4 – 8.4
	Fourth Antenatal Clinic Visit (n): Intervention Sites (Routine U/S) Intervention Sites (No Routine U/S)	562 723	1388 719	147 -0.6	137 -157 0.0 – 1.1

Footnote: CI- Confidence interval; U/S- Ultrasound

The data in this table were extracted from the original publication. % increases and confidence intervals were calculated from the extracted data.

3.6 Discussion

In this review, only two studies met inclusion criteria and thus no meta-analysis was performed but narrative synthesis only. The Goldenberg et al, 2018 RCT study that compared routine use of antenatal ultrasound during pregnancy with control group without routine ultrasound did not find statistically significant improvements in maternal, fetal, and neonatal outcomes for pregnant women in LMICs although antenatal clinic visits increased by a small amount. In the other included observational study (364), antenatal clinic attendance increased in sites where obstetric ultrasound was integrated into routine antenatal care (ANC) compared to control sites although the denominators (number of pregnant women in the area in the study periods) are not known.

There were no data for this review on maternal outcomes such as antepartum haemorrhage, maternal blood transfusion, maternal admission to intensive care unit (ICU), abnormal umbilical arterial cord gases, gestational age at birth, preterm birth < 37 weeks, low 5-minute Apgar score (< 7 or < 4), although these were outcomes in our review study protocol, and we recommend further research to address these gaps.

In a Cochrane systematic review in 2014 that examined the same topic in later pregnancy (after 24 weeks gestation) (365), no trials were identified in LMICs, and no difference was found in maternal and neonatal outcomes. This finding agrees with Goldenberg et al, the only RCT from low-income settings that our review has identified, who found that routine pregnancy ultrasound did not improve maternal, fetal, and neonatal outcomes compared to no routine ultrasound, although confidence intervals were wide, and a small effect cannot be excluded.

While both the Cochrane systematic review and the study by Goldenberg et al primarily recruited women with low-risk pregnancies, the trial by Goldenberg was conducted in rural and remote regions in low-income settings with a high baseline risk of maternal and perinatal complications. While it was a large trial, it is the only one available, and it remains possible that future studies will identify benefits of routine prenatal ultrasound in low- and middle-income settings.

In a narrative review, Stefanovic (2020) (357) argues that the routine use of antenatal ultrasound in developing countries could have a positive impact on reducing maternal and neonatal mortality, and the authors of the Cochrane Systematic Review (365) argue that pregnancy ultrasound may be particularly beneficial when used in high-risk pregnancies by diagnosing high-risk pregnancies early that leads to referral; by accurately determining gestational age leading to fewer stillbirths, post-dates pregnancies and early inductions of labour (357). It would be useful to measure these proxy outcomes in future research studies in low-income settings.

The Cochrane systematic review of ultrasound after 24 weeks gestation was dominated by the RADIUS study, a large RCT in the United States which recruited between 1987 and 1991(365). In this trial, 15,151 pregnant women at low risk for perinatal problems received two pregnancy ultrasound examinations (at 15-22 weeks and 31-35 weeks) and the control group received ultrasounds only if medically indicated, with the primary outcome being adverse perinatal outcomes (fetal death, neonatal death, or neonatal morbidity), (366). The authors concluded that routine antenatal ultrasound screening did not result in significant improvements in maternal, fetal, or neonatal outcomes. However, given the substantial advancement in ultrasound technology since this time and different underlying maternal and infant mortality and morbidity, the results may not be generalisable to modern low-income settings.

This assertion is supported by Kim et al. in 2018 (356), whose study was undertaken in LMICs and found that while obstetric ultrasound can improve patient management, it is not associated with reduced maternal, perinatal, or neonatal mortality. This study was excluded in this review due to the study design which was a narrative review and synthesizes and discusses findings from various other studies, rather than presenting original empirical data or findings from a controlled study.

While we have not found that routine prenatal ultrasounds in LMICs improve maternal outcomes, ultrasound in pregnancy still has an important role. For example, they play an important role in enhancing the detection of pregnancy complications and improving the accuracy of gestational age estimation
(357, 367). However, evidence supporting their effectiveness in reducing maternal, perinatal, or neonatal mortality in these regions remains limited (368).

In a study that focused on various low and middle-income countries (LMICs) as the settings for evaluating obstetrics ultrasound's impact on patient care management and training programs (356), indicated that obstetric ultrasound could enhance maternal and neonatal health through improved diagnostic capabilities and training of healthcare providers in LMIC settings.

Although routine late pregnancy ultrasound in low-risk populations does not appear to confer significant benefits (369), early pregnancy ultrasound may improve detection of multiple pregnancies and reduce post-term inductions (354).
While routine perinatal ultrasound has not been directly shown to improve health outcomes for mothers and babies, there is limited evidence from an observational study that was included in our review that it may increase visits to antenatal clinics, implying that antenatal care is improved (364). The 2016 WHO guidelines recommend

a minimum of eight antenatal care visits for positive pregnancy outcomes (370, 371), but many women in low and middle-income countries do not meet this recommendation (372).

In the study by Mbuyita et al (2015) (373), use of a hand-held ultrasound (not routine) was associated with an increase in the proportion of pregnant women who had at least four antenatal visits from 27% to 60%. While increased antenatal visits may be expected to improve outcomes, other barriers to appropriate care such as completing appropriate referrals persisted, including cost, transportation, and communication issues between healthcare providers and patients (374).

In a Nigerian study, (375) that involved at least several thousand women across two states, with specific post-intervention figures of approximately 3,793 in Kano and 2,854 in Bauchi, there was an increase in antenatal visits and an increase in facility births compared with historical controls after the introduction of limited (not routine) obstetric ultrasounds by primary health care providers. However, it was unclear if these changes were due to the ultrasounds or other temporal factors, and the authors did not report on the number of antenatal visits per pregnancy, and the study was not eligible for this review due to the lack of data.

It is possible that use of ultrasound can increase antenatal clinic attendance. In a small observational study involving 100 women in Ghana, the rate of antenatal clinic attendance was 62.5% among women who gave birth during a program that used mobile phones and portable ultrasounds to encourage antenatal clinic attendance compared with 37.5% in the control group (376, 377). Similarly, in an Ethiopian study where limited obstetric ultrasound was introduced to 30 health centres, first antenatal clinic visits increased from 44% to 73% over a four-year period from 2017 to 2020 (378, 379) studies.

This review identified only two eligible studies, a large RCT (Goldenberg et al., 2018) and one observational study, highlighting the scarcity of evidence on the impact of routine prenatal ultrasound in low-resource settings. The RCT found no statistically significant improvements in maternal, fetal, or neonatal outcomes with the introduction of routine ultrasound, although a modest increase in ANC was observed. The observational study similarly reported higher ANC attendance where ultrasound was integrated into routine care, although interpretation was limited by the absence of denominators and potential confounding.

Maternal deaths and severe complications are relatively rare, requiring very large samples to detect differences. In addition, the effectiveness of ultrasound depends on scan quality, operator skill, and the health system's ability to act on abnormal findings.

Where referral systems, emergency obstetric services, and treatment capacity are limited, detection alone is unlikely to translate into improved outcomes.

The consistent signal across both studies that ultrasound may increase ANC attendance is noteworthy. This suggests that the availability of ultrasound could enhance women's engagement with antenatal services, providing an indirect pathway to better outcomes if coupled with timely and effective interventions. However, evidence remains insufficient to conclude that routine prenatal ultrasound alone reduces maternal or perinatal mortality in low-resource settings.

Further large, well-designed studies are needed, with adequate power to assess rare outcomes, standardized reporting of ANC attendance and maternal morbidity, and careful measurement of referral pathways and health system responses. Importantly, future research should evaluate ultrasound not as an isolated tool, but as part of integrated maternal health strategies that strengthen both diagnostic and treatment capacity.

Although the included studies did not demonstrate clear maternal or neonatal survival benefits, this should not be interpreted as evidence that ultrasound lacks clinical utility. Rather, the value of ultrasound may lie in its ability to influence outcomes in specific high-risk populations where timely diagnosis and intervention are most critical. For example, in women with suspected ectopic pregnancy, placenta praevia, multiple gestations, or intrauterine growth restriction, ultrasound provides essential information that can guide life-saving decisions. In these contexts, its benefit is less about universal screening and more about targeted use where complications are more likely to occur.

This suggests that future research should focus not only on evaluating population-wide effects of routine ultrasound but also on studying its role within high-risk groups. By identifying which subgroups benefit most, such as women with limited access to emergency obstetric care, those with comorbid conditions like diabetes or hypertension, or those in malaria-endemic regions, research can clarify the true value of ultrasound in improving maternal and perinatal outcomes.

The observed association between ultrasound examinations and higher ANC raises an important question: is it the scan itself that improves outcomes, the increased frequency of clinic visits, or both? Ultrasound may act as a catalyst for health-seeking behaviour, encouraging women to return for follow-up once they receive reassurance or visual confirmation of fetal well-being. Increased visits, in turn, provide greater opportunities for essential interventions such as blood pressure monitoring, malaria prophylaxis, iron supplementation, and early detection of complications.

At the same time, ultrasound has intrinsic diagnostic value. Its ability to detect conditions such as multiple gestation, fetal growth restriction, or placenta praevia can directly influence clinical management and referral decisions. It is therefore plausible that the technology exerts a dual effect: indirectly by fostering greater engagement with antenatal care and directly by identifying high-risk conditions. Future research should attempt to disentangle these pathways to better understand the unique and combined contributions of ultrasound and antenatal visits to maternal and neonatal outcomes.

3.7 Strengths and Limitations

The review employed a sensitive search strategy across multiple databases, ensuring a wide range of relevant studies were considered and it is unlikely that relevant studies were missed. The systematic review was conducted in accordance with PRISMA guidelines, which promotes transparency and reproducibility in the review process.

By including both RCTs and observational studies, the review aimed to capture a broader spectrum of evidence regarding the impact of routine prenatal ultrasound. The emphasis on low-resource settings addresses a critical gap in the literature, providing insights that are particularly relevant for regions with high maternal and neonatal mortality rates.

The small number of included studies and the lack of reporting of our prespecified outcomes limited the ability to draw definitive conclusions and perform meta-analyses. There was a notable lack of data on certain maternal outcomes, such as antepartum haemorrhage and maternal admission to intensive care units, which could provide a more comprehensive understanding of the implications of routine ultrasound. The observational study included in the review had inherent biases related to lack of detailed demographic data to strengthen the assessment of comparability between the intervention and control groups or confounding factors, which could affect the validity of the findings

3.8 Conclusion

This systematic review highlights paucity of evidence to support the use of routine prenatal ultrasounds in low-income settings. Further studies, including qualitative and quantitative, with sample sizes sufficiently powered to detect differences in major perinatal outcomes are required to assess the potential value of routine prenatal ultrasounds in low-income settings.

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Not applicable

Conflicts of Interests

None

Author Contribution

YY and BdV conceptualized the primary research goals and objectives for this systematic review. YY, BdV, NN, and RM designed the methodological framework and developed the protocol. YY, in collaboration with BdV, NN and RM, formulated the search terms. YY conducted the search, managed the importation of identified studies into Covidence, and removed duplicates. Screening and data extraction were performed by YY and MA using extraction template created on Covidence by YY and BdV. All conflicts at the title and abstract screening, full text screening and data extraction stages were resolved by BdV and HP. YY and MA assessed the quality of studies contributing to the evidence on routine prenatal ultrasound with no routine prenatal ultrasound on maternal and neonatal health outcomes, and all conflicts were resolved with BdV and HP. YY synthesized the findings narratively, incorporating extensive methodological and intellectual input from BdV, HP, NN and RM. YY prepared the manuscript and drafted the initial version. BdV and HP critically reviewed and provided feedback on the initial and subsequent drafts, verifying data from the studies contributing to evidence on routine prenatal ultrasound with no routine prenatal ultrasound on maternal and neonatal health outcomes during the review process. All authors had full access to the included studies and reviewed and provided feedback on the final draft. YY submitted the manuscript for publication, and all authors have read and approved the final version of the manuscript.

Ethical Approval Data

Ethics approval is not required for this systematic review, as it entails the analysis of data from previously conducted published studies

Availability Statement

A report of this review will be shared through publication in peer-reviewed journals and presentations at conference.

CHAPTER 4: Review of the Ghana Demographic Health Survey on Maternal Mortality in Ghana: Causes, Trends, and the Potential Role of Obstetric Ultrasound (2012–2017)

4.1 Introduction

In Ghana, maternal mortality in the 7 years from 2010 to 2017 was estimated to be 310 deaths per 100,000 live births (380). This compares with a global declining trend from 2010 to 2017, with a stable maternal mortality ratio of 8.6 fatalities per 100,000 births in Australia (381, 382), and 17.4 deaths per 100,000 live births in the United States in 2018 with significant racial disparities (383).

In the five years from 2012 to 2017, obstetrical haemorrhage was the most common direct cause of maternal mortality in Ghana, responsible for 30% of maternal deaths (380), although it is unknown what proportion of these were due to PPH and what proportion were due to antepartum haemorrhage.

In assessing the potential impact of obstetric ultrasound on maternal mortality in low-income countries, it is important to understand the breakdown of causes. For example, ultrasound, particularly transvaginal ultrasound (TVUS), has become the gold standard for diagnosing ectopic pregnancy, offering high sensitivity and specificity (352, 384, 385), and is effective screening tool for placenta praevia with high sensitivity and specificity using specific placenta-cervix distance cutoffs (386). In the case of the former, life-threatening intraabdominal haemorrhage can occur if an ectopic pregnancy ruptures (387, 388), an event that is preventable or treatable through urgent surgical intervention (389). In the case of the latter, skilled antenatal care and planned caesarean section can prevent life-threatening antepartum haemorrhage (390).

The aim of this study was to assess the causes of maternal mortality in Ghana between 2012 and 2017 using verbal autopsies conducted by the Demographic and Health Surveys (DHS) program in 2017 (380), and to describe causes of maternal death deaths potentially preventable using prenatal ultrasound.

4.2 Methods

This was a retrospective descriptive cohort study of women with reported maternal deaths in Ghana in the five years preceding a survey administered by the Demographic Health Survey (DHS) Program in 2017. The primary study factor was direct and indirect causes of maternal death.

The DHS surveyed households in 2017 and asked about family members who died in the 5 years preceding the survey (5 years before the date of the interview) at age 12-49.

The survey used the frame of the 2010 Population and Housing Census maintained by the Ghana Statistical Service using a sampling strategy targeting a population representative of the Ghana urban and rural populations (380). The sample was stratified by separating Ghana into urban and rural areas in 10 geographic regions, yielding 20 sampling strata. Samples of enumeration areas (geographic areas with an average of 161 households each) were selected independently in each stratum by using a probability proportional to size selection.

Nine-hundred enumeration areas (466 in urban areas and 434 in rural areas) were selected. Lists of households in each area then served as a sampling frame for the selection of households. Inquiries were made of each household if there had been any deaths in that household since January 2012 and, if so, the name, sex, and age at time of death of the deceased person(s). Verbal autopsies were conducted by trained personnel, defined in this survey as fieldworkers and health-related staff (including interviewers with prior DHS experience, nurses, midwives, and social science graduates) who underwent intensive training workshops before field deployment. Training covered the content and purpose of the Verbal Autopsy Questionnaire, ethical interviewing skills, culturally sensitive approaches to bereaved families, and standardized probing techniques to elicit consistent and accurate responses. Mock interviews, role-play, and pilot testing were conducted to ensure uniformity, while supervisors closely monitored interviews and carried out random back-checks to confirm accuracy. These measures were designed to minimize interviewer bias and ensure comparability of information collected nationally.

We were granted permission by the DHS to analyse verbal autopsy data from the 2017 Ghana survey (380). The Verbal Autopsy Questionnaire was used to collect information on the deaths of women who died while aged 12-49. Questions were asked on background characteristics, narrative of illness/events leading to death, history and details of injuries/accidents, whether the deceased had been diagnosed with any of a list of specific illnesses/conditions, whether the deceased exhibited particular signs/symptoms, including signs/symptoms associated with pregnancy, with detailed questions on signs/symptoms associated with maternal causes of death, consumption of alcohol and tobacco, treatment received, details of the deceased's contact with health services before death, access to and quality of services, information on timing and cause of death from the death certificate and burial permit (if available).

Deaths were coded according to the International Statistical Classification of Diseases and Related Health Problems, 10th revision (ICD-10; WHO 2016) by six Ghanaian physicians who were trained to review the 2017 Ghana Maternal Health Survey (GMHS) Verbal Autopsy Questionnaires, to determine the final underlying cause of death. Each questionnaire was independently reviewed and assigned a cause (or causes) of death by two different physicians. When the two physicians had discordant results, the questionnaire was re-reviewed by two other physicians. This multi-review process, together with training in WHO verbal autopsy guidelines and ICD-10 coding, further ensured consistency and reliability in the classification of causes of maternal death across the survey.

Data were included in the analysis as a death during pregnancy, childbirth or the puerperium if the respondent answered "Yes" to any of the following questions: "Was (NAME) pregnant when she died?", "Did (NAME) die during childbirth?", "Did (NAME) die within two months after the end of a pregnancy or childbirth?", "Did she die during labour or delivery?", "Did (NAME) die after delivering a baby?", or "Did (NAME) die within 24 hours after delivery?", "Did (NAME) die within 6 weeks of childbirth?", or "Did (NAME) give birth to a live baby within 6 weeks before death?"

Deaths during pregnancy were classified as direct maternal deaths, indirect maternal deaths or deaths unrelated to the pregnancy according to the WHO's recommendations for applying ICD-10 classifications (391), (Appendix 2). Maternal deaths were tabulated by causes, including those due to conditions that may have been prevented by earlier ultrasound diagnosis such as ICD code O00.9 (Ectopic pregnancy, unspecified) and ICD codes O67, O67.0, O67.8, and O67.9 (Intrapartum haemorrhage).

Figure 6: Map of Administrative Regions of Ghana (2010–2017)

As illustrated in Figure 6, the map encompassed Ghana's ten administrative regions as of 2010. Appendix 3 provides the 2010 census population breakdown by region, highlighting population density disparities relevant to the stratified sampling.

Ethical permission: An official request was sought from the Ghana DHS to use the study data and written permission was granted.

Statistical analysis:

All analyses were conducted using Statistical Analysis Software Version 9.4. Categorical variables were summarized as frequencies and percentages. Maternal

deaths were further classified into direct, indirect, or non-maternal causes using ICD-10 categories.

Ninety-five percent confidence intervals (CIs) were estimated for the proportions of maternal deaths attributable to each cause, using the normal approximation method (upper and lower limits of the 95% CI = p ± 1.96 x square-root of [p(1-p)/n] where p = proportion and n = sample size).

4.3 Results

There were 1,817 deaths among women and girls aged 12 to 49 reported between 2012 and 2017, including 247 deaths within 5 years of the date of the survey occurring during or within six weeks of pregnancy. Of these 146 were direct maternal deaths, 13 were indirect maternal deaths, 21 were unable to be classified based on ICD-10 Codes, and 67 were unrelated to the pregnancy.

Among the 159 direct and indirect maternal deaths, Table 4 shows the relationship of the respondent with the deceased woman, most commonly a partner or direct family member. The place of birth was recorded in 111 (Table 5). Of these, the birth occurred in a government or private hospital or clinic in 88 (79%), and in a home environment in 23 (21%).

Of the 159 direct and indirect maternal deaths, and as shown in Table 6, PPH was the leading cause of direct and indirect maternal deaths, accounting for 27.0% of cases (95% CI: 20.7–34.4%). Hypertensive disorders followed at 20.8% (95% CI: 15.2–27.7%), and maternal disease at 15.1% (95% CI: 10.4–21.5%). The 95% CIs show the range in which the reported percentages fall with 95% certainty.

Eleven (6.9%; 95% CI: 3.9-12.0%) were due to unspecified obstetric causes and 16 (10.1%; 95% CI: 6.3-15.7%) were due to other obstetric causes listed in Table 7.

Among the 43 women reported to have died due to a PPH, the question about the woman receiving (or needing) a blood transfusion was answered by 36 respondents. Of these, 18 (50%) were reported to have no blood transfusion.

TABLE 7: Relationship of the main respondent with the deceased among 159 women with a direct or indirect cause of maternal death.

RELATIONSHIP WITH MAIN RESPONDENT		
	FREQUENCY	**PERCENT**
Husband or partner	44	28
Parent	22	14
Child	25	16
Sibling	33	21
Other family member	31	19
Friend	1	0.6
Another relationship	3	2
TOTAL	**159**	

TABLE 8: Place of birth among 159 women with a direct or indirect cause of maternal death.

	FREQUENCY	PERCENT
Government hospital	72	65
Government health centre/clinic	11	10
Private hospital/clinic	5	5
Deceased woman's home	9	8
Other home	1	1
Traditional birth attendant's home	4	4
Other	9	8

TABLE 9: Causes of direct and indirect maternal deaths in Ghana, 2012 to 2017.

Causes of Death	Frequency	Percent	95% CI Lower	95% CI Upper
Antepartum haemorrhage	13	8.0	4.8	13.4
Early pregnancy	9	6.0	3.0	10.4
Hypertension	33	20.8	15.2	27.7
Maternal disease	24	15.1	10.4	21.5
*Other obstetric	16	10.1	6.3	15.7
Postpartum haemorrhage	43	27.0	20.7	34.4
Sepsis	10	6.3	3.5	11.2
Unspecified obstetric cause	11	6.9	3.9	12.0
Total	**159**	**100.0**		

CI- Confidence interval. 95% CI = 95% confidence interval. The lower and upper bounds indicate the statistical range within which the true population proportion for each cause of death

is expected to lie with 95% confidence. Narrower intervals reflect greater precision, while wider intervals reflect more uncertainty due to smaller sample sizes.
[a] Early pregnancy represents those with estimated gestational age less than 13 weeks. Early pregnancy deaths include ectopic pregnancy (n=3) and miscarriage/abortion-related complications (n=4); the remainder were unspecified.
[b] Maternal disease refers to deaths from pre-existing medical conditions aggravated by pregnancy (e.g., anaemia, malaria, HIV/AIDS, cardiovascular disease).

TABLE 10: Other obstetric causes of direct and indirect maternal deaths in Ghana, 2012 to 2017.

Other obstetric causes of Death	Frequency n=16	Percent
Complication of labour and delivery- unspecified	3	19
Complications of anaesthesia during puerperium	1	6
Disseminated intravascular Coagulation	1	6
Hypovolaemic shock	1	6
Intentional self-poisoning	1	6
Other complications of obstetric surgery and procedures	1	6
Other maternal infectious and parasitic diseases	1	6
Other specified complications of labour and delivery	1	6
Other specified maternal diseases	3	19
Placenta accreta spectrum disorder	1	6
Pulmonary embolism	1	6
Uterine rupture in labour	1	6

4.4 Discussion

Our main findings were that in Ghana between 2012 and 2017, postpartum` haemorrhage was the most common cause of maternal death, causing 27% of deaths, followed by hypertensive disease in pregnancy (21%), maternal disease (15%), other obstetric causes (10%), and antepartum haemorrhage (8%). The cause of death was an unspecified obstetric cause in 7% of cases.

Antepartum haemorrhage was responsible for 13 maternal deaths, but it was not clear if these were due to placental abruptions or placenta praevias. As placental abruption is more common than placenta praevia, then placenta praevia might be expected to cause less than half of these cases, representing six or less of 159 maternal deaths or less than 4% of cases. Thus, accurate prenatal ultrasound diagnosis of placenta praevia might be expected to prevent less than 10% of maternal deaths.

Vasa praevia represents a critical example where ultrasound screening can dramatically improve outcomes. This condition, involving unsupported fetal vessels near the cervix, carries very high perinatal mortality rates when undiagnosed (392). However, antenatal detection through ultrasound markedly reduces the risk of fetal loss, with one study reporting only a single loss among 34 diagnosed cases (392). The condition can be excluded in under a minute during routine scanning (393).

The relatively small numbers of maternal deaths due to miscarriage or ectopic pregnancies could be due to under-reporting as family members may not have been aware of the pregnancy at the time of the maternal death. Most ectopic pregnancy cases are diagnosed after rupture, with rates as high as 98.1% reported (394). Many of these would be potentially preventable by ultrasound, through aiding in the diagnosis of ectopic pregnancy, or incomplete miscarriage or planned abortion. Due to potential under-reporting, it was not possible to assess the possible impact of ultrasound services on maternal deaths due to ectopic pregnancy.

Rupture rates of ectopic pregnancies vary widely across studies. A study reports that only 5.43% of ectopic pregnancies at the Korle Bu Teaching Hospital in Ghana were diagnosed before rupture, implying a rupture rate of approximately 94.57%. The setting is a tertiary teaching hospital in Ghana, reflecting a developing country context where early diagnosis remains challenging. This high rupture rate underscores difficulties in timely detection within this environment, as compared to developed countries where nearly 90% or more of ectopic pregnancies are diagnosed unruptured (394).

In another systematic review that included studies from diverse countries, such as the USA, Turkey, Iran, Pakistan, Canada, France, Lithuania, Greece, Sudan, India, Taiwan,

and Ghana, covering various healthcare settings and populations worldwide. The review aggregated data from these different settings to assess the prevalence of rupture among ectopic pregnancy cases and associated factors. A total of 5,269 women with ectopic pregnancy participated in 17 studies, and the study found that 56.4% of women with ectopic pregnancy experienced rupture, with various factors influencing its prevalence (395).

Early diagnosis is vital for reducing rupture rates and associated morbidity and transvaginal ultrasonography serves as a highly sensitive (87-99%) and specific (94-99.9%) tool for early detection of ectopic pregnancy (396). Establishing a dedicated Early Pregnancy Assessment Unit (EPAU) can significantly increase ultrasound visualization of ectopic pregnancies raising detection rates from 22% to 61% (397).

In Ghana, there is no evidence that dedicated EPAUs are yet widely established as separate named units. However, tertiary hospitals provide equivalent clinical functions (rapid ultrasound, emergency gynaecology and early pregnancy management) within their gynaecology or emergency services rather than in formally designated EPAUs. Implementing EPAU principles such as fast-track referral, trained midwife-sonographers, rapid human chorionic gonadotropin testing and clear outpatient pathways, is likely to be feasible and clinically beneficial in Ghana and would mostly require organisational change and targeted training rather than large capital outlays.

PPH was the most common cause of maternal death, consistent with other reports in low-income settings (398-400). Ultrasound could be useful in this setting in the context of diagnosing retained placental tissue which can lead to manual evacuation of retained tissue and or transfer to a maternity hospital. However, uterine atony is the most common cause of post-partum haemorrhage, and the most important treatments are uterotonics including oxytocin, ergometrine, and misoprostol; tranexamic acid; uterine compression devices (e.g., balloons); intravenous fluid and blood product replacement; and surgical intervention. Critically, these treatments must be readily available, and healthcare staff require training to recognize haemorrhage promptly, initiate first-line measures, and escalate care as warranted. This underscores the importance of both resource allocation and workforce development in mitigating maternal mortality from postpartum haemorrhage.

We noted that 50% of the reported maternal deaths due to post-partum haemorrhage were not associated with a blood transfusion, which is often life-saving (401). In one study, 119 of 195 countries and territories had insufficient supplies of blood products to meet their needs, including every country in sub-Saharan Africa (402) and it is common for those who need a blood transfusion not to receive one

(403). Globally, inequities in availability of blood transfusion may be due to fewer local blood donors, as well as a lack of resources and infrastructure.

Ghana has a universal health care system for which pregnant women are exempt from the annual membership payment (404). Despite this, our data suggest blood transfusion is often not available for the treatment of post-partum haemorrhage, an observation that is consistent with previous studies in sub-Saharan Africa (405).

In Ghana, and other sub-Saharan countries, many births occur in rural or remote areas (406), where blood products, medications and surgical management may not be readily available. One relatively new treatment is uterine packing with chitosan covered 'combat gauze' (407). This gauze could potentially be carried by primary carers such as midwives, who could be trained in its use. Packing with haemostatic gauze could potentially buy enough time for women to be transferred to a health centre with treatment facilities such as intravenous fluids, blood products and surgical facilities.

The strengths of this study included the survey sampling methodology which weighted the numbers of participants according to the population size in predefined rural and urban geographic areas, a ensuring a sample which is expected to be representative of the Ghanaian population base, and standardised training for interviewers. The weaknesses include the small numbers of maternal deaths, resulting in relatively wide confidence intervals for the point estimates of maternal deaths attributable to each cause. For example, 27% of maternal deaths were due to PPH, but the 95% CI ranged from 21% to 34%.

4.5 Conclusions

Maternal mortality in Ghana remains a critical issue, with postpartum haemorrhage (27%), hypertensive disorders (21%), and maternal disease (15%) being the leading causes. Limited access to emergency care, blood transfusions, and essential medications contributes to these preventable deaths.

Integration of routine ultrasound screening into antenatal care could enable early diagnosis and timely management of placenta praevia, but this would have only a relatively small impact on maternal mortality. As many ectopic pregnancies may be unreported, the potential impact of ultrasound on maternal deaths due to ruptured ectopic pregnancy is unknown.

Strategies to address maternal mortality due to PPH have the potential to impact on maternal mortality. These might include strengthening healthcare infrastructure, ensuring the availability of blood products, and introduction of emerging

interventions such as chitosan-based haemorrhage control, with the aim of improving maternal health in Ghana.

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Not applicable

Conflicts of Interests

None

Author Contribution

Bradley de Vries (BdV) conceived the idea of this chapter. BdV assisted Yusif Yakub (YY) in writing the chapter and conducting the analysis. Hala Phipps (HP) gave editorial review of the chapter. BdV, YY and HP have read and approved the final version of the manuscript.

CHAPTER 5: Evaluating the Effectiveness of Chitosan-Covered Gauze in the Management of Postpartum Haemorrhage in Low-Resource Settings: A Superiority Unblinded Cluster Randomised Controlled Trial Protocol in Ghana.

5.1 Abstract

Background: Post-partum haemorrhage (PPH) is a leading cause of maternal mortality, especially in low- resource settings with limited access to advanced medical/surgical interventions or blood transfusions. Combat gauze, a haemostatic dressing infused with kaolin or chitosan, offers a promising alternative for controlling bleeding quickly. The study aims to evaluate the effectiveness of chitosan-covered gauze compared to standard care (uterine massage and oxytocin administration) in reducing blood loss and maternal mortality.

Methods/design: This cluster randomised controlled trial (RCT) will investigate the effectiveness and safety of chitosan-covered (combat) gauze in managing PPH in Ghana. Eligible centres will have more than 500 births per year. Eligible participants will be women diagnosed with a PPH of ≥750 mL for both vaginal and caesarean births and aged 18- 45 years old in the Bono and Northern regions of Ghana. Centres will be randomised to standard care plus chitosan-covered gauze or standard care alone for PPH according to local guidelines. The primary outcome will be total blood loss within 24 hours of birth as estimated by the clinical staff providing care. The secondary outcomes will be maternal mortality, severe maternal post-partum anaemia (maternal haemoglobin < 7.0g/L) or blood transfusion, or maternal death due to PPH, blood loss > 2L, need for additional interventions, length of stay at hospital, adverse events and maternal satisfaction. The mean difference in blood loss between groups will be analysed using generalised linear mixed models adjusted for stratification variables. A secondary analysis for the primary outcome may be conducted, adjusting for any unbalanced baseline variables that are known to be associated with PPH. Our sample size calculation showed that 570 participants are required for an alpha value of 0.05, beta value of 0.10, mean difference in blood loss 100mL, standard deviation of blood loss 400mL, with 20 clusters. The trial results will be disseminated at medical conferences and submitted to peer-reviewed journals for publication. Findings may inform updates to professional guidelines for the delivery of obstetric health care.

Trial registration: This trial will be registered with the Australian and New Zealand Clinical Trials Registry.

5.2 Administrative information

Title: Evaluating the Effectiveness of Chitosan-Covered Gauze in the Management of Postpartum Haemorrhage in Low-Resource Settings: A Superiority Unblinded Cluster Randomised Controlled Trial Protocol in Ghana.

Trial Registration: (ClinicalTrials.gov or WHO ICTRP)

Trial registration—data set

Table 11: Trial Registration Data	
Data Category	**Information**
Primary registry and trial identifying number	(ClinicalTrials.gov or WHO ICTRP)
Date of registration in primary registry	DD/MM/YYYY
Secondary identifying numbers	
Source(s) of monetary or material support	
Primary sponsor	
Secondary sponsor(s)	
Contact for public queries	Yusif Yakub, MPH (yyak3902@uni.sydney.edu.au)
Contact for scientific queries	Bradley de Vries, MD, A/Prof Sydney Institute for Women, Children, and Families, Sydney Local Health District, Sydney. Australia.
Public title	Evaluating Chitosan-Covered Gauze for Postpartum Haemorrhage in Low-Resource Settings
Scientific title	Evaluating the Effectiveness of Chitosan-Covered Gauze in the Management of Postpartum Haemorrhage in Low-Resource Settings: A Superiority Unblinded Cluster Randomised Controlled Trial Protocol in Ghana.
Countries of recruitment	Ghana
Health condition(s) or problem(s) studied	Excessive bleeding (≥750 mL)
Intervention(s)	Active comparator: Standard care (including uterine massage and uterotonic agents) and uterine packing with chitosan-covered gauze
	Placebo comparator: Standard care alone
Key inclusion and exclusion criteria	Ages eligible for study: 18–45 years, Sex: females,
	Inclusion criteria: adult female patient (18-45years) diagnosed of postpartum haemorrhage ≥ 750mL
	Exclusion criteria: allergy against Shellfish, suspicion of chorioamnionitis or endometritis, Febrile to >38 degrees Celsius in labour, known hypersensitivity to chitosan.
Study type	Interventional
	Allocation: randomised, Intervention model: cluster parallel-group assignment, allocation ratio of 1:1; Masking: unblinded.
	Primary purpose: prevention
Date of first enrolment	To be advised
Target sample size	570
Recruitment status	Yet to recruit
Primary outcome(s)	Total blood loss within 24 hours of birth
Key secondary outcomes	Maternal mortality, Severe maternal anaemia as indicated by post-partum maternal anaemia (<7.0g/L) or blood transfusion, Blood loss > 2L, Need for additional interventions, Incidence of adverse events.

Protocol version

Protocol Number:

Version and Date: (Version 1.0, August 2025)

Sponsor/Funding Agency: No sponsors or external funding as of 2nd January 2025. The authors are fully responsible for the study design, data collection, analysis, interpretation and decisions about publication.

Roles and responsibilities

Principal Investigator: Yusif Yakub, Mr., Sydney Medical School, Faculty of Medicine and Health, The University of Sydney, Science Rd., Camperdown, NSW 2050, Australia. (YY)

Co-Investigators:

1. Hala Phipps, Clinical Associate Professor. Susan Wakil School of Nursing and Midwifery, Faculty of Medicine and Health, The University of Sydney, Science Rd., Camperdown, NSW 2050, Australia. (HP)
2. Ritu Mogra, Medical Doctor. Central Clinical School, Faculty of Medicine and Health, The University of Sydney, Science Rd., Camperdown, NSW 2050, Australia. (RM)

3. Bradley de Vries, Associate Professor.

   a. Sydney Institute for Women, Children, and Families, Sydney Local Health District, Sydney. Australia.
   b. Reproduction and Perinatal Centre, Faculty of Medicine and Health, The University of Sydney, Sydney, Australia. (BdV)

Authors' contributions: BdV conceived of the study. YY drafted the manuscript. BdV, HP contributed intellectual input into the study design. BdV provided statistical expertise in clinical trial design. All authors contributed to refinement of the study protocol and approved the final manuscript.

Contact information for the trial sponsor

Trial Sponsor:
Sponsor's Reference:
Contact name:
Address:
Telephone:
Email:

Roles and responsibilities—sponsor and funder

The funding source will have no role in the design of this study and will not have any role during its execution, analyses, interpretation of the data, or decision to submit results.

Roles and responsibilities—committees

Principal investigator and research physicians
Design and conduct of trial
Preparation of protocol and revisions
Preparation of investigators brochure (IB) and CRFs [case report forms]
Organising steering committee meetings
Managing CTO [clinical trials office]
Publication of study reports
Members of TMC [Trial Management Committee]
Steering committee (SC)
Members include independent chair, principal investigator, co-investigators, patient/public representatives and representatives of the funder or sponsor (non-voting members)
Agreement of final protocol
All lead investigators will be steering committee members. The lead investigator will be nominated as national coordinator
Recruitment of patients and monitor budget adherence, and milestone achievements.
Reviewing progress of study and if necessary, agreeing changes to the protocol and/or investigators brochure to facilitate the smooth running of the study
Trial management committee (TMC)
(Lead investigators, research physicians, administrator)
Study planning
Organisation of steering committee meetings
Provide annual risk report ethics committee
Responsible for trial master file
Budget administration and contractual issues with individual centres
Advice for lead investigators Audit of (monthly feedback forms and decide when site visit to occur.
Assistance with international review, board/independent ethics committee applications
Data verification
Randomisation
Data manager
Maintenance of trial IT system and data entry
Data verification
Lead investigators
In each participating centre a lead investigator (senior Obstetrician Gynaecologist) will be identified, to be responsible for identification, recruitment, data collection and completion of CRFs, along with follow up of study patients and adherence to study protocol and investigators brochure. Lead investigators will be steering committee members.

Table 12: Roles and responsibilities—committees

5.3 Introduction

5.3.1 Background and rationale

Background

Maternal mortality remains a pressing concern in low-income countries, with stark inequities between high- and low-income nations. The maternal mortality ratio (MMR) exhibits a wide disparity, ranging from 12.1 per 100,000 live births during 1993-2005 to 6.2 per 100,000 live births in 2006-2018 in the Netherlands (408), to 1,461-2,105 per 100,000 in 2007-2014 in tertiary hospitals in The Gambia (409).

Sub-Saharan Africa has an MMR of over 450 per 100,000 live births (410). A study conducted in seven LMICs reported an overall MMR of 168 per 100,000 live births, with 29% of the deaths occurring during the delivery period (411). While some progress has been made, numerous countries remain off course to achieve the Sustainable Development Goal target of reducing maternal mortality to 70 deaths per 100,000 live births by 2030 (412). Haemorrhage continues to be a major contributor to maternal mortality worldwide, especially in LMICs (413, 414).

Postpartum haemorrhage (PPH) is a leading cause of maternal mortality worldwide, with higher risks in low-resource settings (415). In low-resource settings like Ghana, PPH is a major contributor to maternal mortality (398, 416), due to delayed access to advanced care, including blood transfusions and surgical interventions (406). In Ghana, PPH accounted for 24% of maternal deaths in one study (102) and we confirmed in Chapter 4 of this thesis that PPH was the most common cause, responsible for 27% of maternal deaths. In Ghana maternal mortality continues to be a critical concern, with estimates varying between 200 and 1,004 deaths per 100,000 live births, depending on the years studied and region (417, 418).

Chitosan-covered gauze has shown effectiveness in trauma-related haemorrhage across various clinical scenarios. In obstetric and gynaecological settings, it has successfully managed cervical and vaginal bleeding (419, 420). Its efficacy extends to military trauma, where it has been used to treat injuries in combat situations (421, 422). Chitosan-covered or combat gauze has shown superior performance compared to standard gauze in controlling haemorrhage (423, 424). Its mechanism of action involves reducing clotting time (424). While some studies suggest the need for further research to conclusively establish its effectiveness (425), its versatility and efficacy make it a promising and may offer a practical solution for obstetric emergencies (426).

Rationale

This study seeks to bridge the lack of evidence for using combat (chitosan) gauze in obstetric care, specifically in low-resource settings where other interventions may be unavailable. The rationale for using chitosan gauze include the theoretical mechanisms of benefit, such as chitosan's ability to promote rapid haemostasis through electrostatic interactions with red blood cell membranes, its biocompatibility, and potential antimicrobial properties. In addition, there is limited but promising existing evidence, including case series and small trials where chitosan dressings have demonstrated effectiveness in trauma and surgical bleeding contexts. These properties and the urgent need for low-cost, easily deployable solutions for postpartum haemorrhage PPH in low-resource settings would be good for testing this intervention in Ghana.

Choice of comparator

Standard care was chosen as the comparator as this will be easier to implement in this pragmatic RCT. This choice is also because the clinical staff are used to this care, and it would be difficult to get every centre to introduce a new type of standard care for the control group. It's easier for them to do what they usually do and then add chitosan gauze for some participants.

5.4 Objectives.

Primary Objective:

- To evaluate the effectiveness of chitosan-covered gauze in reducing blood loss in women experiencing PPH compared to standard care.

Secondary Objectives:

- To evaluate maternal outcomes, including the need for additional interventions (e.g., surgical procedures, blood transfusion).
- To assess safety and adverse events associated with chitosan-covered gauze use.

Study Hypothesis

Null Hypothesis (H_0): Among women who have a primary PPH of 750mL or more, uterine packing with chitosan-covered gauze in addition to standard care is not more effective than standard care for reducing total blood loss.

Alternative Hypothesis (H_1): Among women who have a primary post-partum haemorrhage of 750mL or more, uterine packing with chitosan-covered gauze is more effective than standard care for reducing total blood loss.

Trial Design

- **Type:** Superiority, unblinded cluster RCT with an allocation ratio of 1:1.
- **Population:** Women aged 18–45 years with PPH ≥ 750mL after vaginal delivery or caesarean section after the placenta has been removed.
- **Duration**: Maximum time of 3-4 years (including recruitment, follow-up, and analysis).

5.5 Methods: Participants, interventions, and outcomes

Study Setting:

Community and Teaching healthcare facilities in Northern and Bono regions of Ghana.

Northern region of Ghana, it is the largest region by land area predominantly rural, with many communities relying on subsistence farming. The region has several district and sub-district health facilities, though access to tertiary care is limited.

Many facilities are under-resourced, with shortages of staff, supplies, and medications. The region has high maternal mortality rates, primarily due to PPH and delays in accessing care. Cultural practices and beliefs influence maternal healthcare utilization.

The limited availability of advanced interventions makes the region ideal for new, cost-effective solutions like chitosan-covered gauze. Bono region is found in the middle belt of Ghana and is smaller in land area compared to the Northern region but more densely populated. The region is mix of urban and rural communities, with agriculture being a major economic activity.

The region benefits from relatively better healthcare infrastructure than the Northern region, but rural areas still face significant challenges. Hospitals and health centres provide basic maternal health services, but specialized care is scarce.

Though slightly better than in the Northern region, maternal mortality and morbidity are of greater concern due to delays in accessing care and limited resources. The

region provides a balance of rural and peri-urban settings for evaluating the intervention's generalisability.

Eligibility Criteria

Inclusion Criteria:

- Women diagnosed with a PPH of ≥750 mL for both vaginal and caesarean births.
- Aged 18–45 years.
- Study centres will include district, regional and teaching hospitals in rural and urban Ghana where women give birth.
- Singleton and multiple pregnancies

Exclusion Criteria:

- Known hypersensitivity to chitosan and or shellfish.
- Placenta still in situ.
- Suspicion of chorioamnionitis or endometritis.
- Febrile to >38 degrees Celsius in labour

Interventions

The Treatment:

The gauze will be inserted into the uterine cavity through the vagina or through the uterine incision in the case of a caesarean section. The application will be performed by a trained Midwife or Obstetrician, and when feasible, ultrasound guidance will be utilized to ensure proper placement and to confirm the absence of retained products in the uterus.

Experimental Group:

In centres randomised to the treatment arm, patients experiencing PPH ≥ 750mL will be offered treatment with the chitosan-covered gauze in addition to routine management of PPH according to local protocols.

Control Group:

Standard care alone: PPH will be managed according to local guidelines (Appendix 4). Management may include, but is not limited to, fluid resuscitation, uterotonic

agents, tranexamic acid, uterine tamponade, and surgical or radiological interventions.

Interventions—modifications

The intervention may be ceased (the chitosan-covered gauze removed) by the treating team or at the request of the participant if there are clinical concerns (such as suspected allergic reaction to the chitosan gauze or other serious adverse event that may be related to the intervention) or if the participant decides she no longer wants the treatment.

Participants may withdraw consent for the intervention or the trial at any point without any repercussions.

The treatment may be ceased if the clinical team determines that continuing the allocated intervention is causing harm to the participant.

The presence of life-threatening conditions such as uterine rupture, severe infection, or cardiovascular collapse, or other adverse events will be treated at the discretion of the treating team and may include removal of the chitosan-covered gauze.

All instances of discontinuation or modification will be documented in detail, including the reason and the timing, review by the trial's Data Monitoring Committee (DMC), and reported in line with Good Clinical Practice (GCP) guidelines as outlined in the protocol and appendices.

Even if an intervention is discontinued or modified, the participant will remain in the trial for safety monitoring and follow-up unless they explicitly withdraw consent from all trial-related activities.

Interventions—adherence

Adherence improvement strategies

Structured training sessions will be conducted for all healthcare providers on the trial protocol, on proper application of the chitosan-covered gauze, and documentation requirements.

Simulation exercises, visual aids, quick-reference guides, and videos will be used to familiarize staff with intervention procedures for those centres allocated to the treatment arm of the trial.

User-friendly Standard Operating Procedures (SOPs) outlining every step of the intervention process will be develop in detail and will be readily accessible at all trial sites.

There will be regular check-ins (one to three monthly) between the trial coordinating team and site staff to address challenges.

There will be a site investigator at each participating site to oversee adherence to protocols, provide immediate feedback, and troubleshoot issues.

Adherence assessments

Standardized checklists will be developed for healthcare providers and local investigators to document adherence to key steps in the protocol, and case report forms (CRFs) will be regularly reviewed to ensure complete and accurate documentation of intervention steps. CRFs will be cross-checked with hospital records for consistency.

Audits will be conducted at trial sites to observe practices and evaluate adherence to protocols and identify deviations and provide local support, feedback, and action plans.

Adherence data will be analysed during interim monitoring visits and provide tailored feedback to sites with low adherence and develop specific action plans for improvement.

Interventions—concomitant care

All local treatments for PPH are permitted at the discretion of the treating clinicians in combination with local guidelines.

5.6 Outcome Measures

Primary Outcome:

- Total blood loss within 24 hours of birth as estimated by the clinical staff providing care.

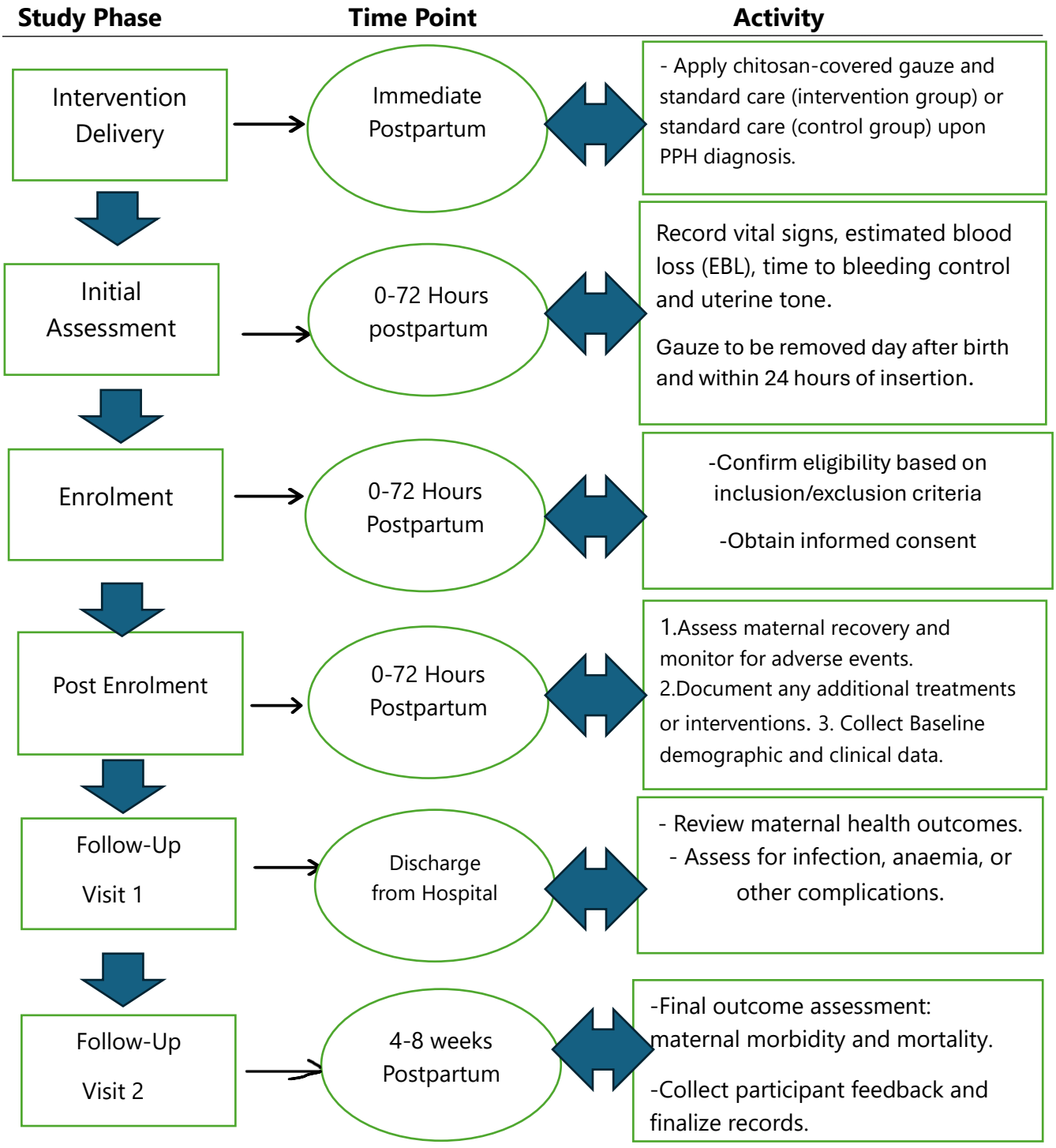
Secondary Outcomes:

- Maternal mortality.
- Severe maternal post-partum anaemia (maternal haemoglobin < 7.0g/L) or blood transfusion, or maternal death due to post-partum haemorrhage.
- Blood loss > 2L.
- Need for additional interventions:

    - Use of medical treatment in addition to a bolus of oxytocin e.g., ergometrine, carbetocin, oxytocin infusion, misoprostol, carbeprost, or tranexamic acid)
    - Use of other tamponade methods (e.g., intrauterine balloon catheter).
    - Surgical intervention (e.g., uterine compression suture, uterine artery ligation, hysterectomy).
- Length of Hospital Stay
- Adverse events
- Maternal satisfaction

5.7 Participant timeline

Figure 6: Flow of Participants



5.8 Sample size calculation and recruitment

Sample Size Calculation

For the primary outcome of volume of primary postpartum haemorrhage: For an alpha value of 0.05, beta value of 0.10, mean difference in blood loss 100mL, standard deviation of blood loss 400mL, with 20 clusters, a total sample size of **570 participants** is required. This calculation used a traditional sample size calculation for an individual superiority randomised trial for a continuous outcome multiplied by a design effect to account for clustering and variation in cluster size as described by Eldridge et al (2006) (427).

Recruitment

Recruiting centres:

Heads of department at each eligible centre will be approached and asked if they would like to participate. Study investigators will be available to discuss the trial protocol and potential benefits of introducing the use of chitosan-covered gauze for treating PPH.

Recruiting individual participants:

Within the catchment area of each participating centre, local leaders, health committees, and traditional birth attendants will be identified and approached. Educational materials will be made available and birth attendants in the community and in each centre will be offered educational sessions about the use of chitosan-covered gauze for PPH.

Trained healthcare providers at participating facilities will identify eligible participants and trial recruitment will be integrated into routine maternity care workflows. Potential participants will be approached in the post-partum period and asked if they would like to participate, and informed consent taken if they agree.

Incentives, such as free maternal health check-ups, transportation reimbursement, or small care packages for newborns, may be offered, to encourage participation.

Recruitment progress will be monitored every one to three months to identify and address barriers to enrolment promptly and provide regular feedback to the recruitment teams to maintain motivation and accountability.

Recruitment materials and communication will be culturally appropriate and available in local languages and will respect cultural norms and engage with participants' families where necessary.

We will establish a referral network involving community health workers and traditional birth attendants to identify eligible participants.

5.9 Methods: Assignment of interventions

Allocation:

Sequence generation

Centres will be randomly assigned to either the control or intervention group with a 1:1 allocation ratio using a computer-based random number generator stratified by geographic region (Northern vs. Bono regions of Ghana) and facility type (rural clinic vs. district hospital).

Allocation concealment mechanism

As this is an unblinded trial, there will be no allocation concealment.

Implementation

An independent statistician or a member of the research team not involved in recruitment will generate the random allocation of centres. The allocation will be made available to the study investigators.

Site investigators and trained research staff at the trial sites will oversee participant enrolment in collaboration with medical staff and birth attendants.

Clinicians in each centre will administer treatment for PPH according to local policies and guidelines (Appendix 4).

Blinding (masking)

Trial participants will not be blinded, as the intervention (chitosan-covered gauze) is visibly distinct from standard care. To reduce observer bias, all participating clinical staff will undergo standardized training on blood loss estimation using predefined visual aids and calibrated drapes or collection containers where feasible.

Care providers will not be blinded and must know the intervention to deliver it appropriately. This includes applying standard care plus chitosan-covered gauze or administering standard care alone for postpartum haemorrhage (PPH).

Outcome assessors responsible for collecting and adjudicating trial outcomes (e.g., blood loss, maternal recovery) will be blinded to the intervention allocation. These independent reviewers will adjudicate outcomes based on de-identified case report forms, partograms, and clinical records. The allocation status of the center will not be

disclosed in these documents. While full blinding at the point of data collection is not possible in an open-label, cluster trial, the adjudication process remains blinded to make the outcome classification as impartial as possible.

Data analysts performing statistical analyses will remain blinded to group allocation by using coded identifiers such as "Group A" and "Group B" until the analysis is finalized.

Blinding (masking)—emergency unblinding

As the trial is not blinded to participants or clinicians, emergency unblinding will not be required.

Cluster randomization bias mitigation and baseline care heterogeneity

We selected cluster randomization to avoid contamination within centres and to reflect the operational delivery of PPH care at facility level. We acknowledge that cluster designs introduce specific risks of bias. To address these concerns, clusters will be consented to participate before allocation disclosure. Randomization will be stratified by geographic region and facility type.

To mitigate baseline imbalance and enable transparent assessment of risk of bias, a structured baseline facility survey will be performed for each centre prior to randomization disclosure. This survey will document PPH standard care practices and capacity variables, including availability of uterotonics (type and stock), tranexamic acid availability, surgical/caesarean capability, blood transfusion services, staff composition, and average monthly delivery volume.

For every PPH enrolment, a standard care checklist will record contemporaneous co-interventions (e.g., uterotonics administered, tranexamic acid, balloon tamponade, laparotomy, transfusion).

We would rely on staff training to prevent cross-contamination. We would supply chitosan gauze only to the centres randomised to this arm, and that would minimise contamination (as the gauze would not be available to centres randomised to standard care)

Analytical methods will explicitly account for clustering and adjust for stratification variables and important baseline facility covariates. All primary analyses will be by intention-to-treat at the cluster level, with sensitivity analyses evaluating the effects of contamination, per-protocol adherence, and loss of clusters.

These measures aim to increase the internal validity of the cluster trial while preserving external relevance to routine care settings.

5.10 Methods: Data collection, management, and analysis

Data collection fields

To ensure comprehensive and high-quality data collection in this trial, the following key data fields will be recorded:

Participant Demographics & Baseline Characteristics

- Age, parity, and gravidity
- Medical and obstetric history (e.g., history of PPH, anaemia)
- Socioeconomic factors (education, income level, access to healthcare)

Enrolment & Randomization Data

- Inclusion/exclusion criteria confirmation
- Cluster assignment (intervention vs. control)
- Date and time of enrolment

Intervention Details

- Type of intervention received (chitosan-covered gauze +standard care or standard care)
- Method and duration of gauze application (if applicable)

Clinical Assessments & Outcomes

- Estimated blood loss after 24 hours of birth
- Haemodynamic status (blood pressure, heart rate)
- Need for additional interventions (uterotonics, blood transfusion, surgery)
- Maternal complications (infection, anaemia, organ failure)
- Maternal mortality (if applicable)
- Maternal satisfaction
- Severe maternal postpartum anaemia (maternal haemoglobin < 7.0g/L) or blood transfusion, or maternal death due to post-partum haemorrhage.
- Length of stay at hospital

- Adverse effect

Follow-Up Assessments

- (0-72) hours postpartum, day of discharge from hospital, and (4-8) weeks postpartum follow-up data
- Presence of adverse effects (e.g., infection, allergic reactions)
- Recovery status and final maternal health outcomes

Data Quality & Monitoring Fields

- Adherence to protocol (compliance checks, deviations)
- Data completeness and verification (duplicate entries flagged)
- Adverse event reporting and classification

Data collection methods

Outcome Data Collection: *O*utcome data will be collected using standardized forms.

Measurements of blood loss: like the E-MOTIVE Trial, we will use calibrated drapes to aid in the estimation of blood loss. This would provide a balance between feasibility and accuracy of measurements. For free blood, a measuring container or jug will be used. Visual estimation will be used only if more accurate methods are not available.

Haemoglobin levels will be measured using validated laboratory equipment on postpartum Day 1, at 12 to 36 hours after the birth. Infection rates will be assessed on maternal temperature of >= 38 degrees, or on at least one occasion in the first 48 hours after birth, requirement for antibiotics or clinical diagnosis of post-operative endometritis.

Maternal satisfaction with their management of PPH will be assessed using a visual analogue scale.

Baseline Data Collection: Demographics, medical history, and obstetric history will be captured at enrolment using a structured case report form (CRF).

Follow-Up Data Collection: Follow-up visits on day of discharge from hospital. Then another visit or phone call at 4 to 8 weeks.

Postpartum assessments will include clinical assessments such signs of infection, anaemia, or complications. *Data Quality Assurance*: All staff involved in data collection will undergo rigorous training on the conduct of the study, completing CRFs and electronic data capture systems, and adhering to GCP guidelines.

SOPs will guide data collection, handling, and storage to ensure consistency across trial sites.

Data Collection Forms: CRFs and electronic data capture templates will be used.

Data collection methods—retention

To maximise data collection, follow-up data will be collected at two time-points – one to three days after the birth and a short follow-up visit or phone call at four to eight weeks after the birth. The primary outcome can be ascertained after 24 hours from the time of the birth, minimising loss to follow-up.

Each participant will be assigned a study coordinator to address any questions or concerns throughout the trial and who will be responsible for collecting follow-up data. Follow-up data may be collected through an on-line survey, by a follow-up phone call or in a face-to-face visit. The multiple options aim at maximising the collection of follow-up data.

Data management

All study data will be entered into a secure electronic data capture system, with critical data fields subject to double data entry to ensure accuracy. Range checks and validation rules will be applied to identify out-of-range values. Data will be encrypted and backed up regularly on secure servers. Access rights will be role-based, ensuring that only authorized personnel can modify or review records. Detailed processes for data handling, including coding schemes, audit trails, and discrepancy resolution, are outlined in the Data Management Plan, which is maintained separately from the protocol.

Statistical methods

Statistical methods—outcomes

- **Primary Outcome:** The mean difference in blood loss between groups will be conducted using generalised linear mixed models adjusted for stratification variables: geographic region (Northern vs. Bono regions of Ghana) and facility type (rural clinic vs. district hospital).
- **Secondary Outcomes:** Odds ratios for binary outcomes will be estimated using generalised linear mixed models adjusted for stratification variables:

geographic region (Northern vs. Bono regions of Ghana) and facility type (rural clinic vs. district hospital).

- A secondary analysis for the primary outcome may be conducted, adjusting for any unbalanced baseline variables that are known to be associated with PPH.

Statistical methods—additional analyses

Subgroup analyses may be conducted within the stratification variables: geographic region (Northern vs. Bono regions of Ghana) and facility type (rural clinic vs. district hospital).

Statistical methods—analysis population and missing data

All randomised participants will be included in the primary analysis on an intention-to-treat basis, regardless of their level of adherence to the study protocol. For missing data, multiple imputation methods will be used for missing primary outcome data between 5% and 40% of observations.

5.11 Methods: Monitoring

Data monitoring - formal committee

DMC Composition

The DMC will include experts in obstetrics and midwifery, biostatistics, and ethics. Members will have no direct involvement with the day-to-day conduct of the study, no competing financial or professional interests, and will be independent from the sponsor to minimize bias.

DMC Role and Responsibilities

The DMC will regularly review aggregated safety data including serious adverse events. DMC shall make recommendations to the trial steering committee on continuing, modifying, or terminating the trial based on emerging data.

Reporting Structure

The DMC will meet after a quarter of the number of participants have been enrolled to review study progress and data. After each meeting, the DMC will issue a written report to the study sponsor and the principal investigator, summarizing any findings, concerns, or recommendations. Only the DMC will have access to unblinded interim data.

Independence from the Sponsor and Competing Interests

The DMC members will have no financial or scientific conflicts of interest related to this study. Full disclosure statements from each member will be collected to confirm independence and manage any potential competing interests.

DMC Charter

Detailed procedures for the DMC's operations, decision-making processes, and conflict-of-interest policies will be described in the DMC terms of reference, which will be maintained separately from this protocol. The DMC terms of reference can be accessed upon request by authorized stakeholders such as ethics committee, regulatory authorities.

Data monitoring—interim analysis

Interim analyses will be conducted after 50% of participants have been enrolled. The DMC will evaluate both efficacy and safety endpoints. Stopping guidelines, including pre-specified boundaries for efficacy, futility, and safety concerns, are detailed in this protocol. The DMC will make formal recommendations to the sponsor and principal investigator regarding trial continuation. However, the final decision to continue or terminate the trial rests with the study's steering committee.

Harms

Adverse events will be systematically collected and documented throughout the study period. All events will be captured via participant diary cards and may be reported as they occur during or between study visits. Investigators will assess each event for severity, causality, and expectedness. Serious adverse events (SAEs) will be reported to the sponsor within 24 hours to the DMC. The sponsor, in consultation with the study team, will monitor cumulative safety data, ensuring that any unexpected trends or serious risks are addressed promptly.

Auditing

Audits will be conducted during the trial to ensure compliance with General Clinical Practice (GCP) and relevant regulations. These audits will be performed by independent auditors who are not involved in the study's design or conduct. A risk-based schedule will be used to determine the frequency of audits, although additional audits may be triggered if concerns about participant safety or data integrity arise. Investigators and site staff are expected to cooperate by granting auditors access to all relevant documents and data. Findings will be documented in an audit report, and any required corrective actions will be implemented promptly by the study team.

5.12 Ethics and dissemination

Research ethics approval

The study will be conducted in accordance with the National Statement on Ethical Conduct in Human Research (2007) (https://www.nhmrc.gov.au/about-us/publications/national-statement-ethical-conduct-human-research-2007-updated-2018), consistent with the principles that have their origin in the Declaration of Helsinki.

Ethical Approval: Approval will be sought from the Ghana Health Service Ethics Review Committee.

Informed Consent: Written informed consent will be obtained from all participants before enrolment.

Safety Monitoring: The independent DMC will oversee adverse events and trial conduct.

Protocol amendments

Changes to the protocol—such as modifications to eligibility criteria, outcome measures, or analytical methods—will be documented in an amended protocol version and submitted for review and approval by the Institutional Review Board (IRB) and, if applicable, regulatory authorities. Once approved, the updated protocol and any revised consent documents will be distributed to site investigators and research staff, who will receive training on the changes. Trial participants will be notified if the amendments directly affect their participation. Further, trial registrations will be updated, and any future publications or presentations will clearly reference the amended protocol version.

Consent

Informed consent to use the trial participants' data in the study will be obtained by qualified study personnel who have received training on the protocol and ethical guidelines. The training will be given to personnel assigned to be at the centres that are randomised to using the chitosan-gauze, and to staff from centres randomised to routine care. The consent process will occur in a private setting, allowing sufficient time for questions and deliberation. In cases where a participant is unable to provide informed consent, a legally authorized representative will be approached. Signed consent forms will be maintained in under lock and key in a secure location.

Confidentiality

Participant confidentiality will be safeguarded throughout this trial. All personal identifiers collected at screening and during participation will be stored on secure, password-protected servers with limited user access. A unique study ID will be assigned to each participant, and all data analyses will be conducted on de-identified datasets. Paper records will be kept under lock and key in a secure location, and direct access to these documents is limited to authorized personnel only. At the conclusion of the study, records will be archived for at least five years per the Ghana Health Service regulatory requirements. No identifying information will be released publicly or shared with any external parties without specific IRB approval or participant consent.

Declaration of interests

All principal investigators and sub-investigators at each participating site will complete a Conflict-of-Interest Disclosure Form before their involvement in this trial. The sponsor's Conflict of Interest Committee will review these disclosures to determine whether any financial or other interests could influence the conduct or reporting of the study. If a conflict is identified, appropriate management steps such as additional oversight, or limited involvement in data analysis will be implemented to protect the integrity of the trial. Investigators are required to promptly update their disclosures if new interests arise during the study. All conflicts of interest will be disclosed in any publications or presentations resulting from this research.

Access to data

Upon completion of data collection and final database lock, the sponsor and the principal investigators will have full access to the final trial dataset. Site investigators will have access to their own site's data and, where appropriate, pooled anonymized data for analysis. Any agreements that could restrict the release of data or delay publication, such as sponsor-required review periods, will be disclosed to the Research Ethics Committee and specified in the clinical trial agreement. In cases where the sponsor retains the right to approve or comment on publications, the investigators will ensure that such provisions do not unreasonably interfere with the publication of trial results.

Ancillary and post-trial care

Participants who experience any injury or harm as a direct result of this trial will have access to appropriate medical care and compensation in accordance with local regulations and our clinical trial insurance policy.

Dissemination policy -trial results

Participants will have the opportunity to see the results of this clinical trial in a clear and understandable format once final analyses are complete. A lay summary will be provided on request via postal mail or secure email. In addition, the principal investigators will submit manuscripts derived from this study to peer-reviewed journals and presented in international conferences. The trial's outcome data will be uploaded to ClinicalTrials.gov within 12 months of final data collection. Prior to publication, the study investigators may review the manuscript to ensure accuracy and protection of proprietary information but will not unreasonably delay or prevent release of the results. If any provisions in our clinical trial agreement limit or delay public disclosure, these will be disclosed to the research ethics committee and documented in the trial's registry.

Dissemination policy—authorship

Authorship on any publication arising from this study will be based on the International Committee of Medical Journal Editors (ICMJE) criteria. All investigators and contributors must satisfy all four criteria to be recognized as authors. The order of authorship will reflect individual contributions, and any changes after initial submission will require agreement from all co-authors. Professional writers assisting in manuscript preparation will be acknowledged, with their funding source disclosed, unless they qualify for full authorship by meeting the ICMJE criteria.

Dissemination policy—reproducible research

We plan to deposit the full study protocol, in an open-access repository upon publication of the primary manuscript. De-identified participant-level data will be made available within 12 months after publication in a secure repository, subject to data use agreements ensuring participant confidentiality.

Specific instructions for requesting access will be outlined in the published manuscripts and on the trial's registration page.

5.13 Discussion

PPH remains one of the leading causes of maternal morbidity and mortality worldwide (428, 429), with the burden being particularly high in low-resource settings (415, 430). In Ghana, where maternal mortality rates are still of significant concern, innovative yet practical interventions are required to enhance bleeding control strategies. The proposed trial investigates a chitosan-covered gauze dressing, an easily deployable, low-cost haemostatic adjunct, that could potentially reduce blood loss and improve maternal outcomes when conventional measures prove insufficient.

Chitosan is a naturally derived polysaccharide with documented haemostatic properties. Chitosan-based dressings have been used effectively in trauma care and military settings due to their ability to promote clot formation and adhere to tissues, thus helping to stabilize and control bleeding (431, 432). While data exist on the effectiveness of chitosan dressings for acute haemorrhage control in trauma, evidence for their utility specifically in postpartum bleeding is limited. In 2013, a case series study of 19 women with PPH from various causes, such as uterine atony and placenta accreta, examined the use of chitosan-covered gauze for uterine packing. The treatment effectively stopped bleeding in all but one case, indicating its potential as a viable option for managing severe PPH (433).

A retrospective case-control study in 2022 analysed outcomes in women treated for PPH using medical therapy alone, balloon tamponade, or chitosan tamponade. Results showed that the chitosan tamponade group had a significantly lower hysterectomy rate compared to the balloon tamponade group, with no notable differences in secondary outcomes or adverse events. The use of chitosan tamponade was linked to a 77.8% reduction in PPH-related hysterectomies (307).

A multicentre registry review of 98 severe PPH cases treated with chitosan-covered gauze demonstrated successful outcomes, reinforcing its potential effectiveness as a haemostatic agent in obstetric care (434).

The findings from these studies indicate that chitosan-covered gauze holds promise as an intervention for PPH, providing advantages such as ease of application, cost-effectiveness, and a decreased reliance on invasive procedures like hysterectomy. However, the current evidence remains limited, highlighting the need for further research, including large-scale RCTs, to confirm its efficacy and safety in managing postpartum haemorrhage.

This study has the potential to fill an important gap by evaluating chitosan-coated gauze in the real-world obstetric context, particularly where resources for advanced interventions may be minimal.

In a cluster randomised design to randomise health facilities rather than individual patients, the trial reflects a more natural clinical environment and reduces the risk of cross-contamination of practices within the same site. This design allows the intervention (chitosan gauze use along with training and implementation) to be integrated more seamlessly into routine obstetric workflows without the need for repeated on-site randomisation decisions.

Interventions targeting refractory PPH such as uterine artery embolisation may be high-cost or require sophisticated equipment and highly trained personnel. The chitosan gauze evaluated here has the potential to be a simple, scalable tool for bleeding control, making it highly relevant to under-resourced healthcare settings. Control of severe PPH in settings where women need to travel to a hospital with blood products or personnel capable of performing a hysterectomy could prove lifesaving. Blood products are often not available in low-income settings (435, 436) and chitosan-covered gauze has the potential to stop or delay the PPH while blood products are being sought.

In this superiority unblinded trial, there is a possibility of performance or detection bias. Healthcare providers aware of the intervention could either under or over report outcomes like blood loss and maternal status or could treat participants in the two arms differently in ways than addition of the chitosan-covered gauze. To mitigate this risk, data collectors and outcome assessors would be as independent as feasible, and standardized measurements may help improve data accuracy.

Although randomising by cluster helps streamline implementation, there is still a risk of contamination if providers share knowledge or materials across facilities. Rigorous training protocols, clear site allocation procedures, and maintaining strong lines of communication can reduce contamination.

Even within the same region, maternal healthcare facilities may differ in staff expertise, availability of uterotonics, and supportive care resources. Stratified randomisation or balancing by facility size and baseline performance could help account for site-level differences.

If effective, chitosan-covered gauze could offer an additional, easily administered method to control PPH before resorting to invasive procedures or referral to higher-level care. It could also buy time for health care workers to source blood products or

for the woman to travel an appropriate health care facility. The findings could potentially shift policies and guidelines on PPH management, particularly in low-resource contexts where timely advanced interventions may be unavailable.

Positive results from this trial would warrant further investigation into the broader integration of chitosan dressings. For example, scale-up studies could explore their utility in pre-hospital or community birth settings, where immediate resources are lacking, and evaluate cost-effectiveness at a national level. Adverse event data and real-world feedback from clinicians and patients would help refine protocols for safe and efficient deployment. Additionally, research on the biochemical mechanisms of chitosan adherence in the postpartum uterus and potential synergy with uterotonics would further elucidate best practices for maximizing haemorrhage control.

5.14 Conclusion

This superiority unblinded cluster RCT has the potential to generate robust evidence on the practical use of chitosan-covered gauze in reducing postpartum haemorrhage in low-resource settings. By actively observing routine clinical scenarios and involving frontline obstetric staff, the study design aims to deliver pragmatic insights that can translate into meaningful maternal health improvements. The trial's outcomes will guide policymakers, clinicians, and global health stakeholders in deciding whether and how to adopt chitosan-based dressings in strategies for managing PPH and reducing preventable maternal deaths.

CHAPTER 6: Summary

Maternal mortality remains a critical public health challenge in low- and middle-income countries (LMICs). This thesis aimed to investigate the causes of maternal mortality in these settings, assess the role of prenatal ultrasound in mitigating adverse pregnancy outcomes and explore innovative interventions to improve maternal health. The findings and discussions from the preceding chapters collectively contribute to understanding the multifaceted nature of maternal mortality and the potential for targeted interventions to address this pressing issue. This chapter synthesizes insights and highlights key implications for practice, policy, and future research.

Literature Review

Chapter 1 provides a detailed review of existing literature on maternal mortality in low-and middle-income countries (LMICs). It highlights the primary causes, including PPH, hypertensive disorders, infections, obstructed labour, and unsafe abortions. This chapter also discusses the challenges in reducing maternal mortality, such as limited access to skilled healthcare providers, inadequate healthcare infrastructure, and sociocultural factors. Additionally, the literature review explores the potential benefits of using prenatal ultrasound for improving maternal and perinatal outcomes, particularly in low-resource settings.

Assessing the Impact of Routine Prenatal Ultrasound: Systematic Review Protocol

In Chapter 2, a systematic review protocol was developed using Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P) 2015 checklist guidelines to investigate the impact of routine prenatal ultrasound on pregnancy and perinatal outcomes in low-resource settings. This chapter detailed the methodology, including the inclusion and exclusion criteria, data sources, search strategies of respective databases, and analytical framework. The protocol emphasized the importance of examining maternal and neonatal outcomes to provide a comprehensive assessment of the utility of prenatal ultrasound in these settings. The systematic review protocol resulted from the apparent research gap around the utility of routine prenatal ultrasounds for improving maternal outcomes in low-income settings.

Systematic Review of Routine Prenatal Ultrasound

Chapter 3 presented the systematic review results using the protocol outlined in Chapter 2. The review highlighted the lack of high-quality evidence to support the use of routine prenatal ultrasounds in low-income settings. The review identifies gaps in the existing literature, particularly regarding important maternal and perinatal outcomes. It recommended need further research to explore the full spectrum of benefits of routine prenatal ultrasound and to develop standardized protocols for its use across diverse healthcare settings.

Ghana Demographic Health Survey: Maternal Mortality Analysis

Due to the lack of data around the utility of prenatal ultrasound for improving maternal mortality and other adverse outcomes, Chapter 4 focused on maternal mortality in Ghana using data from the Ghana Demographic Health Survey (2012–2017). Describing the causes of maternal mortality was expected to give some insight into the potential preventative role that prenatal ultrasound could play, particularly with respect to conditions identifiable on ultrasound such as placenta praevia and ectopic pregnancy.

The analysis identified PPH (as there were 43 maternal deaths due to PPH), hypertensive disorders, and infections as the leading causes of maternal deaths, while antepartum haemorrhage, sometimes caused by placenta praevia, played a smaller role. Early pregnancy complications were not a common cause of maternal mortality, potentially because the families may not have been aware of the early pregnancy. The chapter further discussed the trends in maternal mortality over the five years and explored the potential role of obstetric ultrasound in reducing these deaths.

There may be the need for integrating ultrasound into routine antenatal care and improving access to emergency obstetric services in Ghana. Data on first trimester pregnancies in the survey were particularly lacking (ectopic pregnancies, miscarriages, terminations) and is an area that needs improvement. The data also outlined that PPH, is a leading cause of maternal mortality in Ghana, representing 27% of maternal deaths in this series. This highlights the importance of exploring methods of effective management during the third stage of labour towards reducing maternal mortality related to PPH. This finding led to the ideas described in Chapter 5.

Combat Gauze for Postpartum Haemorrhage: Randomised Controlled Trial Protocol

In Chapter 5, a RCT protocol was developed to evaluate the effectiveness of combat gauze in managing PPH in low-resource settings. The protocol outlined the study design, including participant recruitment, intervention procedures, and outcome measures. This chapter highlighted PPH as a major contributor to maternal mortality and the potential of combat gauze as an affordable, effective, and easily deployable intervention in LMICs. While this Chapter does not focus on obstetric ultrasound, it followed from the findings of Chapter 4. If chitosan-covered gauze were to be introduced into practice, obstetric ultrasound would be an important adjunct. For example, ultrasound could be used before or after uterine packing with gauze, or after its removal to assess for the presence of retained placental tissue. It would also be useful in rare cases where there is difficulty removing the gauze or if there is a clinical suspicion that some has been left behind.

Key Findings and Implications

The findings of this thesis underscore the critical role of evidence-based interventions in addressing maternal mortality in LMICs. Routine prenatal ultrasound is a potential tool for early risk identification and improved pregnancy outcomes. However, its widespread adoption requires addressing implementation challenges, including cost, training, and infrastructure. Additionally, innovative solutions like combat gauze may offer hope for managing life-threatening complications like PPH in resource-constrained environments.

Recommendations for Policy and Practice

1. Recommend improvements in data collection around maternal mortality, especially in the first trimester pregnancies.
2. Strengthening Health Systems: Investments in healthcare infrastructure, particularly in rural and underserved areas, are essential to improve access to emergency obstetric care and skilled birth attendants.
3. Community Education: Awareness campaigns are needed to inform women and families about the benefits of antenatal care and ultrasound and thereby increase utilization rates.
4. Innovative Interventions for PPH: Combat gauze and similar interventions should be evaluated further and, if proven effective, incorporated into maternal health programs to address PPH.

Key Findings in the Context of the Existing Literature

Following an extensive review of the literature in Chapter 1, this thesis addressed important research gaps in the fields of ultrasound for preventing maternal mortality in LMICs and the management of PPH. A systematic review was conducted that showed very limited research on the impact of routine prenatal ultrasound on pregnancy and perinatal outcomes in low-resource settings, with only one RCT identified (363). This demonstrated the importance of conducting more research in this field. For example, when resources are limited, the value of point of care ultrasound and the use of ultrasound through telehealth services (437), are lacking and need to be assessed in high-quality observational studies or RCTs.

When the dearth of literature on prenatal ultrasound for preventing maternal mortality became apparent, publicly available data from the DHS were examined to assess the causes of maternal mortality in Ghana (380), with reference to causes such as placenta praevia that can be diagnosed by ultrasound and lead to preventative measures. While the contribution of PPH could be estimated, mortality due to antepartum haemorrhage could not be subdivided into placenta praevia and placental abruption. This lack of knowledge is reflected in the medical literature and remains an important research gap, for example as in the Ghana DHS (380). Importantly in other studies, approximately half of women presenting with APH, no firm diagnosis of placental abruption or placenta praevia can be made despite thorough investigations (438, 439).

In Chapter 4, PPH was confirmed as the leading cause of maternal mortality in Ghana, consistent with reports from other low-income countries (315, 440).The literature was therefore reviewed with respect to potentially useful treatments for PPH in low-income settings and chitosan-gauze, approved for the treatment of PPH in Europe (407), was identified as a potentially important method of saving maternal lives in low-income countries as it can be stored at room temperature, is portable, and is relatively easy to use (306). A potential role for POCUS was identified, with sonographically identifying that the uterus is empty before packing the uterus with chitosan-gauze being a useful but not essential adjunct.

A protocol of rapid detection and response to PPH was identified as an important prevention measure that could be used in LMICs (304) and there is potential for widespread implementation of this intervention.

One critically important finding in Chapter 4 was that 50% of mothers who died from PPH did not have a potentially life-saving blood transfusion, which is consistent with known systemic issues in blood transfusion services in low-income settings (441, 442). Chitosan-gauze could theoretically delay, slow-down or even fully treat a severe PPH while transportation and/or blood transfusion are arranged (306, 433).

Finally, encouraged by the success of another cluster trial of PPH management in low-income settings (304), a protocol for a cluster trial of chitosan-gauze was developed and reported in Chapter 5. An individual RCT was not considered feasible due to the potential for contamination where chitosan-gauze might be used to treat some participants allocated to the non-gauze arm if perceived to be superior, or it might not be given by clinicians who did not believe in its usefulness. Additionally, as severe PPH is uncommon, it would not be feasible to consent potential participants before a PPH occurred, and not possible to obtain informed consent in an emergency setting. While ultrasound may be considered peripheral to the use of chitosan-gauze, there would be a role in confirming the uterus is empty before offering the treatment (407).

Strengths

- The thesis covered multiple dimensions of maternal mortality, including causes, diagnostic tools (ultrasound), and innovative interventions (chitosan gauze), providing a broad yet interconnected perspective.
- The thesis highlights clear gaps in evidence on routine prenatal ultrasound and its role in preventing maternal mortality, guiding future research priorities.
- The systematic review protocol was written and registered with PROSPERO using the PRISMA checklist, and actual systematic review was conducted using the predetermined protocol and standardised tools for assessing study quality. This methodologically rigorous approach reduced the risk of bias and contributed to transparency and replicability.
- By focusing on highly prevalent causes of maternal death (especially PPH), the findings are directly applicable to health systems and policy in LMICs and have the potential to impact on maternal mortality.
- The sampling methods for the Ghana DHS provided population-level insights that enhance the generalizability of findings within Ghana and comparable LMICs.
- The proposal of an RCT to evaluate chitosan gauze introduces an innovative, context, appropriate intervention with potential for real-world implementation.
- The thesis not only identifies problems but also suggests actionable policy and practice recommendations, making it relevant to decision-makers.

Limitations

- The paucity of high-quality studies on routine prenatal ultrasound in LMICs restricted the ability to draw strong conclusions on its effectiveness.

- DHS datasets lacked detailed information on first-trimester complications (e.g., ectopic pregnancy, miscarriages, unsafe abortions) and did not distinguish between causes of antepartum haemorrhage such as placenta praevia and placental abruption, limiting analysis of ultrasound's potential preventive role.

- Reliance on existing survey data meant being constrained by the quality, completeness and categorization of variables in the DHS.

- The thesis did not include the collection of new clinical data or real-world trial implementation, which would have added depth to the findings.

- While Ghana DHS is nationally representative, findings may not fully generalize to all LMICs due to variations in health systems, cultural practices, and resources.

- The chitosan gauze RCT remains at the protocol development stage; hence conclusions about its efficacy are hypothetical rather than evidence-based at this point.

- While recommendations are made, detailed cost-effectiveness analyses and implementation feasibility studies were beyond the scope of the thesis.

Future Research Directions

Future research should focus on:

- Conducting large-scale trials to evaluate the long-term impact of routine prenatal ultrasound on maternal and neonatal health outcomes.
- Investigating cost-effective models for scaling up prenatal ultrasound services in LMICs.
- Exploring the cultural and sociological factors that influence the acceptance and utilization of maternal health interventions.
- Assessing the effectiveness of innovative interventions like combat gauze in diverse low-resource settings.

Conclusions

This thesis contributes to the growing body of evidence on the causes and prevention of maternal mortality in LMICs, emphasizing the role of ultrasound and other targeted interventions. By addressing the gaps identified in this research, stakeholders can make significant strides toward achieving sustainable reductions in maternal mortality and improving mothers' and their children's overall health and well-being.

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7.0 APPENDICES

APPENDIX 1: Search Strategy for Systematic Review

Search Strategy for Ovid MEDLINE(R) ALL <1946 to May 30, 2024

1. ((ultraso*) adj3 (pregnan* or gestation or cyesis or antenatal or prenatal or obstetric*)).mp or Ultrasonography, Prenatal/

2. developing countries/
3. (developing countr* or low* income countr* or low* resource countr* or low* middle income countr* or LMIC or Ghana or Ethiopia or Afghanistan or Benin or Rwanda or Zimbabwe or Niger or Somalia or South Sudan or Sierra Leone or Tanzania or Togo or Uganda or Zambia or Guinea or Guinea-Bissau or Haiti or Democratic People's Republic of Korea or North Korea or Liberia or Madagascar or Malawi or Mali or Mozambique or Eritrea or Democratic republic of Congo or Burundi or Burkina Faso or Chad or Comoros or Central African Republic).mp
4. 2 or 3
5. 1 and 4

The search technique/strategy for Cochrane Library/CENTRAL database will be as follows:

1. ((ultraso*) adj3 (pregnan* or gestation or cyesis or antenatal or prenatal or obstetric*)).mp or Ultrasonography, Prenatal/

2. developing countries/
3. (developing countr* or low* income countr* or low* resource countr* or low* middle income countr* or LMIC or Ghana or Ethiopia or Afghanistan or Benin or Rwanda or Zimbabwe or Niger or Somalia or South Sudan or Sierra Leone or Tanzania or Togo or Uganda or Zambia or Guinea or Guinea-Bissau or Haiti or Democratic People's Republic of Korea or North Korea or Liberia or Madagascar or Malawi or Mali or Mozambique or Eritrea or Democratic republic of Congo or Burundi or Burkina Faso or Chad or Comoros or Central African Republic).mp.
4. 2 or 3
5. 1 and 4

Search Strategy for Global Index Medicus

(((ultraso*) AND (obstetric* OR antenatal OR prenatal OR pregnancy OR gestation OR cyesis)))

AND (("low middle income countr*" OR Ghana OR Ethiopia OR Afghanistan OR Benin OR Rwanda OR Zimbabwe OR Niger OR Somalia OR “South Sudan” OR “Sierra Leone” OR Tanzania OR Togo OR Uganda OR Zambia OR Guinea OR “Guinea-Bissau” OR Haiti OR “Democratic People’s Republic of Korea” OR “North Korea” OR “Liberia” OR Madagascar OR Malawi OR Mali OR Mozambique OR Eritrea OR “Democratic Republic of Congo” OR Burundi OR ”Burkina Faso” OR Chad OR Comoros OR “Central African Republic”))

Search Strategy for Embase (Ovid)

1. ((ultraso*) adj3 (pregnan* or gestation or cyesis or antenatal or prenatal or obstetric*)).mp or fetus echography/

2. developing countries/ or exp western Africa/

3. (developing countr* or low* income countr* or low* resource countr* or low* middle income countr* or LMIC or Ghana or Ethiopia or Afghanistan or Benin or Rwanda or Zimbabwe or Niger or Somalia or South Sudan or Sierra Leone or Tanzania or Togo or Uganda or Zambia or Guinea or Guinea-Bissau or Haiti or Democratic People’s Republic of Korea or North Korea or Liberia or Madagascar or Malawi or Mali or Mozambique or Eritrea or Democratic republic of Congo or Burundi or Burkina Faso or Chad or Comoros or Central African Republic).mp.
4. 2 or 3
5. 1 and 4

Search Strategy for CINAHL via EBSCO

1. "((ultraso*) N3 (pregnan* OR gestation OR cyesis OR antenatal OR prenatal OR obstetric*))"

2. "low-resource settings" OR "resource-limited settings" OR "developing countries" OR LMICs OR “Ghana” OR “ Ethiopia” OR “Afghanistan” OR “Benin” OR “Rwanda” OR “Zimbabwe” OR “Niger” OR “Somalia” OR “South Sudan” OR “Sierra Leone” OR “Tanzania” OR “Togo” OR “Uganda” OR “Zambia” OR “Guinea” OR “Guinea-Bissau” OR “Haiti” OR “Democratic People’s Republic of Korea” OR “North Korea” OR “Liberia” OR “Madagascar” OR “Malawi” OR “Mali” OR “Mozambique” OR “Eritrea” OR “Democratic republic of Congo” OR “Burundi” OR ”Burkina Faso” OR “Chad” OR “Comoros” OR “Central African Republic”

3. 1 AND 2

SCOPUS Search Strategy

(ultraso*) W/3 (obstetric* OR antenatal OR prenatal OR pregnancy OR gestation OR cyesis)

AND

"low middle income countr*" OR Ghana OR Ethiopia OR Afghanistan OR Benin OR Rwanda OR Zimbabwe OR Niger OR Somalia OR “South Sudan” OR “Sierra Leone” OR Tanzania OR Togo OR Uganda OR Zambia OR Guinea OR “Guinea-Bissau” OR Haiti OR “Democratic People’s Republic of Korea” OR “North Korea” OR “Liberia” OR Madagascar OR Malawi OR Mali OR Mozambique OR Eritrea OR “Democratic republic of Congo” OR Burundi OR ”Burkina Faso” OR Chad OR Comoros OR “Central African Republic”

Maternity and Infant Care Search Strategy

1. (ultraso* adj3 (pregnan* or gestation or cyesis or antenatal or prenatal or obstetric*)).mp
2. (developing countr* or low* income countr* or low* resource countr* or low* middle income countr* or LMIC or Ghana or Ethiopia or Afghanistan or Benin or Rwanda or Zimbabwe or Niger or Somalia or South Sudan or Sierra Leone or Tanzania or Togo or Uganda or Zambia or Guinea or Guinea-Bissau or Haiti or Democratic People's Republic of Korea or North Korea or Liberia or Madagascar or Malawi or Mali or Mozambique or Eritrea or Democratic republic of Congo or Burundi or Burkina Faso or Chad or Comoros or Central African Republic).mp
3. 1 AND 2

APPENDIX 2: ICD Classifications and Classifications of Maternal Death

ICD-10 Code	Description	Classification of maternal death	Type of maternal death	Cause of maternal death
A01.0	Typhoid fever	Infection	Unrelated	Unrelated
A05.9	Bacterial foodborne intoxication, unspecified	Infection	Unrelated	Unrelated
A09.9	Gastroenteritis and colitis of unspecified origin	Infection	Unrelated	Unrelated
A16.2	Tuberculosis of lung, without mention of bacteriological or histological confirmation	Infection	Unrelated	Unrelated
A41.9	Sepsis, unspecified	Sepsis	Direct	Sepsis
A93.9	A93 is other arthropod-borne viral fevers, not elsewhere classified	Infection	Unrelated	Unrelated
B18.1	Chronic viral hepatitis B without delta-agent	Gastroenterology	Unrelated	Unrelated
B20.1	HIV disease resulting in other bacterial infections	Infection	Unrelated	Unrelated
B20.8	HIV disease resulting in other infectious and parasitic diseases	Infection	Unrelated	Unrelated
B22.0	HIV disease resulting in encephalopathy	Infection	Unrelated	Unrelated
B23.2	HIV disease with haematological and immunological abnormalities not classified elsewhere	Infection	Unrelated	Unrelated
B24	HIV disease resulting in haematological and immunological abnormalities, not elsewhere classified	Infection	Unrelated	Unrelated
B54	Unspecified malaria	Infection	Unrelated	Unrelated
C50.9	Malignant neoplasm of breast of unspecified site	Cancer	Unrelated	Unrelated
D37.6	Neoplasm of uncertain behaviour of liver, gallbladder and bile ducts	Cancer	Unrelated	Unrelated
D48.6	Neoplasm of uncertain or unknown behaviour of breast	Cancer	Unrelated	Unrelated
D57.0	Hb-SS disease with crisis	Haemaological	Indirect	Haematologic

D58.9	Hereditary haemolytic anaemia, unspecified	Haemaological	Unrelated	Unrelated
D64.9	Anaemia, unspecified	Haemaological	Unrelated	Unrelated
D65	Disseminated intravascular coagulation [defibrination syndrome]	DIC	Direct	Other obstetric
G03.9	Meningitis, unspecified	Infection	Unrelated	Unrelated
G40.9	Epilepsy, unspecified	Epilepsy	Unrelated	Unrelated
I10	Essential (primary) hypertension	Hypertension	Direct	Hypertension
I11.0	Hypertensive heart disease with heart failure	Hypertension	Direct	Hypertension
I13.2	Hypertensive heart and chronic kidney disease with heart failure and with stage 5 chronic kidney disease, or end stage renal disease	Hypertension	Direct	Hypertension
I21.9	Acute myocardial infarction, unspecified	Cardiac	Indirect	Cardiac
I26.9	Pulmonary embolism without acute cor pulmonale	Pulmonary embolism	Direct	Pulmonary embolism
I50.0	Congestive heart failure	Cardiac	Indirect	Cardiac
I51.9	Heart disease, unspecified	Cardiac	Indirect	Cardiac
I64	Stroke, not specified as haemorrhage or infarction	Stroke	Indirect	Neurological
J18.9	Pneumonia, unspecified organism	Infection	Unrelated	Unrelated
J90	Pleural effusion, not elsewhere classified	Pulmonary embolism	Unrelated	Unrelated
K65.9	Peritonitis, unspecified	Infection	Unknown	Unknown
K72.1	Chronic hepatic failure	Gastroenterology	Unrelated	Unrelated
K76.9	Liver disease, unspecified	Gastroenterology	Unknown	Unknown
L02.2	Cutaneous abscess, furuncle and carbuncle of trunk	Infection	Unrelated	Unrelated
L03.0	Cellulitis of finger and toe	Infection	Unrelated	Unrelated
L03.1	Cellulitis and acute lymphangitis of other parts of limb	Infection	Unrelated	Unrelated
M06.9	Rheumatoid arthritis, unspecified	Rheumatology	Unrelated	Unrelated
N18.9	Chronic kidney disease, unspecified	Renal	Indirect	Renal

N71.9	Inflammatory disease of uterus, unspecified	Endometritis	Direct	Sepsis
O00.0	Abdominal pregnancy	Obstetric	Direct	Ectopic
O00.9	Ectopic pregnancy, unspecified	Obstetric	Direct	Ectopic
O03.0	Genital tract and pelvic infection following incomplete spontaneous abortion	Obstetric	Direct	Miscarriage/abortion
O03.1	Delayed or excessive haemorrhage following incomplete spontaneous abortion	Obstetric	Direct	Miscarriage/abortion
O03.6	Delayed or excessive haemorrhage following complete or unspecified spontaneous abortion	Obstetric	Direct	Miscarriage/abortion
O04.1	Medical abortion, incomplete, complicated by delayed or excessive haemorrhage	Obstetric	Direct	Miscarriage/abortion
O05	Other abortion	Obstetric	Direct	Miscarriage/abortion
O06	Unspecified abortion	Obstetric	Direct	Miscarriage/abortion
O06.8	Unspecified abortion, complete or unspecified, with other and unspecified complications	Obstetric	Direct	Miscarriage/abortion
O07.5	Other and unspecified failed attempted abortion, complicated by genital tract and pelvic infection	Obstetric	Direct	Miscarriage/abortion
O07.6	Other and unspecified failed attempted abortion, complicated by delayed or excessive haemorrhage	Obstetric	Direct	Miscarriage/abortion
O07.8	Other and unspecified failed attempted abortion, with other and unspecified complications	Obstetric	Direct	Miscarriage/abortion
O10.0	Pre-existing essential hypertension complicating pregnancy, childbirth and the puerperium	Obstetric	Direct	Hypertension
O14	Pre-eclampsia	Obstetric	Direct	Hypertension
O14.1	Severe pre-eclampsia	Obstetric	Direct	Hypertension
O14.2	HELLP syndrome	Obstetric	Direct	Hypertension
O14.9	Pre-eclampsia, unspecified	Obstetric	Direct	Hypertension
O15.0	Eclampsia in pregnancy	Obstetric	Direct	Hypertension

O15.1	Eclampsia in labour	Obstetric	Direct	Hypertension
O15.2	Eclampsia in the puerperium	Obstetric	Direct	Hypertension
O15.9	Eclampsia, unspecified as to time period	Obstetric	Direct	Hypertension
O16	Unspecified maternal hypertension	Obstetric	Direct	Hypertension
O21.2	Vomiting in late pregnancy	Obstetric	Direct	Gastroenterology
O24.4	Diabetes mellitus arising during pregnancy	Obstetric	Direct	Diabetes
O43.2	Morbidly adherent placenta	Obstetric	Direct	Other obstetric
O46.9	Antepartum haemorrhage, unspecified	Obstetric	Direct	APH
O67	Labour and delivery complicated by intrapartum haemorrhage, not elsewhere classified	Obstetric	Direct	Labour APH
O67.0	Intrapartum haemorrhage with coagulation defect	Obstetric	Direct	Labour APH
O67.8	Other intrapartum haemorrhage	Obstetric	Direct	Labour APH
O67.9	Intrapartum haemorrhage, unspecified	Obstetric	Direct	Labour APH
O71.1	Rupture of uterus during labour	Obstetric	Direct	Other obstetric
O72	Third stage and postpartum haemorrhage	Obstetric	Direct	PPH
O72.0	Third-stage haemorrhage	Obstetric	Direct	PPH
O72.1	Other immediate postpartum haemorrhage	Obstetric	Direct	PPH
O72.2	Delayed and secondary postpartum haemorrhage	Obstetric	Direct	PPH
O73.0	Retained placenta without haemorrhage	Obstetric	Direct	PPH
O75.4	Other complications of obstetric surgery and procedures	Obstetric	Direct	Surgery
O75.8	Other specified complications of labour and delivery	Obstetric	Direct	Other obstetric
O75.9	Complication of labour and delivery, unspecified	Obstetric	Direct	Other obstetric
O85	Puerperal sepsis	Obstetric	Direct	Sepsis
O89.2	Central nervous system complications of anaesthesia during the puerperium	Obstetric	Direct	Anaesthetic
O90.3	Cardiomyopathy in the puerperium	Obstetric	Direct	Cardiac
O95	Obstetric death of unspecified cause	Obstetric	Direct	Other obstetric

O98.8	Other maternal infectious and parasitic diseases in pregnancy, childbirth and the puerperium	Obstetric	Direct	Other obstetric
O99.0	Anaemia in pregnancy, childbirth and the puerperium	Obstetric	Direct	Haematologic
O99.6	Diseases of the digestive system in pregnancy, childbirth and the puerperium	Obstetric	Direct	Gastroenterology
O99.8	Other specified diseases and conditions in pregnancy, childbirth and the puerperium	Obstetric	Direct	Other obstetric
Q24.9	Congenital malformation of heart, unspecified	Cardiac	Indirect	Cardiac
R51	Headache	Headache	Unrelated	Neurological
R57.1	Hypovolaemic shock	Hypovolaemic shock	Direct	Shock
R60	Oedema, not elsewhere classified	Unknown	Unrelated	Unrelated
R96.1	Death occurring less than 24 hours from onset of symptoms, not otherwise explained	Unknown	Unknown	Unknown
R99	Other ill-defined and unspecified causes of mortality	Unknown	Unknown	Unknown
T50.9	Poisoning by other and unspecified drugs, medicaments and biological substances	Poison	Unrelated	Physical trauma
T63.0	Snake venom	Animals	Unrelated	Physical trauma
V04.1	Pedestrian injured in collision with heavy transport vehicle or bus, traffic accident	Physical trauma	Unrelated	Physical trauma
V33.6	Occupant of three-wheeled motor vehicle injured in collision with car, pick-up truck or van, passenger injured in traffic accident	Physical trauma	Unrelated	Physical trauma
W06.2	Fall involving cot	Physical trauma	Unrelated	Physical trauma
W18	Other fall on same level	Physical trauma	Unrelated	Physical trauma
W20	Struck by thrown, projected or falling object(s)	Physical trauma	Unrelated	Physical trauma
W34	Discharge from other and unspecified firearms	Physical trauma	Unrelated	Physical trauma
W69	Drowning and submersion while in natural water	Drowning	Unrelated	Physical trauma

X20	Contact with venomous snakes and lizards	Animals	Unrelated	Physical trauma
X49	Accidental poisoning by and exposure to other and unspecified chemicals and noxious substances	Poison	Unrelated	Physical trauma
X69	Intentional self-poisoning by and exposure to other and unspecified chemicals and noxious substances	Suicide	Direct	Suicide
Y19	Poisoning by and exposure to other and unspecified chemicals and noxious substances, undetermined intent	Poison	Unknown	Physical trauma
Y60.0	Unintentional cut, puncture, perforation or haemorrhage during surgical operation	Surgery	Unknown	Surgery
Y61.0	Foreign object accidentally left in body during surgical operation	Surgery	Unknown	Surgery

APPENDIX 3: Ghana Population Distribution by Region (2010 Census)

Below is a structured table based on official 2010 census data:

Region	Population (2010 Census)	Share of National Population (%)
Ashanti	4,780,380	19.4%
Greater Accra	4,010,054	16.3%
Eastern	2,633,154	10.7%
Northern	2,479,461	10.1%
Western	2,376,021	9.6%
Brong-Ahafo	2,310,983	9.4%
Volta	2,118,252	8.6%
Central	2,201,863	8.9%
Upper East	1,046,545	4.2%
Upper West	702,110	2.8%
Total (Ghana)	**24,658,823**	**100%**

REFEREFNCE

Ghana Statistical Service. (2012). *2010 Population & Housing Census: Summary Report of Final Results*. Accra, Ghana: Ghana Statistical Service

Census2010_Summary_report_of_final_results.pdf

APPENDIX 4: Ghana Local Guidelines for Management of Postpartum Haemorrhage

POSTPARTUM HAEMORRHAGE (PPH)
Definition: Blood loss ≥500 mL after vaginal birth (≥1000 mL after CS) or any blood loss causing shock.

STEP 1: IMMEDIATE ACTIONS (0–10 min)

- CALL FOR HELP (OB, anaesthetist, senior midwife, blood bank).
- Airway + Oxygen (6–10 L/min).
- Two large-bore IV lines.
- Rapid IV fluids: 500–1000 mL crystalloid bolus.
- Monitor vitals (pulse, BP, SpO_2).
- Crossmatch blood.
- Empty bladder (catheter).
- Uterine massage.

STEP 2: UTEROTONICS (give immediately)

- Oxytocin 10 IU IM (or 10 IU slow IV bolus if IV access).
  → Continue with 20–40 IU in 500 mL fluid IV infusion.
- If no response or oxytocin unavailable:
  - Ergometrine 0.5 mg IM (avoid if HTN/preeclampsia).
  - Misoprostol 800 µg sublingual.
  - Carbetocin (if available, single IV dose).

STEP 3: ANTIFIBRINOLYTIC

- Tranexamic Acid (TXA): 1 g IV over 10 min (within 3 hrs of birth).
- May repeat 1 g IV if bleeding persists after 30 min or recurs

STEP 4: RESUSCITATION

- Continue IV fluids.
- Blood transfusion: initiate early if shock/ongoing bleeding.
- Correct coagulopathy with FFP/platelets/cryoprecipitate as available.

STEP 5: IDENTIFY CAUSE (4 T's)

- Tone (uterine atony) → uterotonics, massage, balloon tamponade.
- Tissue (retained placenta/membranes) → manual removal.
- Trauma (tears) → inspect & repair.
- Thrombin (coagulopathy) → correct with blood products.

STEP 6: IF BLEEDING PERSISTS

- Balloon tamponade (Bakri or condom-catheter).
- Surgical options: B-Lynch sutures, uterine/artery ligation.
- Hysterectomy if uncontrolled.

REFERRAL / ESCALATION

- Bleeding persists after uterotonics + balloon tamponade.
- Blood products not available.
- Surgical capacity not available.

REMEMBER

- Document: blood loss, drugs (dose/time), fluids, transfusions, vitals.
- Report all PPH cases per Maternal Death Surveillance & Response (MDSR).

End of Poster

Ghana Health Service Guidelines for PPH management.