10-14-2020 2:00 PM

Maternal and Neonatal Mortality Associated With Caesarean Section

Areej A. Hezam, *The University of Western Ontario*

Supervisor: Martin, Janet, *The University of Western Ontario*

A thesis submitted in partial fulfillment of the requirements for the Master of Science degree in Epidemiology and Biostatistics

Abstract

Universal access to safe caesarean section is vital. The objective of this thesis was to quantify the risks of maternal and neonatal mortality, and causes of caesarean-related deaths.

Our initial systematic overview of pre-existing meta-analyses found no interventions that significantly reduced the risk of all-cause maternal or neonatal mortality. However, many interventions have been understudied.

Our systematic review and meta-analysis of 196 studies identified that the risk of perioperative maternal mortality has decreased over time and according to country development index, and the risk of perioperative neonatal mortality has fluctuated. We also found that the proportion of reported causes of caesarean-related deaths due to pregnancy-related infection and non-obstetric complications have decreased while obstetric haemorrhage and hypertensive disorders have increased over the past 70 years. Initiatives to reduce perioperative neonatal mortality and caesarean-related deaths due to obstetric haemorrhage and hypertensive disorders should be a global priority.

KEYWORDS: Caesarean, maternal mortality, neonatal mortality, cause of death, systematic review, meta-analysis, women's health.

Summary for Lay Audience

Throughout the world, 18.5 million caesarean sections are performed every year. Compared to other forms of delivery, caesarean sections have higher risks of complications, including death of the mother and newborn. The rates of caesarean sections have been increasing globally and are more frequent in high resource countries. Additionally, maternal mortality has been found to be higher in low resource settings. This study aims to provide a better understanding of maternal and neonatal death during or after caesarean section over time and by country development status, through comprehensive systematic searches of prior studies and analyses. Our first study summarized the findings from 20 prior systematic research studies and found that none of the treatments or strategies assessed in the pooled analyses resulted in a lower risk in maternal or neonatal mortality during or after caesarean section. The subsequent study, which pooled the findings from 196 previous studies, determined that the risk of mothers dying during or following caesarean section reduced over time, whereas the risk of neonatal death after caesarean section showed no change over time. Furthermore, there was a relationship between the risk of mothers dying during or following caesarean section and country development status. In our final study, we found that the proportion of maternal deaths during or after caesarean section due to obstetric haemorrhage and hypertensive disorders increased over the past 70 years, and maternal deaths due to pregnancy-related infection and non-obstetric complications decreased over time. Additionally, deaths attributed to obstetric haemorrhage were higher in countries with low development status. By identifying areas that need improvement, adverse maternal and neonatal outcomes after caesarean section may be enhanced.

Acknowledgments

This thesis would not have been possible without the support and encouragement from the people that continually pushed me to give it my all, my parents. They were there for me every step of the journey throughout these 2 years, they framed me into the person that I am today and always taught me to reach for my goals and for that I am forever grateful. Also, I would like to thank all my siblings for their love and support.

I would like to express my sincere gratitude to my supervisor Dr. Janet Martin for providing me with the opportunity to perform this research and make an impact globally. Your guidance, knowledge, motivation and continued support throughout the design, analysis and writing process has turned our research vision into a reality.

I would also like to thank Dr. Kelly Anderson and Dr. Davy Cheng for providing insight in areas of my thesis where gaps were present. Additionally, I would like to thank Jessica Moodie for her help in formulating database search strategies for the systematic reviews and for continually arranging meetings between myself and Dr. Martin.

Lastly, to all the amazing friends that I have made throughout this journey thank you for the light-hearted chats, the laughs, and for always keeping me motivated.

Table of Contents

List of Tables

List of Figures

List of Appendices

Abbreviations

AMSTAR 2: A Measurement Tool to Assess Systematic Reviews 2

CI: Confidence Interval

CS: Cesarean Section

EGM: Evidence Gap Map

ERAS: Enhanced Recovery After Surgery Society

H&MIC: High-and Middle-Income countries

HDI: Human Development Index

HELLP: Hemolysis, Elevated Liver Enzymes, and a Low Platelet Count

HIC: High-Income Countries

ICD-MM: International Classification of Diseases-Maternal Mortality

IV: Intravenous

LIC: Low-Income Countries

LMHIC: Low-, Middle-and High-Income Countries

LMIC/ L&MIC: Low- and Middle-Income Countries

LMWH: Low-Molecular-Weight Heparin

MDG: Millennium Development Goals

MeSH: Medical Subject Heading

MIC: Middle-Income Countries

MMR: Maternal Mortality Ratio

NICE: The National Institute for Health and Care Excellence

NMR: Neonatal Mortality Rate

OR: Odds Ratio

p: p-value

PACU: Post-Anesthesia Care Unit

POMMR: Perioperative Maternal Mortality Ratio

POMR: Perioperative Mortality Rate

PONMR: Perioperative Neonatal Mortality Ratio

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

PROSPERO: Prospective Register of Systematic Reviews

RCTs: Randomized Controlled Trials

RoB: Risk of Bias

RR: Relative Risk

SDG: Sustainable Development Goals

SSI: Surgical Site Infection

UN: United Nations

WHO: World Health Organization

Chapter 1 - Introduction

1 WHAT IS CAESAREAN SECTION, CLINICAL NEED AND RISKS

A caesarean section is an obstetric surgical procedure that is used in the delivery of a fetus through an incision of the abdomen and uterus of the mother.[1] During the procedure, an incision is made at the lower segment of the mother's abdomen through the skin, through the abdominal wall, and into the uterus; the incision may be conducted by means of a vertical or a transverse opening.[47] A transverse incision extends across the pubic line while a vertical incision spans from the navel to the pubic hairline.[47] The most common form of incision conducted is the transverse uterine incision as it results in a reduction of blood loss and faster healing.[47]Although the type of incision varies depending on the conditions of the mother and fetus, transverse uterine incisions increase the chance for vaginal birth after caesarean section.[47] Caesarean sections may be classified as either elective or emergency; elective cases are usually undertaken in women with low risk pregnancies often upon maternal request without a specific medical or obstetrical indication (i.e. scheduled). [4,18] Other elective cases include those with previous history of caesarean delivery along with women that decide to undergo the obstetric procedure >24hrs before delivery due to nonurgent conditions of the mother and fetus.[4,18] Emergency cases are undertaken in women with high risk pregnancies, it is not scheduled or pre-planned; the decision to undergo the procedure is made within 24 hours of the delivery when complications with the mother or neonate occur in which a vaginal delivery is likely to be unsafe.[4,18]

In most cases, this form of intervention is performed to prevent complications that arise due to childbirth through vaginal delivery[2,3]. Caesarean sections are the most commonly performed obstetric procedure. Indications for this form of delivery include but are not restricted to previous caesarean section, dystocia (non-progressive labour), abnormalities in fetal position or size, breech birth, and non-reassuring fetal heart rate.[3] The likelihood of undergoing a caesarean section is affected by various aspects which include maternal, neonatal and obstetric factors.[3] Maternal factors are composed of pre-

existing health conditions, obesity, hypertension, age, previous caesarean section, pre-eclampsia, eclampsia, maternal preference, and health conditions that arise throughout the pregnancy.[3] Infant factors are composed of multiple births, malposition, suspected macrosomia along with antenatal issues which may include intrauterine growth restriction and fetal anomalies.[3] Finally, obstetric factors are characterized as conditions that arise due to the current intrauterine pregnancy which includes placental abruption, placenta accreta, placenta previa, prolapsed cord, and non-reassuring fetal heart tracing.[3] According to the recommendations of national clinical societies as well as global societies of Obstetricians and Gynaecologists when maternal or fetal indications for caesarean section are absent a vaginal delivery is safe and recommended.[4] Caesarean deliveries should only be conducted when there is an excessive increase in risk to the mother or fetus if vaginal delivery is performed that is worthy of the added risk of the surgical procedure itself.[4] The National Institute for Health and Care Excellence (NICE) indicated in their evidence update in 2013 "that if a woman requests a CS [caesarean section] when there is no other indication; discuss the overall risks and benefits of CS compared with vaginal birth. If necessary, a discussion should be held with other members of the obstetric team (including the obstetrician, mid-wife and anaesthetist) if necessary, to explore the reasons for the request, and ensure the woman has accurate information. If after discussion and offer of support (including perinatal mental health support for women with anxiety about childbirth), a vaginal birth is still not an acceptable option, offer a planned CS.".[5]

For low risk pregnancies the benefits associated with caesarean delivery compared to vaginal delivery is not clear.[3] Although the procedure in itself may be lifesaving under specific conditions for the mother and the fetus, there is a scarcity of evidence to indicate the benefits of caesarean delivery in women who do not require it.[2] Caesarean delivery, like any other surgical procedure is associated with risks that may include short term and long term effects. The long-term risks may take effect months or years after the index delivery, and may result in consequences to the health of the mother, baby and subsequent pregnancies.[2] Short-term maternal risks include haemorrhage, organ injury, infections, blood transfusion along with anesthesia related complications.[6,7] Caesarean

delivery increases the risk of complications in future pregnancies which includes uterine rupture, issues with placental implementation and hysterectomy.[8,9]

1.1 RATES OF CESAREAN SECTION

The rates of caesarean section vary worldwide depending on country income status (low, middle, high-income setting). [2] Overall, the rates of caesarean section have been increasing, leading to public health concerns, and resulting in considerable debate due to the potential adverse risks of surgery pre-dominantly low-risk mothers and neonates where caesarean section is chosen out of preference rather than of necessity.[2] The average caesarean section rate globally has increased three-fold from 6.7% to 19.1% during the timespan of 1990 to 2014; the average rate increase per year is 4.4%. Within this time, the average rates of caesarean section have increased from 22.8% to 42.2% in Latin American and the Caribbean, 18.5% to 32.6% in Oceania, 22.3% to 32.3% in North America, 11.2% to 25% in Europe, 4.4% to 19.5% in Asia, and 2.9% to 7.4% in Africa.[10] The world health organization (WHO) released a consensus statement in 1985 that indicated that population rates for caesarean section above 10% to 15% are unlikely to be associated with any additional health benefits for the mother or fetus.[11] A systematic review of population-based studies published by WHO in 2015 investigated at the population-level the ideal rate of caesarean sections.[12] From this review it was found that although caesarean sections can be a life-saving procedure and should be performed when indications and complications are present, at the population level caesarean rates that are greater than 10% do not reduce maternal and neonatal mortality. A complementary global longitudinal ecological study reaffirmed the results of the above systematic review.[13] The increasing rate in caesarean section is thought to be multifactorial with contributions from various factors such as clinical factors as well as technological, professional, legal, ethical, and cultural factors.[14]

1.2 MATERNAL MORTALITY

Maternal mortality is defined by WHO as “the death of a woman whilst pregnant or within 42 days of delivery or termination of pregnancy, from any cause related to, or

aggravated by pregnancy or its management, but excluding deaths from incidental or accidental causes".[15] The most common measure for maternal mortality is the maternal mortality ratio (MMR), it is defined as "the number of maternal deaths during a given time period per 100,000 live births during the same time period".[19] MMR and neonatal mortality rate (NMR) along with other health indices are used by the United Nations and the World Health Organization as proxy measures for overall health status. We propose that assessments of the causes of morbidity and death along with investigations of the impact of health interventions may be conducted with health indices. The safety and quality of surgery and anesthesia is assessed through a health indication known as the perioperative mortality rate (POMR).[44] POMR is defined as the death rate from all causes prior to discharge in patients that have underwent a procedure within an operating theatre, over the total number of procedures.[33]

The concept of POMR in the setting of caesarean sections has been understudied, and consensus on unique parameters for defining POMR are needed. For the purposes of this thesis, we will combine the concept of POMR with maternal and neonatal mortality to formulate measures known as the perioperative maternal mortality ratio (POMMR) and the perioperative neonatal mortality ratio (PONMR). POMMR was defined as the death of a woman from any cause, occurring any time between the start of the procedure or the start of anesthesia until hospital discharge or 42 days of follow-up after caesarean section. If anesthesia is not provided, then the initial point will change to the point of first incision until hospital discharge or 42 days post-caesarean section. PONMR was defined as death of a neonate during the first 28 days of life per births by obstetric surgery.

$$\text{POMMR} = \frac{\text{Number of maternal deaths}}{\text{Total number of caesarean sections}} \quad (1)$$

$$\text{PONMR} = \frac{\text{Number of neonatal deaths}}{\text{Total number of caesarean sections}} \quad (2)$$

These measures will be used to illustrate both the safety and access of the procedure, since access can be conveyed indirectly via the number of procedures performed, which is the denominator of the POMMR and PONMR metrics.[44] Higher rates of maternal and neonatal mortality and fewer procedures are correlated with delayed presentations which occur due to an absence in access to safe surgical procedures and anesthesia.[44] When measuring POMMR the numerator is the number of deaths from obstetric surgery and the denominator is the number of patients undergoing obstetric surgery, as seen in (1).[44] Additionally, for PONMR the numerator is the number of deaths of neonates born through obstetric surgery within the first 28 days of life and the denominator is the number of women undergoing obstetric surgery, as seen in (2). During a patient's hospital admission, they may have more than one obstetric surgical procedure conducted (e.g. having a caesarean section and hysterectomy). This may, result in a slight overestimation in the total number of obstetric surgical procedures as compared to the total number of patients, albeit this overestimation is likely inconsequential at a population-level.[44] However, the numerator which represents the number of deaths will only be counted once even if the patient has multiple obstetric procedures.[44]

1.2.1 Global efforts to improve maternal mortality

The improvement in maternal health, specifically the reduction in maternal mortality is a priority in global health initiatives. The UN Millennium Development Goals (MDG) framework highlighted the urgency of this issue in MDG5 which emphasized the need to reduce the maternal mortality ratio by three quarters, between 1990 and 2015.[20] When examining the targets of the MDG5 and the data from 1990 until 2015, it is clear that progress has been made; however, the target was not reached in many countries. Globally, the maternal mortality ratio decreased by 44%, going from a value of 385 to 216 maternal deaths per 100,000 live births from 1990 to 2015.[21] While encouraging, the 44% reduction fell short of the named MDG5 target of reduction in MMR by 75% by 2015.[21] Furthermore, inequalities based on geographic settings were still present. For example, the region of sub-Saharan Africa suffers the highest MMR of 546 maternal deaths per 100,000 live births, whereas in high resource settings, average MMR is a mere

12 maternal deaths per 100,000 live births.[21] After 2015, the MDG have been superseded by the sustainable development goals (SDG). The health-related SDG (SDG3) includes metrics for the reduction of MMR globally to less than 70 per 100,000 live births by 2030, and that no country will have a maternal mortality more than double the global average.[21]

In 2017, an estimated 295,000 women died during or after pregnancy and childbirth. Of, those, 810 women died due to preventable causes of pregnancy and childbirth.[22] Low- and middle-income countries (LMIC) were responsible for a larger amount of these maternal deaths, with 94% of the above maternal deaths occurring within LMIC settings, with large discrepancies within and between regions and countries.[22] Two regions of Sub-Saharan Africa and South Asia together accounted for 86% of the estimated global maternal deaths within 2017.[22] Independently, the region of Sub-Saharan Africa was responsible for nearly two thirds of maternal mortalities, whereas South Asia was responsible for an estimated one fifth.[22] Throughout the decades, MMR has decreased. From 2000 to 2017, there was a decrease in the maternal mortality ratio by 38% globally.[22] The greatest overall reduction in the maternal mortality ratio (MMR) was seen in Southern Asia as it went from 384 down to 157 (60% decline).[22] Sub-Saharan Africa has reduced its MMR by 40% within this time span.[22] The MMR of other regions such as Central Asia, Eastern Asia, Europe and Northern Africa have reduced by half from 2000 until 2017.[22] A decline of the MMR in all low resource regions has decreased almost by 50%.[22]

From these values it may be seen that conscious efforts have been implemented in order to reduce maternal mortality globally. Throughout various areas of the world, inequalities are still present in terms of the access to health services which causes variations in MMR. Overall, in low-income countries the MMR in 2017 was 462 per 100,000 live births whereas in high-income countries it was only 11 per 100,000 live births.[22] 15 countries that were identified as high alert or very high alert of being a fragile state based on the Fragile States Index in 2017 included South Sudan, Somalia, Central African Republic, Yemen, Syria, Sudan, the Democratic Republic of the Congo, Chad,

Afghanistan, Iraq, Haiti, Guinea, Zimbabwe, Nigeria and Ethiopia.[22] The MMR from these 15 countries in 2017 varied from 31 (Syria) to 1150 (South Sudan).[22] The global disproportion in maternal mortality is present across countries, within continents, between different income settings along with urban and rural regions within individual countries. These were evident at the end of the MDG and continue to occur while the SDGs are in effect.

Higher rates of maternal mortality in LMIC may be largely driven by inequalities in terms of access to healthcare provisions and healthcare services.[45] The majority of maternal deaths may be prevented with the use of good quality obstetric care. However, in regions where women do not have access to this type of care, a higher amount of maternal deaths are present.[45] For example, in high-resource countries almost all births are attended by skilled birth attendants and almost all the women receive the WHO recommended four antenatal visits resulting in lower rates of maternal mortality.[46] Comparatively, in low-resource countries skilled birth attendance is received by less than half of women and only one third receive the WHO recommended four antenatal visits causing these countries to have higher rates of maternal mortality.[46]

1.2.2 Maternal mortality during or following caesarean Section

The risk of overall maternal mortality as well as death due to complications associated with delivery are increased when a caesarean section is conducted as compared to a vaginal birth independent of geographical area and clinical characteristics.[16] Maternal mortality during or following caesarean section in low- and middle-income countries is 100 times higher than in high-income countries.[17]Access to caesarean section worldwide is a necessity when considering the improvement in maternal outcomes, and is a key component of the comprehensive emergency obstetric care package by WHO.[18] Globally, it is paradoxical that caesarean sections are generally overused in high-resource settings or underused in low-resource settings, and both extremes result in adverse outcomes for the mother.[17] Maternal mortality during or following caesarean section occurs in LMICs due to the lack of trained personnel and resources to conduct the procedure.[17]Although the outcomes of caesarean sections are

safer now than it was previously due to advances in technology and research, women throughout the world are still dying during or after the obstetric procedure. Clinicians as well as pregnant women need to weight the risks and benefits when deciding on the mode of delivery. Various studies that investigated the association between caesarean section rate and maternal mortality have yielded inconsistent results that vary from different countries.[23] Some studies have concluded that there is no association, while most studies have found that there is a positive association present between maternal mortality and caesarean section, although, to different degrees. Studies report caesarean section compared with vaginal birth was associated with maternal mortality ratio 10 times higher in the USA, 3.6 times higher in France, 5.5 times higher in Peru, and 3.01-fold higher in India.[24,25,26,16]

Studies that were conducted in regions of the world that have high rates of maternal mortality and caesarean section rates that are lower than 15% (e.g. Sub-Saharan Africa) suggest a protective effect of the procedure as it was associated with lower maternal mortality ratios.[28] However, in countries where the caesarean section rates are greater than 30% (e.g. Latin America and USA), the rates of caesarean section are associated with higher maternal mortality ratios.[27,28] Nevertheless, given the nature of epidemiologic and descriptive studies, these results may be also confounded by other variables that are present within the relationship between maternal mortality and the mode of delivery.[28]

1.3 NEONATAL MORTALITY

The neonatal period which encompasses the timeframe between birth and 28 days of life is the most vulnerable period in the life of an infant.[48] Neonatal mortality is defined by WHO as “deaths among live births during the first 28 completed days of life”.[48] It can be further broken down into early neonatal death (deaths that occur within 0-7 days of birth) and late neonatal death (deaths that occur within 7-28 days of birth).[47] 2.6 million babies died throughout the neonatal period; this encompasses 46% of all under-five deaths in 2016.[49] These values translate to the death of approximately 7000 newborns everyday.[49] A larger number of neonatal deaths occur in the first day or within the first week of life, 36% of neonates die in the first 24hrs of life, 37% die in between the first

and seventh day of life and 27% die between 7-27 days.[47] Globally, neonatal mortality rates have declined from 31.9 deaths per 1000 live births in 1990 to 18.4 deaths per 1000 live births in 2013.[47] The 40% rate of decline falls behind the rate of change in mortality in children aged 1–59 months as there is a 56% decline within the same time period.[47] If the current trends continue, more than 60 countries will not reach the SDG target of reducing neonatal mortality under 12 deaths per 1000 live births by 2030, and nearly half of them will be unable to reach this goal by 2050.[49] In 2016, these countries were responsible for 80% of the burden of neonatal deaths.[49]

1.3.1 Relationship between neonatal mortality and maternal mortality

Often, the death of a mother may have a spillover effect on the health of the child through obstetric complications and feeding behaviour of infants. For this reason, it is important to look beyond MMRs to fully characterize the harm that results from the loss of a mother. There are various mechanisms through which a maternal death has an impact on the outcomes of infants and children. An increase in the risk of neonatal mortality is seen when the main direct causes of maternal mortality are present, including, obstetric complications such as sepsis, hemorrhage, eclampsia and obstructed labour.[50] In cases where the mother dies but the infant survives, the lack of nutritional support commonly provided through breastfeeding puts that baby at risk of malnutrition. This can be detrimental to the infant as it may increase the risk of disease and death due to infection.[50] A cohort study conducted in Benin on women who experienced critical complications during childbirth (including near-miss cases), found that even in the absence of maternal mortality there is still an elevated risk of neonatal mortality.[51] Research in Kenya found an increased rate in neonatal mortality in babies of mothers who died after childbirth.[52] From this it may be seen that neonatal mortality is one of many potential adverse outcomes that are associated with maternal mortality.

1.3.2 Neonatal mortality and caesarean section

Studies that examined the association between neonatal mortality and caesarean sections have yielded inconsistent results. Two ecological studies that used country-level

data identified that caesarean section was associated with lower rates of neonatal mortality. Whereas an additional two ecological studies found there was no association between caesarean section and neonatal mortality when the rates of caesarean section were greater than 10%.[53-56] This inconsistency is also present in individual-level data. A study conducted in eight Latin American countries found that the odds of neonatal mortality were 1.66 and 1.99 times higher when mothers underwent intrapartum and elective caesarean with cephalic presentation.[57] However, another study examining nine countries in Asia identified an improvement in neonatal outcomes after breech presentation for both pre-labour and intrapartum caesarean sections.[58] A study that incorporated both country-level and individual-level data discovered that there was an increase in the risk of neonatal mortality following caesarean section as compared to vaginal delivery in low (<5%) and medium (5%-15%) rates of caesarean section.[59] From these data it may be deduced that the impact of caesarean section on neonatal mortality is unclear when the outcome is not investigated alongside maternal mortality. The indications for caesarean section and contextual factors such as health inequalities in terms of unequal access and constraints in the infrastructure of healthcare facilities and health workforce may play a role in the association between neonatal mortality and caesarean section.

1.4 CHARATERISTICS OF MATERNAL MORTALITY DURING OR FOLLOWING CAESAREAN SECTION

1.4.1 Causes of death during or following caesarean section

A vast number of maternal deaths, including those during or following caesarean section, are likely preventable. In order to provide a better understanding and to reduce maternal mortality related to the procedure, insight into the causes of death during or following caesarean section is required to allow for effective policy and health program decisions. Causes of death can be broken down into direct and indirect causes. Direct obstetric deaths include those that occur due to obstetric complications in the state of pregnancy (during pregnancy, childbirth and puerperium up to 42 days); examples of these are deaths due to eclampsia and obstetric haemorrhage.[29] Indirect obstetric deaths

are comprised of maternal deaths that occur due to previously existing diseases or diseases that are not due to direct obstetric causes as it developed during pregnancy and was heightened as a result of the physiological effects of pregnancy (i.e. cardiac conditions heightened by pregnancy).[29] As noted above, the maternal mortality rates have been seen to vary through time and geographically. This pattern is also present in the causes of maternal mortality during or following caesarean section. As there is no current evidence that examines the trends and distribution in cause of death during or following caesarean section this thesis will further investigate this topic. WHO conducted a systematic review to investigate the global, regional, and sub-regional estimates of the causes of maternal death; they published one review that examined the causes and trends from 1998–2002 and an updated review from 2003–09.[30,31] From this study it was suggested that the point estimates of the various causes of deaths were substantially different across the numerous regions. Haemorrhage was the leading cause of death in northern Africa, accounting for 36·9% of all maternal deaths within that region.[31] In Latin America and the Caribbean hypertension disorders was a key cause of maternal mortality, accounting for 22·1% within that region.[31] Sepsis-related maternal deaths were mainly seen in low resource settings, with the largest proportion of sepsis-related deaths (13·7%) reported in Southern Asia.[31] Embolism was reported as the cause of death in 14·8% of maternal deaths in Oceania.[31] These causes of death for overall maternal mortality overlap with the causes of maternal mortality during or following caesarean section. The common causes of death during or following caesarean section include haemorrhage, hypertensive disorders, complications of anesthesia, and embolism.[24,32] These varying causes of death globally may be attributed to differences in the experience and attitude of the attending medical personnel along with variations in the efficiency of administration.

1.4.2 Contributors of death during or following caesarean section

The varying rates of maternal mortality along with the distribution of the causes of maternal death throughout various regions of the world often provide insight into the quality of healthcare services available, along with the access to healthcare

provisions.[34,35] The clinical causes of overall maternal mortality, together with common causes of maternal mortality during or following caesarean section discussed above did not necessarily identify or account for, the underlying causes that lead to maternal mortality. These key factors include gender inequality, lack of access to knowledge and education, or lack of autonomy in decision making.[36,37] Another significant factor that was found to be closely linked with maternal mortality was poverty.[37,38]

The three delays model examines the societal causes of maternal mortality. It aims to examine the three groups of factors that impede or prevent women from accessing maternal health care.[35] The three steps are linked to one another, where a delay in one stage often results in delays in subsequent stages (Figure 1.1). The three delays described by the model include; delay 1: a delay in the decision to seek care (e.g. in cases of emergency caesarean section), this delay is primarily due to low social status of women, financial issues, acceptance of death, bad experience with healthcare and lack of awareness to seek care.[35] Delay 2: a delay in reaching care (e.g. appropriate facilities to perform caesarean section), this may be due to affordability of transportation to the facility, distance to health centres and hospitals, poverty, and poor roads and infrastructure.[35] Delay 3: delay in receiving adequate health care (e.g. receiving a required caesarean section), this delay is mainly due to inadequate referral systems, facilities that are poorly managed, maintained and staffed, lack of medical supplies and inadequately trained medical staff.[35] The following model emphasizes the need for consideration of a wide range of issues that are associated with caesarean section that not only include clinical factors but also societal factors (Figure 1.1). This will in turn provide guidance to what issues to address in terms of maternal mortality and how to approach solutions to these issues.

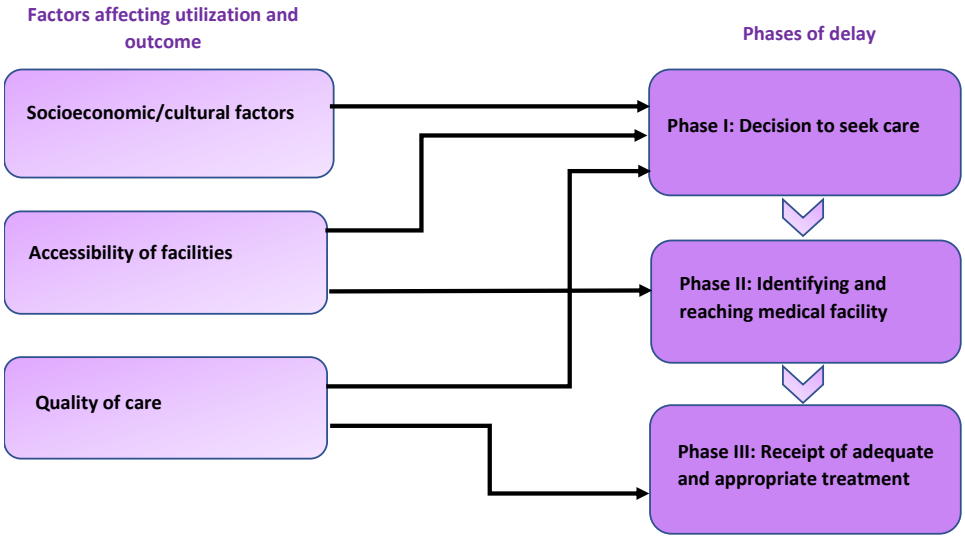


Figure 1.1 The three delays model

1.5 PERIOPERATIVE INTERVENTIONS FOR CAESAREAN SECTION

In low-resource countries, it was estimated that half of the adverse events in surgical care that occurred were preventable.[39] These avoidable mistakes may occur not only during the procedure, but also before and after the surgical operation.[39] The perioperative period is composed of pre-, intra-, and postoperative patient care.[39] Within the preoperative period the patient is prepared for surgery, the intraoperative period is composed of anesthesia management, conduct of the procedure, and monitoring of the patient.[39] Finally, the postoperative phase begins when the patient is admitted to the recovery room where ideally there is constant monitoring of vital signs and continues until discharge (though this may be limited in low-resource settings).[39] A study that was conducted in the Netherlands found that a large number of critical incidents do not occur intraoperatively, but rather pre and postoperatively.[39] From the study it was indicated that quality of care in the pre- and postoperative periods were neglected and that patient safety in the intraoperative phase alone is insufficient.[39] Traditionally, the operation was the main concern of surgery[39]. In order to improve patient safety and other patient outcomes all three phases of perioperative care are equally significant.[39] This applies to both high and low resource settings.[39]

In terms of caesarean section, the interventions that are conducted throughout the perioperative phase are key in ensuring the safety of the mother as well as the neonate. Preoperatively interventions may include, but are not limited to preanesthetic medication, fasting, carbohydrate supplementation, skin wash/ vaginal cleansing, anti-fibrinolytic drugs, and antibiotic prophylaxis [40]. Intraoperative interventions may include anesthetic management, uterotonic drugs, cord clamping, operative techniques, maternal position, surgical personnel and wound drainage.[40] Within the postoperative phase interventions may include nutritional care/ feeding, nausea and vomiting management, mobilization, anti-fibrinolytic drugs, urinary drainage management, and analgesia[40]. Interventions that are conducted throughout all three phases of the obstetric procedure of caesarean section include hypothermia management, glucose management, fluid and hemodynamic management, anti-fibrinolytic drugs, surgical safety checklist and sometimes thromboembolism prevention.[40] All these interventions play a part in ensuring the safety of the mother throughout the procedure of caesarean section. They are often required in emergencies to treat complications of pregnancy and delivery such as hemorrhage, hypertensive disorder, wound infections as well as other complications. When evidence-based interventions are not provided in a timely manner, the risk of adverse outcomes increases.[41] For health care solutions used to prevent or manage complications of caesarean section that are well-proven by high-quality evidence, any failure to provide them may lead to preventable maternal deaths.

The effect of interventions has been evaluated most often in high resource countries. However, it is ironic that the burden of unmet need is highest in the lower-resource settings, where the least amount of research has been conducted. Until recently, the lack of reliable data, incomplete reporting of maternal deaths, and issues with assessment of the causality of each individual maternal death has limited capacity to conduct research in most low and middle-income settings.[42,43]

While some interventions have been studied across the spectrum of low and high-resource settings, constraints such as economic, geographic and social factors that are most relevant to low resource settings have been neglected when examining

interventions. This in turn leads to results that may be less relevant or less reliable in these contexts. Interventions that are contextually-relevant are likely to be more effective in terms of estimates of effect, success of implementation, and generalizability.

1.6 APPROACHING MATERNAL MORTALITY DURING OR FOLLOWING CAESAREAN SECTION

Obtaining and measuring maternal and neonatal mortality during or following caesarean section, along with assessing the impact of caesarean-related interventions on maternal mortality within certain settings is challenging. When attempting to investigate the trends in maternal and neonatal mortality associated with caesarean section various sources of evidence may lack adequate information. The implementation and study design of interventions and their effect on reducing maternal mortality may lack sufficient detail as they are poorly documented. Given the difficulties in assessing maternal and neonatal mortality along with the effects of interventions, the most effective approach is to examine data from various sources and various settings. In order to allow for evidence-based decision making and guide clinical practice, the highest grade of evidence may be achieved through well designed and executed systematic reviews and meta-analyses.

1.7 TOOLS FOR APPROACHING MATERNAL MORTALITY DURING OR FOLLOWING CAESAREAN SECTION

After identifying the gaps and burden in the evidence base for measuring maternal mortality during or following caesarean section, consideration should be given to pre-existing tools for the identification of causes of death and the impact of maternal mortality during or following caesarean section. In order for new findings to be implemented into practice an examination through knowledge dissemination is required. Several tools exist that investigate the impact of maternal mortality during or following caesarean section through evidence-based recommendations. These tools include clinical guidelines and knowledge translation. Clinical guidelines can be used to optimize patient care, these recommendations are informed by evidence synthesis along with the

assessment of benefits and harms of alternative care options. Evidence-based clinical practice guidelines that incorporate the best available evidence and conduct synthesis through rigorous and unbiased methodology allow for an impactful influence on the reduction in the maternal mortality during or following caesarean as well as the reduction in the rate of caesarean sections.

A recognizable gap is present between knowledge produced though research and application of the evidence to the population; this gap can be addressed through knowledge transfer. The gaps in knowledge-to-action results in consequences such as substandard use of treatments that are effective, poor health outcomes and health inequalities that cause negative effects on quality of life and the use and distribution of resources. Strategies in knowledge translation may be used to formulate methods that diminish the gap present between evidence and application into clinical practice. Since the highest proportion of maternal mortality and morbidity occurs during childbirth; in the case of caesarean section during the obstetric procedure and the postoperative period, strategies in knowledge translation need to be formulated in order to resolve these issues. Although some complications that occur during pregnancy and childbirth may not be preventable, a decrease in negative effects in maternal outcomes and a lower proportion of complications may be achieved through monitoring and early intervention throughout the antenatal and postpartum stages. Strategies implemented for the reduction in the number of maternal mortalities during or following caesarean section should not only target institutions and health professionals but also patients and the community.

1.8 CONCLUSIONS, IMPACT, AND THESIS OUTLINE

There remains a paucity of research concerning the trends in maternal and neonatal mortality during or following caesarean section along with the causes of caesarean-related deaths. Caesarean section is a surgical procedure that may be a necessity for women undergoing childbirth in emergency cases when risks in spontaneous childbirth or the indications of caesarean section arise and clinicians must take action to ensure the safety of the mother and the neonate. Unfortunately, caesarean section imposes various dangers to the overall health of the mother throughout the actions

of multiple factors that occur throughout the procedure, and may result in maternal mortality. The risk in maternal mortality during or following caesarean section may be improved with an understanding of the magnitude of risk and causes of caesarean-related deaths throughout time and in high and low-resource countries. These data will provide a measure that represents the global safety efforts for caesarean section. Additionally, various regions of the world will be able to identify the distribution and trends of causes of maternal mortality during or following caesarean section and take action in order to reduce the risk associated with the outcome. This may be conducted through implementation of guidelines, policies and interventions that target the physiology of the specific cause of maternal mortality.

Research through data synthesis has mainly been focused on overall maternal mortality. It was not until recently that investigations have more commonly expanded to include maternal mortality during or following caesarean section.

This thesis provides an in-depth analysis of maternal and neonatal mortality during or following caesarean section and the process of formulating a strategy for the investigation of the causes of maternal mortality during or following caesarean section. This investigation will contribute to the field of perioperative medicine by identifying key aspects that will allow for an improvement in maternal safety throughout the obstetric procedure of caesarean section. This strategy will serve as a guidance for further research in the investigation of the specific causes and to guide clinicians in evidence-based decision making, potentially reducing the risk of maternal and neonatal mortality during or following caesarean section. The initial introduction chapter provides an overview of the framework of caesarean section, maternal mortality and neonatal mortality along with concepts that will be discussed in subsequent chapters. The second chapter provides a systematic overview of systematic reviews and meta-analyses along with an evidence gap map (EGM) to illustrate the gaps in perioperative interventions for caesarean section and their impact on maternal mortality during or following caesarean section. The third chapter contains a systematic review and meta-analysis of perioperative maternal and neonatal mortality over time and by HDI status. Chapter four identifies the proportion of

reported causes of caesarean-related deaths over time and by HDI status through a systematic review and meta-analysis. Chapter 5 assesses the effect of various intervention and comparator groups on the outcome of caesarean attributed maternal deaths. The sixth chapter indicates the impact of the findings, future directions, and the overall conclusions of the thesis.

1.9 BIBLIOGRAPHY

1. American College of Obstetricians and Gynecologists. (2015). Cesarean birth (C-section). FAQ006. Retrieved December 15, 2019, from http://www.acog.org/~/media/For%20Patients/faq006.pdf?dmc=1&ts=20120731T1617495597
2. Chen, I., Opiyo, N., Tavender, E., Mortazhejri, S., Rader, T., Petkovic, J., Yogasingam, S., Taljaard, M., Agarwal, S., Laopaiboon, M., Wasiak, J., Khunpradit, S., Lumbiganon, P., Gruen, R. L., & Betran, A. P. (2018). Non-clinical interventions for reducing unnecessary caesarean section. *The Cochrane database of systematic reviews*, *9*(9), CD005528. https://doi-org.proxy1.lib.uwo.ca/10.1002/14651858.CD005528.pub3
3. Degani, N., & Sikich, N. (2015). Caesarean Delivery Rate Review: An Evidence-Based Analysis. *Ontario health technology assessment series*, *15*(9), 1–58.
4. Cai, M., Loy, S. L., Tan, K. H., Godfrey, K. M., Gluckman, P. D., Chong, Y. S., Shek, L. P., Cheung, Y. B., Lek, N., Lee, Y. S., Chan, S. Y., Chan, J., Yap, F., & Ang, S. B. (2018). Association of Elective and Emergency Cesarean Delivery With Early Childhood Overweight at 12 Months of Age. *JAMA network open*, *1*(7), e185025. https://doi-org.proxy1.lib.uwo.ca/10.1001/jamanetworkopen.2018.5025
5. *Caesarean section: Evidence Update March 2013*. (2013). National Institute for Health and Clinical Excellence (UK). Vol. 35.
6. Cook, J. R., Jarvis, S., Knight, M., & Dhanjal, M. K. (2013). Multiple repeat caesarean section in the UK: incidence and consequences to mother and child. A national, prospective, cohort study. *BJOG : an international journal of obstetrics and gynaecology*, *120*(1), 85–91. https://doi-org.proxy1.lib.uwo.ca/10.1111/1471-0528.12010
7. Marshall, N. E., Fu, R., & Guise, J. M. (2011). Impact of multiple cesarean deliveries on maternal morbidity: a systematic review. *American journal of obstetrics and gynecology*, *205*(3), 262.e1–262.e2628. https://doi-org.proxy1.lib.uwo.ca/10.1016/j.ajog.2011.06.035
8. Keag, O. E., Norman, J. E., & Stock, S. J. (2018). Long-term risks and benefits associated with cesarean delivery for mother, baby, and subsequent pregnancies: Systematic review and meta-analysis. *PLoS medicine*, *15*(1), e1002494. https://doi-org.proxy1.lib.uwo.ca/10.1371/journal.pmed.1002494
9. Timor-Tritsch, I. E., & Monteagudo, A. (2012). Unforeseen consequences of the increasing rate of cesarean deliveries: early placenta accreta and cesarean scar pregnancy. A review. *American journal of obstetrics and gynecology*, *207*(1), 14–29. https://doi-org.proxy1.lib.uwo.ca/10.1016/j.ajog.2012.03.007

10. Betrán, A. P., Ye, J., Moller, A. B., Zhang, J., Gülmezoglu, A. M., & Torloni, M. R. (2016). The Increasing Trend in Caesarean Section Rates: Global, Regional and National Estimates: 1990-2014. *PloS one*, *11*(2), e0148343. https://doi-org.proxy1.lib.uwo.ca/10.1371/journal.pone.0148343
11. World Health Organization. Appropriate technology for birth. (1985). *Lancet (London, England)*, *2*(8452), 436–437.
12. Betran, A. P., Torloni, M. R., Zhang, J. J., Gülmezoglu, A. M., & WHO Working Group on Caesarean Section (2016). WHO Statement on Caesarean Section Rates. *BJOG : an international journal of obstetrics and gynaecology*, *123*(5), 667–670. https://doi-org.proxy1.lib.uwo.ca/10.1111/1471-0528.13526
13. Ye, J., Zhang, J., Mikolajczyk, R., Torloni, M. R., Gülmezoglu, A. M., & Betran, A. P. (2016). Association between rates of caesarean section and maternal and neonatal mortality in the 21st century: a worldwide population-based ecological study with longitudinal data. *BJOG : an international journal of obstetrics and gynaecology*, *123*(5), 745–753. https://doi-org.proxy1.lib.uwo.ca/10.1111/1471-0528.13592
14. D'Souza, R., & Arulkumaran, S. (2013). To 'C' or not to 'C'? Caesarean delivery upon maternal request: a review of facts, figures and guidelines. *Journal of perinatal medicine*, *41*(1), 5–15. https://doi-org.proxy1.lib.uwo.ca/10.1515/jpm-2012-0049
15. WHO. International Classification of Diseases and Related Health Problems. Geneva: World Health Organization, 1992.
16. Kamilya, G., Seal, S. L., Mukherji, J., Bhattacharyya, S. K., & Hazra, A. (2010). Maternal mortality and cesarean delivery: an analytical observational study. *The journal of obstetrics and gynaecology research*, *36*(2), 248–253. https://doi-org.proxy1.lib.uwo.ca/10.1111/j.1447-0756.2009.01125.x
17. Sobhy, S., Arroyo-Manzano, D., Murugesu, N., Karthikeyan, G., Kumar, V., Kaur, I., Fernandez, E., Gundabattula, S. R., Betran, A. P., Khan, K., Zamora, J., & Thangaratinam, S. (2019). Maternal and perinatal mortality and complications associated with caesarean section in low-income and middle-income countries: a systematic review and meta-analysis. *Lancet (London, England)*, *393*(10184), 1973–1982. https://doi-org.proxy1.lib.uwo.ca/10.1016/S0140-6736(18)32386-9
18. Yang, X. J., & Sun, S. S. (2017). Comparison of maternal and fetal complications in elective and emergency cesarean section: a systematic review and meta-analysis. *Archives of gynecology and obstetrics*, *296*(3), 503–512. https://doi-org.proxy1.lib.uwo.ca/10.1007/s00404-017-4445-2
19. Maternal mortality - UNICEF DATA. (2019). Retrieved 11 October 2019, from https://data.unicef.org/topic/maternal-health/maternal-mortality/
20. SDG 3: Ensure healthy lives and promote wellbeing for all at all ages. (2019). Retrieved 11 October 2019, from https://www.who.int/sdg/targets/en/
21. The Sustainable Development Goals and Maternal Mortality. (2019). Retrieved 11 October 2019, from https://www.mhtf.org/topics/the-sustainable-development-goals-and-maternal-mortality/
22. WHO. (2019). Trends in maternal mortality: 2000 to 2017 estimates by WHO, UNICEF, UNFPA, World Bank Group and the United Nations Population Division. Geneva: World Health Organization.

23. Molina, G., Weiser, T. G., Lipsitz, S. R., Esquivel, M. M., Uribe-Leitz, T., Azad, T., Shah, N., Semrau, K., Berry, W. R., Gawande, A. A., & Haynes, A. B. (2015). Relationship Between Cesarean Delivery Rate and Maternal and Neonatal Mortality. *JAMA*, *314*(21), 2263–2270. https://doi-org.proxy1.lib.uwo.ca/10.1001/jama.2015.15553
24. Clark, S. L., Belfort, M. A., Dildy, G. A., Herbst, M. A., Meyers, J. A., & Hankins, G. D. (2008). Maternal death in the 21st century: causes, prevention, and relationship to cesarean delivery. *American journal of obstetrics and gynecology*, *199*(1), 36.e1–e11. https://doi-org.proxy1.lib.uwo.ca/10.1016/j.ajog.2008.03.007
25. Deneux-Tharaux, C., Carmona, E., Bouvier-Colle, M. H., & Bréart, G. (2006). Postpartum maternal mortality and cesarean delivery. *Obstetrics and gynecology*, *108*(3 Pt 1), 541–548. https://doi-org.proxy1.lib.uwo.ca/10.1097/01.AOG.0000233154.62729.24
26. Gonzales, G. F., Tapia, V. L., Fort, A. L., & Betran, A. P. (2013). Pregnancy outcomes associated with Cesarean deliveries in Peruvian public health facilities. *International journal of women's health*, *5*, 637–645. https://doi-org.proxy1.lib.uwo.ca/10.2147/IJWH.S46392
27. Martin, J. A., Hamilton, B. E., Osterman, M. J., & Driscoll, A. K. (2019). Births: Final Data for 2018. *National Vital Statistics Reports, 68*(13). doi:10.7717/peerj.2140/supp-5
28. Fahmy, W. M., Crispim, C. A., & Cliffe, S. (2018). Association between maternal death and cesarean section in Latin America: A systematic literature review. *Midwifery*, *59*, 88–93. https://doi-org.proxy1.lib.uwo.ca/10.1016/j.midw.2018.01.009
29. Say, L., & Chou, D. (2011). Better understanding of maternal deaths--the new WHO cause classification system. *BJOG : an international journal of obstetrics and gynaecology*, *118 Suppl 2*, 15–17. https://doi-org.proxy1.lib.uwo.ca/10.1111/j.1471-0528.2011.03105.x
30. Khan, K. S., Wojdyla, D., Say, L., Gülmezoglu, A. M., & Van Look, P. F. (2006). WHO analysis of causes of maternal death: a systematic review. *Lancet (London, England)*, *367*(9516), 1066–1074. https://doi-org.proxy1.lib.uwo.ca/10.1016/S0140-6736(06)68397-9
31. Say, L., Chou, D., Gemmill, A., Tunçalp, Ö., Moller, A. B., Daniels, J., Gülmezoglu, A. M., Temmerman, M., & Alkema, L. (2014). Global causes of maternal death: a WHO systematic analysis. *The Lancet. Global health*, *2*(6), e323–e333. https://doi-org.proxy1.lib.uwo.ca/10.1016/S2214-109X(14)70227-X
32. Ojo, V. A., Adetoro, O. O., & Okwerekwu, F. E. (1988). Characteristics of maternal deaths following cesarean section in a developing country. *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics*, *27*(2), 171–176. https://doi-org.proxy1.lib.uwo.ca/10.1016/0020-7292(88)90003-3
33. Meara, J. G., Leather, A. J., Hagander, L., Alkire, B. C., Alonso, N., Ameh, E. A., Bickler, S. W., Conteh, L., Dare, A. J., Davies, J., Mérisier, E. D., El-Halabi, S., Farmer, P. E., Gawande, A., Gillies, R., Greenberg, S. L., Grimes, C. E., Gruen, R. L., Ismail, E. A., Kamara, T. B., … Yip, W. (2016). Global Surgery 2030: evidence

and solutions for achieving health, welfare, and economic development. *International journal of obstetric anesthesia*, *25*, 75–78. https://doi-org.proxy1.lib.uwo.ca/10.1016/j.ijoa.2015.09.006
34. World Health Organisation. (2009). WHO Recommended Interventions for Improving Maternal and Newborn Health. Geneva: WHO.
35. Thaddeus, S., & Maine, D. (1991). Too far to walk: maternal mortality in context. *Newsletter (Women's Global Network on Reproductive Rights)*, (36), 22–24.
36. Nieburg, P. (2012). Improving Maternal Mortality and Other Aspects of Women's Health: The United States Global Role. Centre for Strategic and International Studies.
37. Paruzzolo, S. M. R., Kes, A., & Ashbaugh, C. (2010). Targeting Poverty and Gender Inequality to Improve Maternal Health. International Centre for Research on Women.
38. Chirowa, F., Atwood, S., & Van der Putten, M. (2013). Gender inequality, health expenditure and maternal mortality in sub-Saharan Africa: A secondary data analysis. *African Journal of Primary Health Care and Family Medicine*, *5*(1), 471.
39. Bosse, G., Abels, W., Mtatifikolo, F., Ngoli, B., Neuner, B., Wernecke, K. D., & Spies, C. (2015). Perioperative Care and the Importance of Continuous Quality Improvement--A Controlled Intervention Study in Three Tanzanian Hospitals. *PloS one*, *10*(9), e0136156. https://doi-org.proxy1.lib.uwo.ca/10.1371/journal.pone.0136156
40. Wilson, R. D., Caughey, A. B., Wood, S. L., Macones, G. A., Wrench, I. J., Huang, J., Norman, M., Pettersson, K., Fawcett, W. J., Shalabi, M. M., Metcalfe, A., Gramlich, L., & Nelson, G. (2018). Guidelines for Antenatal and Preoperative care in Cesarean Delivery: Enhanced Recovery After Surgery Society Recommendations (Part 1). *American journal of obstetrics and gynecology*, *219*(6), 523.e1–523.e15. https://doi-org.proxy1.lib.uwo.ca/10.1016/j.ajog.2018.09.015
41. Ogboli-Nwasor, E. (2014). Maternal Mortality and Morbidity Will Not Reduce in Low Resource Countries without the Anaesthetists' Involvement. *Open Journal of Obstetrics and Gynecology*, *4*(5), 228-33.
42. World health organisation, UNICEF, UNFPA, Worldbank. (2012). Trends in maternal mortality 1990-2010. Geneva: World health organisation.
43. World Health Organisation. (1996). Coverage of maternity care, a listing of available information. Geneva.
44. Watters, D. A., Hollands, M. J., Gruen, R. L., Maoate, K., Perndt, H., McDougall, R. J., Morriss, W. W., Tangi, V., Casey, K. M., & McQueen, K. A. (2015). Perioperative mortality rate (POMR): a global indicator of access to safe surgery and anaesthesia. *World journal of surgery*, *39*(4), 856–864. https://doi-org.proxy1.lib.uwo.ca/10.1007/s00268-014-2638-4
45. Yaya, S., Uthman, O. A., Amouzou, A., Ekholuenetale, M., & Bishwajit, G. (2018). Inequalities in maternal health care utilization in Benin: a population based cross-sectional study. *BMC pregnancy and childbirth*, *18*(1), 194. https://doi-org.proxy1.lib.uwo.ca/10.1186/s12884-018-1846-6
46. Jacobs, C., Moshabela, M., Maswenyeho, S., Lambo, N., & Michelo, C. (2017). Predictors of Antenatal Care, Skilled Birth Attendance, and Postnatal Care Utilization among the Remote and Poorest Rural Communities of Zambia: A Multilevel

Analysis. *Frontiers in public health*, *5*, 11. https://doi-org.proxy1.lib.uwo.ca/10.3389/fpubh.2017.00011
47. Pathirana, J., Muñoz, F. M., Abbing-Karahagopian, V., Bhat, N., Harris, T., Kapoor, A., Keene, D. L., Mangili, A., Padula, M. A., Pande, S. L., Pool, V., Pourmalek, F., Varricchio, F., Kochhar, S., Cutland, C. L., & Brighton Collaboration Neonatal Death Working Group (2016). Neonatal death: Case definition & guidelines for data collection, analysis, and presentation of immunization safety data. *Vaccine*, *34*(49), 6027–6037. https://doi-org.proxy1.lib.uwo.ca/10.1016/j.vaccine.2016.03.040
48. World Health Organization. (2006). Neonatal and perinatal mortality: country, regional and global estimates. WHO Libr.
49. United Nations Inter-agency Group for Child Mortality Estimation (UNIGME). (2017). Levels and trends in child mortality: report 2017, estimates developed by the UN Inter-agency Group for Child Mortality Estimation. New York: United Nations Children's Fund.
50. Molina, G., Weiser, T. G., Lipsitz, S. R., Esquivel, M. M., Uribe-Leitz, T., Azad, T., Shah, N., Semrau, K., Berry, W. R., Gawande, A. A., & Haynes, A. B. (2015). Relationship Between Cesarean Delivery Rate and Maternal and Neonatal Mortality. *JAMA*, *314*(21), 2263–2270. https://doi-org.proxy1.lib.uwo.ca/10.1001/jama.2015.15553
51. Filippi, V., Goufodji, S., Sismanidis, C., Kanhonou, L., Fottrell, E., Ronsmans, C., Alihonou, E., & Patel, V. (2010). Effects of severe obstetric complications on women's health and infant mortality in Benin. *Tropical medicine & international health : TM & IH*, *15*(6), 733–742. https://doi-org.proxy1.lib.uwo.ca/10.1111/j.1365-3156.2010.02534.x
52. Family Care International, International Center for Research on Women, KEMRI-CDC Research and Public Health Collaboration. (2014). A price too high to bear: The costs of maternal mortality to families and communities.
53. Betrán, A. P., Merialdi, M., Lauer, J. A., Bing-Shun, W., Thomas, J., Van Look, P., & Wagner, M. (2007). Rates of caesarean section: analysis of global, regional and national estimates. *Paediatric and perinatal epidemiology*, *21*(2), 98–113. https://doi-org.proxy1.lib.uwo.ca/10.1111/j.1365-3016.2007.00786.x
54. Molina, G., Weiser, T. G., Lipsitz, S. R., Esquivel, M. M., Uribe-Leitz, T., Azad, T., Shah, N., Semrau, K., Berry, W. R., Gawande, A. A., & Haynes, A. B. (2015). Relationship Between Cesarean Delivery Rate and Maternal and Neonatal Mortality. *JAMA*, *314*(21), 2263–2270. https://doi-org.proxy1.lib.uwo.ca/10.1001/jama.2015.15553
55. Ye J, Zhang J, Mikolajczyk R, Torloni MR, Gülmezoglu AM, Betran AP. Association between rates of caesarean section and maternal and neonatal mortality in the 21st century: a worldwide population-based ecological study with longitudinal data. *BJOG*. 2016;123(5):745-753. doi:10.1111/1471-0528.13592
56. Althabe, F., Sosa, C., Belizán, J. M., Gibbons, L., Jacquerioz, F., & Bergel, E. (2006). Cesarean section rates and maternal and neonatal mortality in low-, medium-, and high-income countries: an ecological study. *Birth (Berkeley, Calif.)*, *33*(4), 270–277. https://doi-org.proxy1.lib.uwo.ca/10.1111/j.1523-536X.2006.00118.x

57. Villar, J., Carroli, G., Zavaleta, N., Donner, A., Wojdyla, D., Faundes, A., Velazco, A., Bataglia, V., Langer, A., Narváez, A., Valladares, E., Shah, A., Campodónico, L., Romero, M., Reynoso, S., de Pádua, K. S., Giordano, D., Kublickas, M., Acosta, A., & World Health Organization 2005 Global Survey on Maternal and Perinatal Health Research Group (2007). Maternal and neonatal individual risks and benefits associated with caesarean delivery: multicentre prospective study. *BMJ (Clinical research ed.)*, *335*(7628), 1025. https://doi-org.proxy1.lib.uwo.ca/10.1136/bmj.39363.706956.55
58. Lumbiganon, P., Laopaiboon, M., Gülmezoglu, A. M., Souza, J. P., Taneepanichskul, S., Ruyan, P., Attygalle, D. E., Shrestha, N., Mori, R., Nguyen, D. H., Hoang, T. B., Rathavy, T., Chuyun, K., Cheang, K., Festin, M., Udomprasertgul, V., Germar, M. J., Yanqiu, G., Roy, M., Carroli, G., … World Health Organization Global Survey on Maternal and Perinatal Health Research Group (2010). Method of delivery and pregnancy outcomes in Asia: the WHO global survey on maternal and perinatal health 2007-08. *Lancet (London, England)*, *375*(9713), 490–499. https://doi-org.proxy1.lib.uwo.ca/10.1016/S0140-6736(09)61870-5
59. Kyu, H. H., Shannon, H. S., Georgiades, K., & Boyle, M. H. (2013). Caesarean delivery and neonatal mortality rates in 46 low- and middle-income countries: a propensity-score matching and meta-analysis of Demographic and Health Survey data. *International journal of epidemiology*, *42*(3), 781–791. https://doi-org.proxy1.lib.uwo.ca/10.1093/ije/dyt081

Chapter 2 - Perioperative interventions for caesarean section: a systematic overview of systematic reviews and meta-analyses

2 INTRODUCTION

Approximately 830 women die every day from preventable causes related to childbirth and pregnancy.[1] Of these maternal deaths, 99% occur in low resource settings, with more than half of the deaths occurring in Sub-Saharan Africa.[1] Rates of caesarean section have been continually rising worldwide – in 2016 the rates were reported to be 24.5% in Western Europe, 32% in North America, and 41% in South America.[10] When maternal and neonatal complications are present, a caesarean section may be beneficial as it may reduce the risk of maternal and neonatal morbidity and mortality.[10] However, a growing number of caesarean sections have been conducted without a medical or obstetric indication.[10] Maternal complications associated with caesarean section, such as infection, haemorrhage, visceral injury, and venous thromboembolism, have decreased in high-income countries. However, in low- and middle-income countries, there is an increased risk of adverse outcomes even with elective caesarean sections.[10] The increasing rate of caesarean sections has become a concern globally and has allowed for a greater emphasis on the investigation of obstetric interventions that reduce maternal mortality and promote maternal health.[6]

An estimated 74% to 98% of maternal mortalities could be averted if evidence-based health-care solutions and interventions shown to prevent or manage complications related to caesarean section were optimally applied.[7] Recent guidelines from the Enhanced Recovery After Surgery (ERAS) Society that have suggested evidence-based recommendations for the perioperative phases of caesarean delivery in terms of maternal outcomes in order to prevent complications that result in maternal mortality.[3,4,5] These interventions may be divided according to perioperative phases throughout the processes and recovery of the surgical procedure. The *preoperative phase* begins when a patient makes the decision to have the caesarean section and ends when the woman is transferred to the operating room.[11] Interventions in this phase are conducted to prepare the patient for surgery. For caesarean section, recent ERAS guidelines suggest preanesthetic

medication, fasting, carbohydrate supplementation, anti-fibrinolytic drugs, and skin wash/ vaginal cleansing.[5] The *intraoperative phase* begins when the patient is taken to the operating room and ends with the transfer to the post-anesthesia care unity (PACU) or other units in which postsurgical recovery is provided.[11] Intraoperative interventions are used to prepare and drape the patient, provide antimicrobial infection prophylaxis, anesthetize, monitor, and conduct the surgical caesarean section. ERAS guidelines propose specific approaches to anesthetic management, uterotonic drugs, cord clamping, maternal position, operative techniques, antifibrinolytic agents, wound drainage, and responsibilities of surgical/perioperative personnel during caesarean section.[4] Finally, the *postoperative phase* begins immediately following surgery, when the patient is transferred to the recovery unit and ends with the resolution of surgical sequelae.[11] The objective of this phase is to monitor and manage the physiologic health of the patient and aid in post-surgical recovery. Interventions conducted following caesarean section include continued fluid management, blood management, analgesia, nausea and vomiting management, urinary drainage management, nutritional care/feeding, thromboembolism prevention, and mobilization.[3] Other interventions such as hypothermia management, glucose management, fluid management, and surgical safety checklist may be applied across the continuum of perioperative phases of caesarean section.[5]

The effectiveness and safety of caesarean section interventions has been assessed by numerous primary studies which encompass randomized controlled trials (RCTs) along with observational studies over various decades. Existing evidence has been summarized in systematic reviews and meta-analyses. However, few of these provide clarity on which interventions apply to maternal and neonatal outcomes in low-, middle-, and high-income settings. In 2019, Smith et al. reported an umbrella review on antenatal and intrapartum interventions on the effectiveness of reducing caesarean section, promoting vaginal birth, and reducing fear of childbirth.[12] However, this review did not assess the impact of perioperative interventions for caesarean section on maternal and neonatal health. Considering the large number of systematic reviews of randomized controlled trials and observational studies regarding the impact of different caesarean-

related interventions and maternal and neonatal outcomes, an overall evaluation of the current evidence is timely.

Evidence-based decision making related to caesarean section requires knowledge of best available research evidence, individual clinical expertise, along with patient values and expectations. Identification of existing systematic reviews and meta-analyses on interventions related to caesarean section, together with evidence mapping, will provide a framework for clinicians and decision makers to visually see which interventions have evidence for safety and effectiveness.[2] It also allows for research priority-setting to address gaps to ensure patients are provided with the best standard of care.

The objective of this systematic overview was to identify, map, and characterize empirical evidence from existing systematic reviews and meta-analyses on the impact of preoperative, intraoperative, and postoperative interventions on maternal mortality in women undergoing, or planning to undergo, a caesarean section across various country income settings. From there, we seek to identify gaps in terms of specific interventions and geographical subgroups to better direct future research, and to summarize the impact of interventions on maternal and neonatal outcomes.

2.1 METHODS

For this systematic overview, a prospective protocol in line with current recommendations was used and we reported the review as per the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines.[34] The study protocol has been registered with PROSPERO, number CRD42020160551.

2.1.1 Search strategy

An extensive search was conducted using multiple sources including scientific and grey literature databases, theses and dissertations, abstracts, as well as forward and backward citation review. Database searches were done from the date of database inception until July 25, 2019, and databases included EMBASE, MEDLINE, Cochrane

database of systematic reviews, Web of science, SCOPUS, WHOLIS, CINHAL, CADTH, NICE, WHO IRIS, Global Index Medicus, and African journals online. The grey literature databases were composed of OAIster/WorldCat, OpenGrey, Centre for Research Libraries Global Resource Network, EU Open Data Portal, and Latin American open Archives Portal. The theses and dissertations databases included Open Access Theses and Dissertations (OATD), EThOS, and DART.

Database searches were conducted with the use of controlled subject terms specific to each database (i.e. caesarean section and maternal mortality). We also used key words and word variants for caesarean section (e.g. c?esar?an*, CSection*, C-Section?*, abdominal deliver*, and abdominal birth*) and maternal mortality (e.g. maternal mortal*, maternal death*, pregnan* death*, and wom?n death*). In addition, subject terms and key words were used to limit study design to systematic review, meta-analysis, and evidence synthesis. Language or date restrictions were not imposed. Detailed search strategies for each database are provided in APPENDIX A.

2.1.2 Screening and inclusion criteria

Selection of studies occurred in two levels. In level one, one reviewer screened the titles and abstracts of all citations for potentially relevant papers with the use of Mendeley. Studies that were not related to interventions during caesarean section and maternal mortality were removed – this level of screening was kept inclusive to avoid errors. In level two, full text articles were assessed by two independent reviewers (AH, KM) who applied the pre-specified inclusion and exclusion criteria. To be included in the systematic overview, all studies had to be systematic reviews, meta-analyses, and evidence syntheses. The reviews must have assessed the impact of preoperative, intraoperative, or postoperative interventions related to caesarean section on maternal mortality in women of all ages who undergo or are planning to undergo an elective or emergency caesarean section. Of the studies that assessed maternal mortality, the primary outcome of neonatal mortality and the secondary outcomes of surgical site infection (SSI), and maternal sepsis were also included. Our primary outcome of maternal mortality was defined as death of a woman from any cause, occurring any time between

the start of the procedure or start of anesthesia until hospital discharge or 42 days of follow-up after caesarean section.[33] If anesthesia was not provided, then the initial point changed to the point of first incision until hospital discharge or 42 days of follow-up after caesarean section. Studies were excluded if they included solely pregnant women undergoing only vaginal delivery, if interventions were not related to caesarean section or were not conducted preoperatively, intraoperatively, or postoperatively, and if they examined maternal mortality during pregnancy, under any other surgical procedure, or beyond 42 days postoperatively. Studies that reported on mixed populations (vaginal delivery and caesarean section) were excluded if data on the caesarean section subgroup was not reported separately. Study designs other than those presented above were not included. No limits were imposed on the comparison group. Studies that reported adjusted rates for our primary and secondary outcomes without crude data were excluded. Abstracts or studies that could not be retrieved after reasonable effort, as well as studies not conducted on humans, were excluded. For systematic reviews with multiple versions published, the most recent version was included.

2.1.3 Data extraction and critical appraisal

Two reviewers (AH, KM) independently extracted data using a data extraction form developed and pilot tested a priori. Discrepancies and disagreements were resolved through discussion and consensus. From the eligible studies we obtained information on the following characteristics: author, aim of the review, year the review was published, number of studies included in the reviews, types of studies in the reviews, sample size, population characteristics, description of the intervention and comparator, outcome data for both groups and the results (narrative or meta-analyzed data, as available), countries in which the primary studies were conducted, and critical appraisal of included studies. Assessment of the quality of the included systematic reviews was conducted by two independent reviewers (AH, KM) with the use of 'A Measurement Tool to Assess Systematic Reviews 2' (AMSTAR 2) tool.[8] AMSTAR 2 is a tool for analyzing the methodological quality of systematic reviews that include randomized studies, non-randomized studies, or both, for healthcare interventions.[8] This tool consists of 16 items

with response categories of yes or no for each item, and has been previously validated.[9] The domains of the AMSTAR 2 tool include: question and inclusion, protocol, study design, comprehensive search, study selection, data extraction, excluded studies justification, included studies details, risk of bias (RoB), funding sources, statistical methods, RoB on meta-analysis, RoB in individual studies, explanation for heterogeneity, publication bias, and conflict of interest.[8]

Classification of country income level according to the World Bank categories was used to assign income settings to reviews.[35] If a systematic review or meta-analysis identified the country income settings that were assessed, then that category was used. If the systematic review or meta-analysis did not explicitly state the country income settings included then it was identified from the countries in which the primary studies were performed, this was obtained either from the review or the original primary studies.

2.1.4 Data analysis

The synthesis of data was narrative due to heterogeneity of the intervention and comparator groups between reviews. This was supplemented by summary tables for the characteristics, along with the results of the included reviews where interventions demonstrating evidence of effect for our primary and secondary outcomes were highlighted. We presented the summary effect estimates provided by the reviews; that is, odds ratio (OR) or relative risk (RR), with 95% confidence intervals (CI) for pair-wise meta-analyses and proportions (%) with 95% confidence intervals (CI) for single-arm meta-analyses. We reanalyzed each pairwise meta-analysis using the DerSimonian and Laird random effects model, which takes into account between and within study variance. This was conducted through the extraction of intervention and outcome data, as published within each systematic review and meta-analysis article. A forest plot presenting the primary and secondary outcomes of the various intervention and comparator groups was generated using a common effect estimate of risk ratio (RR) derived from events data of the included reviews. This was done to provide a visual representation of the net impact on outcomes across various intervention/comparator groups without any intention of pooling the data. Studies were included only once, and we did not combine multiple

meta-analyses with the same intervention and comparison groups. A figure is provided for the AMSTAR 2 quality assessment, and relationships within and between the data were explored according to these domains. An evidence gap map (EGM) was created to present a visual overview of the volume of available systematic reviews and meta-analyses in terms of the types of interventions related to caesarean section for our primary and secondary outcomes across various country income settings. Interventions were listed on the y-axis and country income settings on the x-axis. The bubbles present at intersections between interventions and country income settings denote the existence of systematic reviews and meta-analyses assessing the relevant intervention within the appropriate income settings. Bubbles of different colours indicate different outcome combinations. The size of each bubble quantifies either the number of studies or the number of participants studied within each systematic review.

2.2 RESULTS

A total of 1634 studies were identified from the database search along with 693 studies from other sources, including theses and dissertations, grey literature, and from forward and backward citation. After removing duplicates, 1055 studies remained. A total of 987 titles and abstracts were excluded as they were not systematic reviews, they did not examine the outcome of maternal mortality, or did not examine the effects of perioperative interventions. There were 68 studies remaining for full text screening; of these, 48 were excluded due to the prespecified exclusion criteria. A final sample of 20 systematic reviews and meta-analyses were identified for inclusion in the systematic overview.[13-32] Figure 2.1 provides the PRISMA Flow-Chart for details of the article selection process used for this systematic overview.

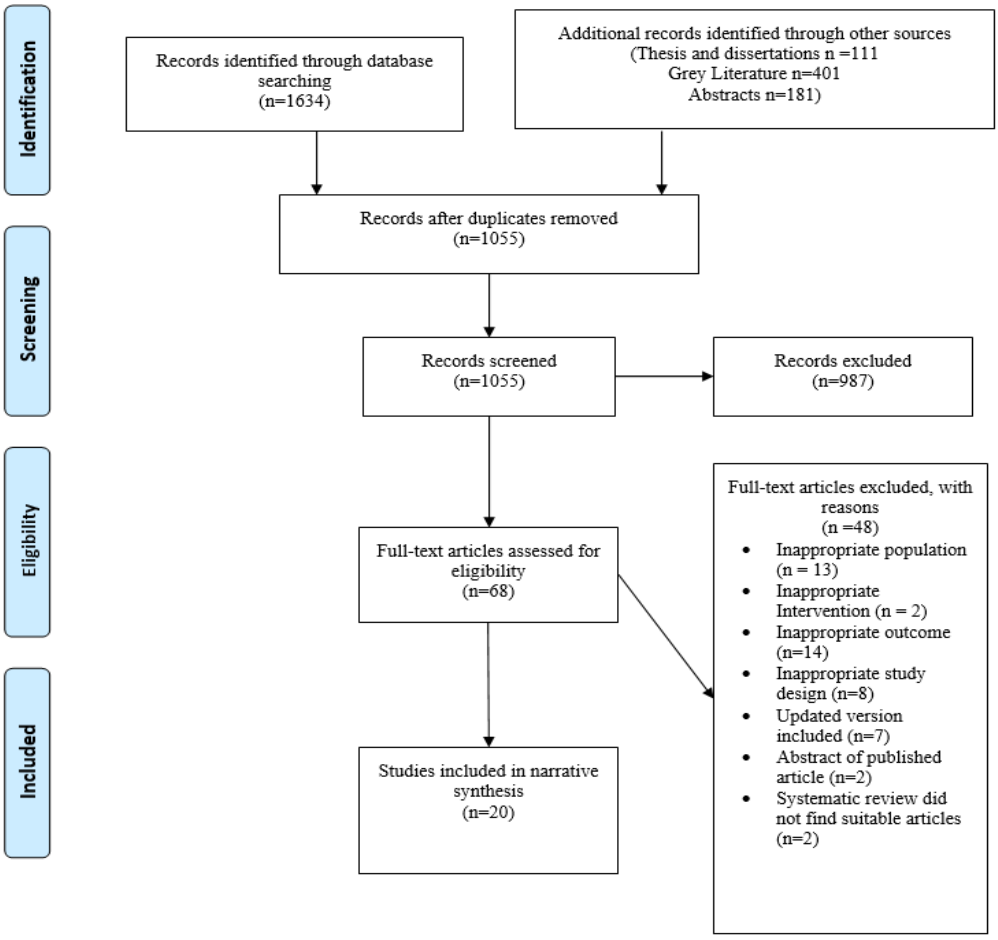


Figure 2.1 PRISMA flow diagram of study selection

2.2.1 Description of studies

Of the 20 included systematic reviews, 16 were of randomized controlled trials (RCTs),[14,15,17-19,21-31] two included only observational studies,[13,20] and two included both observational studies and RCTs.[16,32] For the populations of the included studies, seven reviews were of women undergoing both caesarean section and vaginal delivery,[15,18,19,25,26,28,30] 12 reviews only examined women undergoing caesarean section[13,14,17,20-24,27,29,31,32] and one review evaluated pregnant women undergoing any obstetric procedure.[16] In terms of the caesarean-related interventions, three reviews investigated preoperative interventions,[17,18,24] 12 reviews examined intraoperative interventions,[13-16,20,22,23,26,27,29,31,32] one review investigated postoperative interventions,[25]

and four reviews examined perioperative interventions.[19,21,28,30] Areas of clinical care commonly assessed in the reviews included interventions for preanesthetic management (one review),[17] skin wash/ vaginal cleansing (one review),[24] anesthetic management (three reviews),[16,29,32] uterotonic drugs (two reviews),[15,26] anti-fibrinolytic drugs (four reviews),[18,19,25,30] maternal position (one review),[27] operative techniques (four reviews),[14,20,22,23] surgical personnel (one review),[13] wound drainage (one review),[31] antimicrobial prophylaxis (one review),[21] and thromboembolism prevention (one review).[28] For country income settings, one review was conducted in low-income countries (LIC),[13] two reviews in middle-income countries (MIC),[19,30] two reviews in high-income countries (HIC),[15,28] one review in low-and middle-income countries (L&MIC),[16] 11 reviews in high-and middle-income countries (H&MIC)[14,17,18,20-22,24,27,29,31,32] and three reviews in low-middle and high-income countries (LMHIC).[23,25,26] APPENDIX B: Table1 shows the characteristics of these reviews. Of the included systematic reviews and meta-analyses that investigated the primary outcome of maternal mortality, one additionally examined maternal sepsis,[20] four also investigated neonatal mortality,[20,21,27,29] and 10 also assessed surgical site infection/ wound infection.[13,14,20-24,28,29,31]

2.2.2 Evidence gap map

When examining the evidence base for interventions conducted throughout the perioperative period of caesarean section and their impact on maternal mortality, a total of 11 distinct intervention categories were identified.[13-32] Of these intervention categories, 60% were conducted within the intraoperative phase[13-16,20,22,23,26,27,29,31,32] leaving large gaps within the evidence for pre-, post-, and perioperative interventions; the largest gap is present in the postoperative phase. The most frequently studied intervention categories were operative techniques, accounting for 20% of the reviews[14,20,22,23] followed by anesthetic management (15%),[16,29,32] both of which are in the intraoperative phase. For operative techniques, the studies included in the reviews were from high- and middle-income countries[14,20,22] and across high, middle- and low-income countries,[23] while all other county income settings showed absolute gaps in this type of intervention. Similarly,

reviews of anesthetic management were conducted in low- and middle-income countries[16] and high- and middle-income countries,[29,32] and no studies were found in other country income settings. The most frequently studied country income settings were those of combined groups (low- and middle-income, middle- and high-income, and all country income settings)[14,16-18,20-27,29,31,32,] rather than only including studies focused on one individual setting (LIC, MIC, HIC)[13,15,19,28,30] with most reviews being conducted on studies of middle and high-income settings.[14,17,18,20-22,24,27,29,31,32] The country income settings with the most gaps are low-income[13] and low and middle-income[16] with only one systematic review obtained for each income setting.

The outcome that was more commonly assessed throughout the reviews was the independent investigation of maternal mortality (45%)[15-19,25,26,30,32] followed by the combination of maternal mortality and SSI/wound infection (35%).[13,14,22-24,28,31] The outcome combinations with the largest gaps are maternal mortality, neonatal mortality[27] along with maternal mortality, SSI/wound infection, sepsis, neonatal mortality[20] both with only one review obtained from the evidence base in H&MIC. Figures 2.3 and 2.4 provide further identification of reviews based on intervention categories and income settings along with gaps present within the framework. Two evidence gap maps were created in order to provide perspectives based on the number of studies within the systematic reviews and the number of participants studied who underwent caesarean section; these were depicted by the size of the bubbles.

2.2.3 Quality assessment

AMSTAR 2 ratings representing the quality of the systematic reviews and meta-analyses are displayed in Figure 2.2. Most of the reviews obtained an overall rating of moderate quality (55%). Item 7 “Excluded Studies Justification” was the only domain that was present within all the reviews. Most of the included reviews indicated the types of studies that were to be included within their review. However, none of the studies provided an explanation for their choice of study design. This resulted in the absence of item 3 “Study Design” among 95% of included reviews. Item 15 “Publication Bias” was only present in 15% of included studies. This occurred because the included studies that

performed quantitative synthesis had less than ten studies included in their analysis, preventing them from investigating publication bias. The domains in which the reviews performed well on quality criteria included: “Question and inclusion” (95%), “Study Selection” (95%), “Data extraction” (95%), “Risk of Bias (ROB)” (85%), and “Statistical methods” (75%). Other domains for “Protocol”, “Explanation for Heterogeneity” and “Conflict of Interest” were performed moderately well as they were present in 65% of the included reviews. The domains that were performed poorly including: “Funding Source” (20%) and “ROB analysis” (50%). The two domains with the greatest uncertainty were “Comprehensive Search” and “Included Studies Details” in which a partial yes was given to 60% and 70% of the included reviews. This was primarily due to the lack of grey literature and reference list searches, the limited description of language and publication date restrictions, and the absence of information on study setting and timeframe for follow-up of the studies within the reviews. Complete AMSTAR item ratings for included reviews are available in Appendix C.

2.2.4 Maternal mortality

We identified 20 reviews that assessed maternal mortality.[13-32] APPENDIX B: Table 2 and Figure 1 portray the effects of the various management techniques on the outcome. The estimates for this outcome across various intervention and comparator groups demonstrated substantial variation, with risk ratio values ranging from 0.17 to 14.38.[13,14,20,23,25,26,32] Two intervention and comparator groups showed a significantly higher risk of the intervention on maternal mortality in women who undergo or are planning to undergo caesarean section.[13,32] Compared to regional anesthesia, general anesthesia was associated with a significantly higher risk of maternal mortality [RR 14.38 (95% CI 6.08-34.02)].[32] Further, one review conducted a single arm meta-analysis indicating that anaesthesia was responsible for 13·8% (95% CI 9.0-20.7) of deaths following caesarean section.[16] Clinical officers carrying out caesarean sections were associated with significantly higher risk of maternal mortality, as compared to medical officers [RR 1.57 (95% CI 1.15-2.15)].[13] The following intervention and comparator groups showed no significant difference between the interventions and comparators for

the primary outcome: misoprostol vs oxytocin [RR 0.33 (95% CI 0.01-8.01)],[26] extraperitoneal vs intraperitoneal caesarean section techniques [RR 0.17 (95% CI 0.02-1.37)],[23] classical caesarean section vs low transverse incision [RR 2.38 (95% CI 0.15-37.91)],[20] exteriorized vs in situ [RR 4.76 (95% CI 0.23-98.94)],[14] standard care plus IV tranexamic acid vs placebo or standard care alone (all-cause mortality) [RR 0.93 (0.68-1.26)],[25] and standard care plus IV tranexamic acid vs placebo or standard care alone (mortality due to bleeding) [RR 0.80 (95% CI 0.54-1.18)].[25] The effects of intervention and comparator groups of the following intervention categories on maternal death could not be estimated, as the reviews intended to investigate maternal mortality, however, none of the individual studies included within the reviews reported on the outcome: preanesthetic medication,[17] skin wash/ vaginal cleansing,[24] perioperative anti-fibrinolytic drugs,[30] maternal position,[27] wound drainage,[31] antimicrobial prophylaxis[21] and various comparison groups for uterotonic drugs[15,26] and operative techniques[22] as seen in APPENDIX B: Table 2. Further, the following intervention and comparator groups reported maternal mortality; however, no cases of maternal death were identified, indicating that the study may have been underpowered for a rare outcome like maternal death: carbetocin vs oxytocin,[26] misoprostol plus oxytocin vs oxytocin,[26] misoprostol vs carbetocin,[26] misoprostol plus oxytocin vs carbetocin,[26] perioperative tranexamic acid vs placebo/no treatment,[19] preoperative tranexamic acid vs no treatment,[18] five-day Low-molecular-weight heparin (LMWH) vs 10-day LMWH[28] and manual displacer vs 15º left lateral tilt.[27] Substantial heterogeneity was seen in three meta-analyses reporting this outcome (I^2 =58% to 84%). One review reported a Cochran's Q test and found that there was no evidence of statistical heterogeneity (p=0.51).

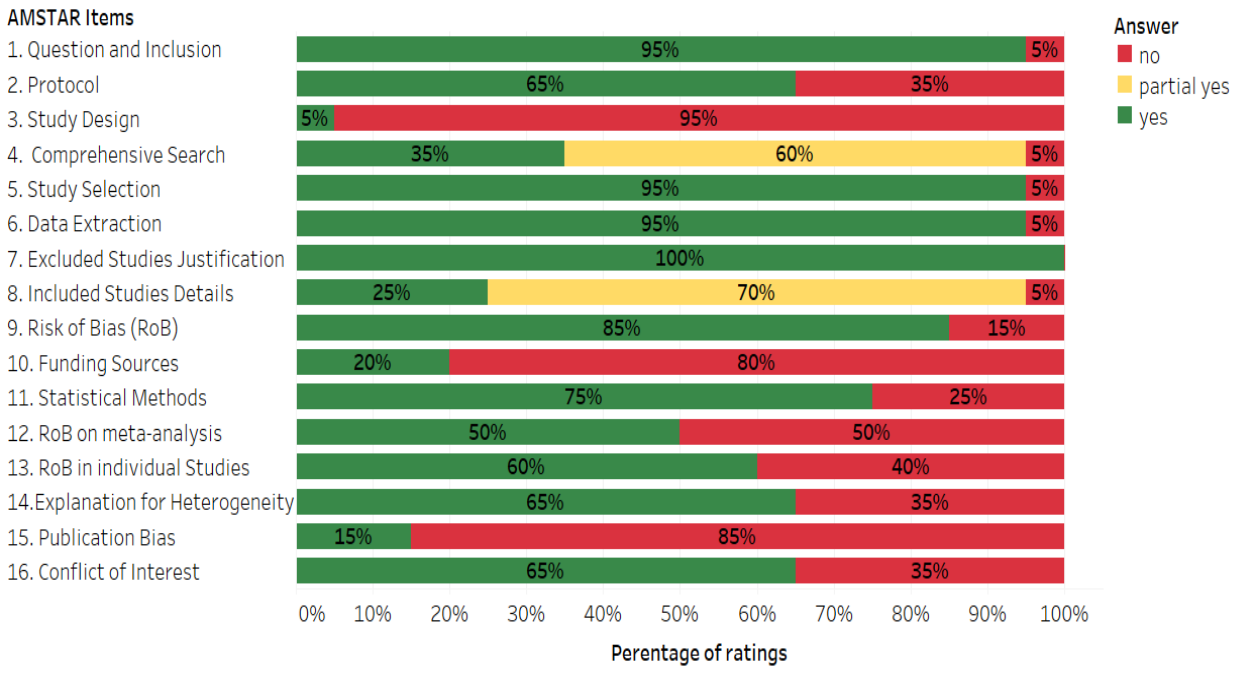


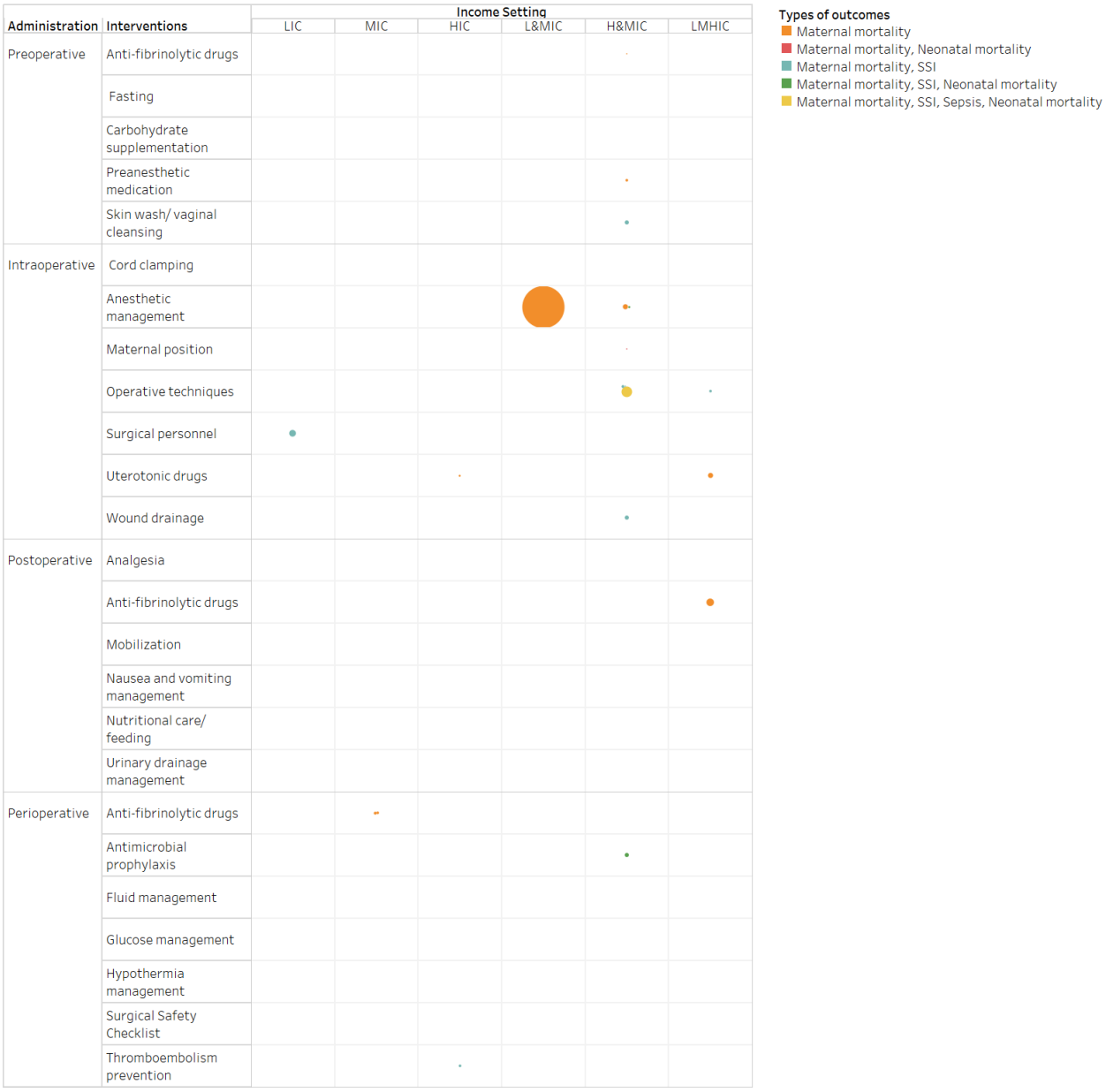
Figure 2.2 Summary of findings from the AMSTAR 2 quality assessment

2.2.5 Neonatal mortality

Four reviews examined neonatal mortality. However, none of these reviews reported results of the outcome in women undergoing a caesarean section.[20,21,27,29] The intervention and comparator groups of regional anaesthesia vs general anaesthesia,[29] manual displacer vs 15º left lateral tilt[27] and prophylactic intravenous (IV) antibiotic administration for caesarean birth 0 to 30 and 30 to 60 minutes prior to skin incision vs prophylactic antibiotic administration for caesarean birth after neonatal umbilical cord clamping[21] intended to investigate the effects on neonatal mortality. However, none of the individual studies included within the reviews reported on neonatal mortality. Neonatal mortality was only reported for one comparison (classical versus low transverse Caesarean section),[20] but was not included in our review since the findings were adjusted without any crude data, preventing its inclusion into our analysis of neonatal mortality.

Abbreviations:
LIC= Low-income countries, MIC= Middle-income countries, HIC=High-income countries, L&MIC=Low and middle-income countries, H&MIC=High and middle-income countries, LMHIC=Low, middle and high-income countries

Figure 2.3 Evidence gap map of perioperative interventions for caesarean section examined by systematic reviews and meta-analyses where maternal mortality was reported (Note: this only includes systematic reviews and meta-analyses where maternal mortality was included as an outcome, and does not represent the totality of the evidence base for studies where maternal mortality was not a focus). The size of each bubble quantifies the number of studies within each systematic review and the colours indicate different outcome combinations.



Abbreviations:
LIC= Low-income countries, MIC= Middle-income countries, HIC=High-income countries, L&MIC=Low and middle-income countries, H&MIC=High and middle-income countries, LMHIC=Low, middle and high-income countries

Figure 2.4 Evidence gap map of perioperative interventions for caesarean section examined by systematic reviews and meta-analyses where maternal mortality was reported (Note: this only includes systematic reviews and meta-analyses where maternal mortality was included as an outcome, and does not represent the totality of the evidence base for studies where maternal mortality was not a focus). The size of each bubble quantifies the number of participants studied who underwent caesarean section within each systematic review and the colours indicate different outcome combinations.

2.2.6 Sepsis reported in reviews that assessed maternal mortality

Only one review that investigated maternal mortality additionally investigated the secondary outcome of sepsis.[20] The results indicated that the risk of maternal sepsis was higher with classical incision as compared to low transverse incision [RR 3.18 (95% CI 1.45-6.96)].[20] Statistical heterogeneity for the outcome of sepsis as analyzed by a single review was low (I^2=0%) (APPNDIX B: Table 2).

2.2.7 Wound infections/surgical site infection reported in reviews that assessed maternal mortality

Ten reviews that investigated maternal mortality additionally assessed wound infection or surgical site infection in women undergoing a caesarean section.[13,14,20-24,28,29,31] Estimates of intervention and comparator groups ranged from RR 0.33 – 5.42;[13,14,20-24,28,31] only two intervention and comparator groups showed significant effects, while the remainder provided no statistically significant effects.[13,31] Subcutaneous drain as compared to sub-sheath drain [RR 5.42 (95% CI 1.28-22.98)][31] and conduct of caesarean section by clinical officers as compared to medical officer [RR 3.65 (95% CI 2.46-5.41][13] were associated with a significantly higher risk of wound infection. The following intervention and comparator groups showed no statistically significant difference on the outcome of wound infection/surgical site infection: drape vs no drape (subgroup iodine) [RR 1.42 (95% CI 0.98-2.04)],[24] drape vs no drape (subgroup chlorhexidine) [RR 1.11 (95% CI 0.70-1.76)],[24] drape vs no drape (overall) [RR 1.28 (95% CI 0.96-1.71)],[24] parachlorometaxylenol with iodine vs iodine alone [RR 0.33 (0.04-2.99)],[24] chlorhexidine gluconate vs povidone iodine [RR 0.80 (95% CI 0.62-1.02)],[24] Joel-Cohen type vs Pfannenstiel (Joel-Cohen subgroup) [RR 1.00 (95% CI 0.07-15.38)],[23] Joel-Cohen type vs Pfannenstiel (Misgav-Ladach subgroup) [RR 3.61 (95% CI 0.79-16.49)],[23] Joel-Cohen type vs Pfannenstiel (modified Misgav-Ladach subgroup) [RR 0.99 (95% CI (0.56-1.76)],[23] Joel-Cohen type vs Pfannenstiel (overall) [RR 1.21 (95% CI 0.73-2.03)],[23] Misgav-Ladach vs lower midline [RR 1.14 (95% CI 0.68-1.91)],[23] classical caesarean section vs low transverse incision [RR 0.72 (95% CI 0.35-1.46)],[20] Joel-Cohen type vs Pfannenstiel [RR 1.56 (95% CI 0.45-5.42)],[22] muscle cutting/Maylard

cutting vs Pfannenstiel incision [RR 1.26 (95% CI 0.27-5.91)],[22] exteriorized vs in situ [RR 0.81 (95% CI 0.54-1.23)],[14] wound drain vs no drain [RR 1.06 (95% CI 0.89-1.26)],[31] wound drain vs subcutaneous suture [RR 0.78 (95% CI 0.41-1.45)],[31] five-day LMWH vs 10-day LMWH RR [1.13 (95% CI 0.63-2.05)],[28] prophylactic intravenous antibiotics administered before caesarean incision vs after neonatal umbilical cord clamping (cephalosporin 1 g subgroup) [RR 0.55 (95% CI 0.30-1.01)],[21] prophylactic intravenous antibiotics administered before caesarean incision vs after neonatal umbilical cord clamping (cephalosporin 2 g subgroup) [RR 0.61 (95% CI 0.43-0.88)][21] and prophylactic intravenous antibiotics administered before caesarean incision vs after neonatal umbilical cord clamping (overall) [RR 0.60 (95% CI 0.44-0.81)].[21] In the comparison of one-minute alcohol scrub with iodophor drape versus five-minute iodophor scrub without drape, surgical site infection was assessed. However, no cases were reported resulting in a RR of zero.[24] One review examined the effects of regional versus general anesthesia on wound infection. However, none of the included studies reported on the outcome.[29] Heterogeneity ranged from low (I^2=0%, nine reviews and Cochran's Q test (P=0.77)) to substantial (I^2=61% and 72%) (APPENDIX B: Table 2).

2.3 DISCUSSION

2.3.1 Summary of main results

In this overview, we summarized the evidence from 20 systematic reviews and meta-analyses that assessed the effectiveness and safety of interventions occurring during the perioperative phases in women who undergo caesarean section.[13-32] Additionally, we summarized the results of the reviews based on the primary outcomes of maternal and neonatal mortality, along with the secondary outcomes of sepsis and wound infection/surgical site infection.

Although all 20 reviews assessed maternal mortality, none of the interventions found a significantly *lower* risk in maternal mortality, and two indicated a significantly *higher* risk in maternal mortality (general vs regional anesthesia; clinical officer versus medical officer).[13,32] Few reviews that assessed maternal mortality also reported on other

outcomes: sepsis, and surgical site infection. For maternal sepsis, one included review indicated a significantly *higher* risk of maternal sepsis (classical incision versus low transverse incision).[20] For wound infection/surgical site infection, none of the included systematic reviews showed a significantly *lower* risk and two interventions indicated a significantly *higher* risk (subcutaneous drain as compared to sub-sheath drain; clinical officers versus medical officer).[13,31] Evidence of interventions examining neonatal mortality in addition to maternal mortality was limited. Although four reviews intended to include studies of this outcome, no studies were identified that provided data on neonatal mortality.[20,21,27,29]

However, the lack of identified interventions with impact on sepsis and surgical site infection should not be interpreted as the totality of the evidence since this systematic overview *only* intended to evaluate the evidence base for studies that assessed maternal mortality. Hence, the secondary outcomes are to be interpreted in this light, where their impact on maternal mortality together with impact on sepsis or surgical site infection is the goal. For example, plenty of systematic reviews have established the impact of antibiotic prophylaxis on reducing the risk of surgical site infection and endometritis. However, these latter systematic reviews and meta-analyses were not included in the present overview if they did not report on maternal mortality. This is not to infer that antibiotic prophylaxis is unimportant, or that the evidence base is lacking. Rather, the results of this overview should be interpreted for its impact on maternal mortality (or lack thereof).

2.3.2 Significance of findings

As caesarean sections are one of the most common surgeries performed worldwide, with the intention of saving the lives of mothers and neonates, the importance of adequately evaluating interventions used throughout the various phases of the procedure cannot be understated. Numerous systematic reviews and meta-analyses have analyzed interventions in relation to caesarean section. However, a limited number have assessed the effects of those interventions on maternal mortality. Therefore, the goal of this systematic overview was to identify areas in which evidence on interventions were

present and where the gaps in the evidence base lie. This systematic overview expands on current knowledge of the extent of the existing evidence base for perioperative interventions for caesarean section on maternal mortality by providing a visualization of the volume of evidence and net effectiveness of these interventions on the primary and secondary outcomes investigated.

Various gaps were identified throughout the evidence base in terms of intervention categories as well as country income settings in which the effects of interventions were analyzed. Given the increased risk of maternal mortality and morbidity linked to caesarean section and the lack of effective interventions within the evidence base as described above, it is imperative that further research along with advancements in interventions are attained in order to reduce the risks associated with this obstetric procedure. Our overview has identified 56 individual interventions administered throughout the perioperative stages for various complications associated with caesarean section.[13-32] These may be considered in practice by clinicians for evidence-based decision making in the context of country income setting. Furthermore, researchers may use the results and map of the evidence base as a guideline in order to fill in the gaps through further research in areas with minimal to no evidence in an effort to increase safety for caesarean section.

2.3.3 Strengths and limitations

The search strategy for this overview was extensive, incorporating various databases, abstracts along with grey literature sources allowing us to capture a wide range of relevant evidence. The main objective of this review was to identify, map, and describe the existing empirical evidence on perioperative interventions in caesarean section. Additionally, study selection and data extraction were undertaken by two independent reviewers, thereby mitigating potential errors or biases.

All systematic reviews and meta-analyses in the review were included irrespective of their quality assessment scoring. However, since the purpose of this overview was to explore the available evidence on the topic, this entails including all studies regardless of

the quality. More than half of the studies included in this review were of moderate quality (55%). This would suggest moderate confidence in the findings and recommendations of the review indicating that the review provides an accurate summary of the studies included. The moderate and low-quality reviews on this topic should indicate that more research of high-quality should be encouraged. Another limitation present of our review relates to the rarity of maternal mortality and rarity of studies powered to address mortality, which prevented the inclusion of these interventions to our summary of effects. However, although these reviews did not provide insight into the safety of the interventions investigated, they did provide insight into the scarcity of the existing evidence base. This highlights the importance of future studies to routinely include mortality and safety of interventions, as systematic review and meta-analysis provides an opportunity to increase the power to detect differences across all studies, even when individually they are underpowered.

Since the methodology of our study was an overview of systematic reviews and meta-analyses on various perioperative interventions that addressed our primary and secondary outcomes, some interventions were not included if they were only assessed through primary studies. However, this provides an efficient framework to inform the existing gaps in research. Therefore, some perioperative interventions may have been missed if they have not yet been included in systematic reviews, though the number of missing interventions is likely to be low.

We identified a number of methodological gaps in the existing evidence base. Various reviews included in our overview did not provide information on the setting of the included studies. In order to identify the setting, we had to manually go back to the individual studies of some systematic reviews and meta-analyses to capture these data. Another gap was the scarcity of information on the types of interventions investigated in the reviews; a small number of reviews, specifically Cochrane reviews provided detailed information on when the intervention was conducted, whereas other review provided insufficient information.

The most significant limitation of our systematic overview is that it included only reviews that assessed maternal mortality. Therefore, the additional secondary outcomes of impact of interventions on sepsis, and wound infection/ surgical site infection should not be interpreted as if they include all studies in this area. The results must be interpreted as those stemming solely from studies where maternal mortality *and* these secondary outcomes are included.

2.3.4 Implications for future work

Future research should aim to add to the knowledge attained from this review by expanding the inclusion criteria to all studies, including those that did not analyze maternal mortality. In addition, future studies should analyze costs along with the health outcomes of the perioperative interventions for caesarean section. A comparison of the various interventions on the basis of costs and effectiveness, and formal economic evaluation would allow for informed priority-setting. Comparing the interventions within each intervention category will provide insight into whether the value of an intervention justifies its costs. When resources are limited, it is important to ensure that they are used for the most cost-effective interventions in order to prevent loss in the potential gain from alternative interventions that may provide more of an impact on the outcome. Priority-setting tools will be informed by this review, as we have identified various perioperative interventions for caesarean section which provides a path toward identifying high priority interventions for implementation into practice, versus interventions which have promise, but which have not been adequately studied and should be prioritized for further research.

2.4 CONCLUSION

This overview of systematic reviews and meta-analyses identified and highlighted perioperative interventions for caesarean section that have been shown to have an impact on maternal mortality along with those that additionally impacted sepsis and wound infection/surgical site infection. No interventions indicated a lower risk in maternal mortality. Interventions which indicated a significantly higher risk of maternal mortality included general anesthesia compared to regional anesthesia, and clinical officer versus

medical officer for maternal mortality.[13,32] In addition, of studies reporting on maternal mortality, classical incision versus low transverse incision for maternal sepsis,[20] and subcutaneous drain as compared to sub-sheath drain and clinical officers versus medical officer suggested a higher risk of wound infection/surgical site infection.[13,31] None of the included reviews included data on neonatal mortality. This overview summarizes existing empirical evidence and may provide an extensive and valuable resource for clinicians when making decisions on practices in terms of which interventions reduce the safety of caesarean section. This overview also highlights research priorities for future studies that are required to increase the safety of caesarean section.

2.5 BIBLIOGRAPHY

1. World Health Organization. Maternal mortality. (2019). Retrieved 25 July 2019, from https://www.who.int/news-room/fact-sheets/detail/maternal-mortality.
2. Smith, V., Devane, D., Begley, C., & Clarke, M. (2011). Methodology in conducting a systematic review of systematic reviews of healthcare interventions. *BMC Medical Research Methodology*, *11*(1). doi: 10.1186/1471-2288-11-15
3. Macones, G., Caughey, A., Wood, S., Wrench, I., Huang, J., & Norman, M. et al. (2019). Guidelines for Postoperative care in Cesarean Delivery: Enhanced Recovery After Surgery (ERAS) Society Recommendations (Part 3). *American journal of obstetrics and gynecology*, *221*(3), 247.e1–247.e9. https://doi-org.proxy1.lib.uwo.ca/10.1016/j.ajog.2019.04.012
4. Caughey, A., Wood, S., Macones, G., Wrench, I., Huang, J., & Norman, M. et al. (2018). Guidelines for intraoperative care in cesarean delivery: Enhanced Recovery After Surgery Society Recommendations (Part 2). *American journal of obstetrics and gynecology*, *219*(6), 533–544. https://doi-org.proxy1.lib.uwo.ca/10.1016/j.ajog.2018.08.006
5. Wilson, R., Caughey, A., Wood, S., Macones, G., Wrench, I., & Huang, J. et al. (2018). Guidelines for Antenatal and Preoperative care in Cesarean Delivery: Enhanced Recovery After Surgery Society Recommendations (Part 1). *American journal of obstetrics and gynecology*, *219*(6), 523.e1–523.e15. https://doi-org.proxy1.lib.uwo.ca/10.1016/j.ajog.2018.09.015
6. Chen, I., Opiyo, N., Tavender, E., Mortazhejri, S., Rader, T., Petkovic, J., Yogasingam, S., Taljaard, M., Agarwal, S., Laopaiboon, M., Wasiak, J., Khunpradit, S., Lumbiganon, P., Gruen, RL., & Betran, AP. (2018). Non-clinical interventions for reducing unnecessary caesarean section. *The Cochrane database of systematic reviews*, *9*(9), CD005528. https://doi-org.proxy1.lib.uwo.ca/10.1002/14651858.CD005528.pub3
7. Nyamtema, A., Urassa, D., & van Roosmalen, J. (2011). Maternal health interventions in resource limited countries: a systematic review of packages, impacts and factors for change. *BMC Pregnancy And Childbirth*, *11*(1). https://doi-org.proxy1.lib.uwo.ca/10.1186/1471-2393-11-30

8. Shea, B., Reeves, B., Wells, G., Thuku, M., Hamel, C., & Moran, J. et al. (2017). AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *BMJ (Clinical research ed.)*, *358*, j4008. https://doi-org.proxy1.lib.uwo.ca/10.1136/bmj.j4008
9. Pieper, D., Puljak, L., González-Lorenzo, M., & Minozzi, S. (2019). Minor differences were found between AMSTAR 2 and ROBIS in the assessment of systematic reviews including both randomized and nonrandomized studies. *Journal Of Clinical Epidemiology*, *108*, 26-33. https://doi-org.proxy1.lib.uwo.ca/10.1016/j.jclinepi.2018.12.004
10. Keag, O., Norman, J., & Stock, S. (2018). Long-term risks and benefits associated with cesarean delivery for mother, baby, and subsequent pregnancies: Systematic review and meta-analysis. *PLOS Medicine*, *15*(1), e1002494. https://doi-org.proxy1.lib.uwo.ca/10.1371/journal.pmed.1002494
11. Goodman, T., & Spry, C. (2017). Chapter 1 Introduction to Perioperative Nursing. In *Essentials of perioperative nursing*. Burlington, MA: Jones & Bartlett Learning.
12. Smith, V., Gallagher, L., Carroll, M., Hannon, K., & Begley, C. (2019). Antenatal and intrapartum interventions for reducing caesarean section, promoting vaginal birth, and reducing fear of childbirth: An overview of systematic reviews. *Plos One*, *14*(10). https://doi-org.proxy1.lib.uwo.ca/10.1371/journal.pone.0224313
13. Wilson, A., Lissauer, D., Thangaratinam, S., Khan, K.S., MacArthur, C., & Coomarasamy, A. (2011). A comparison of clinical officers with medical doctors on outcomes of caesarean section in the developing world: Meta-analysis of controlled studies. *BMJ*, *342*, d2600. https://doi-org.proxy1.lib.uwo.ca/10.1136/bmj.d2600
14. Walsh, C.A., & Walsh, S.R. (2009). Extraabdominal vs intraabdominal uterine repair at cesarean delivery: a metaanalysis. *American Journal of Obstetrics and Gynecology*, *200*, 625.e1-625.e8. https://doi-org.proxy1.lib.uwo.ca/10.1016/j.ajog.2009.01.009
15. Su, L.L., Chong, Y.S., & Samuel M. (2012). Carbetocin for preventing postpartum haemorrhage. *Cochrane database of systematic reviews (Online)*, *2*, CD005457. https://doi-org.proxy1.lib.uwo.ca/10.1002/14651858.CD005457.pub3
16. Sobhy, S., Zamora, J., Dharmarajah, K., Arroyo-Manzano, D., Wilson, M., Navaratnarajah, R., et al (2016). Anaesthesia-related maternal mortality in low-income and middle-income countries: A systematic review and meta-analysis. *The Lancet Global Health*, *4*, e320-e327. https://doi-org.proxy1.lib.uwo.ca/10.1016/S2214-109X(16)30003-1
17. Paranjothy, S., Griffiths, J.D., Broughton, H.K., Gyte, G.M.L., Brown, H.C., & Thomas, J. (2014). Interventions at caesarean section for reducing the risk of aspiration pneumonitis. *Cochrane Database of Systematic Reviews*, *2014*, CD004943. https://doi-org.proxy1.lib.uwo.ca/10.1002/14651858.CD004943.pub4
18. Ferrer, P., Roberts, I., Sydenham, E., Blackhall, K., & Shakur, H. (2009). Anti-fibrinolytic agents in post partum haemorrhage: A systematic review. *BMC Pregnancy and Childbirth*, *9*, 29. https://doi-org.proxy1.lib.uwo.ca/10.1186/1471-2393-9-29
19. Novikova, N., Hofmeyr, G.J., & Cluver C. (2015). Tranexamic acid for preventing postpartum haemorrhage. *Cochrane Database of Systematic Reviews*, *2015*, (6), CD007872. https://doi-org.proxy1.lib.uwo.ca/10.1002/14651858.CD007872.pub3

20. Moramarco, V., Korale Liyanage, S., Ninan, K., Mukerji, A., McDonald, S. D., V., M., … McDonald, S. D. (2019). Classical Caesarean: What Are the Maternal and Infant Risks Compared With Low Transverse Caesarean in Preterm Birth, and Subsequent Uterine Rupture Risks? A Systematic Review and Meta-analysis. *Journal of Obstetrics and Gynaecology Canada : JOGC = Journal d'obstetrique et Gynecologie Du Canada : JOGC*, *42*(2), 179–197.e3. https://doi-org.proxy1.lib.uwo.ca/10.1016/j.jogc.2019.02.015
21. Mackeen, A.D., Packard, R.E., Ota, E., Berghella, V., & Baxter, J.K. (2014). Timing of intravenous prophylactic antibiotics for preventing postpartum infectious morbidity in women undergoing cesarean delivery. *The Cochrane database of systematic reviews*, (12), CD009516. https://doi-org.proxy1.lib.uwo.ca/10.1002/14651858.CD009516.pub2
22. Mathai, M., Hofmeyr, G.J., & Mathai, N.E. (2013). Abdominal surgical incisions for caesarean section. *The Cochrane database of systematic reviews*, (5), CD004453. https://doi-org.proxy1.lib.uwo.ca/10.1002/14651858.CD004453.pub3
23. Hofmeyr, G.J., Mathai, M., Shah, A.N., & Novikova, N. (2008). Techniques for caesarean section. *The Cochrane database of systematic reviews*, (1), CD004662. https://doi-org.proxy1.lib.uwo.ca/10.1002/14651858.CD004662.pub2
24. Hadiati, D.R., Hakimi, M., Nurdiati, D.S., Da Silva Lopes, K., & Ota, E. (2018). Skin preparation for preventing infection following caesarean section. *The Cochrane database of systematic reviews*, *10*(10), CD007462. https://doi-org.proxy1.lib.uwo.ca/10.1002/14651858.CD007462.pub4
25. Shakur, H., Beaumont, D., Pavord, S., Gayet-Ageron, A., Ker, K., & Mousa, H.A. (2018). Antifibrinolytic drugs for treating primary postpartum haemorrhage. *The Cochrane database of systematic reviews*, *2*(2), CD012964. https://doi-org.proxy1.lib.uwo.ca/10.1002/14651858.CD012964
26. Gallos, I.D., Papadopoulou, A., Man, R., Athanasopoulos, N., Tobias, A., Price, M.J., et al. (2018). Uterotonic agents for preventing postpartum haemorrhage: a network meta-analysis. *The Cochrane database of systematic reviews*, *12*(12), CD011689. https://doi-org.proxy1.lib.uwo.ca/10.1002/14651858.CD011689.pub3
27. Cluver, C., Novikova, N., Hofmeyr, G.J., & Hall, D.R. (2013). Maternal position during caesarean section for preventing maternal and neonatal complications. *The Cochrane database of systematic reviews*, (3), CD007623. https://doi-org.proxy1.lib.uwo.ca/10.1002/14651858.CD007623.pub3
28. Bain, E., Wilson, A., Tooher, R., Gates, S., Davis, L.J., & Middleton, P. (2014). Prophylaxis for venous thromboembolic disease in pregnancy and the early postnatal period. *The Cochrane database of systematic reviews*, (2), CD001689. https://doi-org.proxy1.lib.uwo.ca/10.1002/14651858.CD001689.pub3
29. Afolabi, B.B., & Lesi, F.E. (2012). Regional versus general anaesthesia for caesarean section. *The Cochrane database of systematic reviews*, *10*, CD004350. https://doi-org.proxy1.lib.uwo.ca/10.1002/14651858.CD004350.pub3
30. Alam, A., & Choi, S. (2015). Prophylactic Use of Tranexamic Acid for Postpartum Bleeding Outcomes: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Transfusion medicine reviews*, *29*(4), 231–241. https://doi-org.proxy1.lib.uwo.ca/10.1016/j.tmrv.2015.07.002

31. Gates, S., & Anderson, E.R. (2013). Wound drainage for caesarean section. *The Cochrane database of systematic reviews*, (12), CD004549. https://doi-org.proxy1.lib.uwo.ca/10.1002/14651858.CD004549.pub3
32. Sobhy, S., Dharmarajah, K., Arroyo-Manzano, D., Navanatnarajah, R., Noblet, J., Zamora, J., et al. (2017). Type of obstetric anesthesia administered and complications in women with preeclampsia in low- and middle-income countries: A systematic review. *Hypertension in pregnancy*, *36*(4), 326–336. https://doi-org.proxy1.lib.uwo.ca/10.1080/10641955.2017.1389951
33. World Health Organization. Maternal mortality ratio (per 100 000 live births). (2014, March 11). Retrieved August 14, 2020, from https://www.who.int/healthinfo/statistics/indmaternalmortality/en/
34. Liberati, A., Altman, D. G., Tetzlaff, J., Mulrow, C., Gøtzsche, P. C., Ioannidis, J. P., Clarke, M., Devereaux, P. J., Kleijnen, J., & Moher, D. (2009). The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ (Clinical research ed.)*, *339*, b2700. https://doi.org/10.1136/bmj.b2700
35. The World Bank. World Bank Country and Lending Groups. Retrieved September 15, 2019, from https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups

Chapter 3 - Perioperative maternal and neonatal mortality associated with caesarean section: a systematic review and meta-analysis

3 INTRODUCTION

Mortality remains one of the most-feared complications of caesarean section. However, the magnitude of risk of death and temporal patterns associated with caesarean section across global contexts is not fully understood. Reduction in maternal mortality was a high priority during the time of the millennium development goals (MDGs) and continues to be a key aspect of the sustainable development goals (SDGs).[1] In 2017, approximately 295,000 women died during and following pregnancy and childbirth.[2] Of these deaths, 94% took place within low resource settings.[2] Safe access to caesarean section for women who require the procedure, as well as a reduction in the rates of unnecessary caesarean sections, are crucial for improving maternal outcomes.[2] The World Health Organization (WHO) released guidelines in 2018 with the aim of steadily reducing excessive rates of caesarean section globally in an effort to decrease preventable maternal mortality.[3]

Worldwide, approximately 18.5 million caesarean sections are performed each year.[33] Caesarean section rates exceed 15% in half of countries globally.[9] In the most severely resource-restricted regions of the world, the rate of caesarean sections was approximately 6% from 1990-2014, which is significantly lower than other regions globally.[5] Due to the fact that a small proportion of these obstetric procedures are conducted in resource-restricted settings, there is a considerable scarcity of research to evaluate caesarean attributed mortality across the full spectrum of global regions.[6,7] A global, comprehensive systematic analysis of the trends in caesarean attributed maternal and neonatal mortality over time and according to country development status is required.

A summary of the magnitude of perioperative maternal and neonatal mortality is vital to allow for the improvement and development of health policies geared towards maternal and neonatal health. A previous systematic review of maternal and perinatal mortality was exclusively focused on low and middle-income countries, without assessment across the full range of low to high-income countries. [10] Our analysis aims to

update this review by further investigating maternal and neonatal mortality associated with caesarean section over time across the spectrum of low, middle, and high-income countries. As the safety of caesarean sections increases, maternal mortality associated with the obstetric procedure is becoming increasingly rare. This rarity highlights the need for pooled effects through comprehensive systematic review and meta-analysis in order to achieve sufficient power to detect trends over time and across settings. Thus, we undertook a systematic review to provide updated estimates of the risk of maternal and neonatal mortality during or following caesarean section, and to analyze whether the magnitude of effect for mortality changes over time and by the human development index (HDI) status of the country.

3.1 METHODS

For this systematic review and meta-analysis, a prospective protocol in line with current recommendations was used and we reported the review as per the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines.[11,12] The study protocol has been registered with PROSPERO, number CRD42020164224.

3.1.1 Search strategy

An extensive search was conducted using multiple sources, including scientific and grey literature databases, from inception until November 21, 2019. The databases searched included EMBASE, MEDLINE, Cochrane Central, Web of science, SCOPUS, CINHAL, WHOLIS, WHO IRIS, WHO Reproductive Health Library, CAB Direct, PAIS Index, Global Index Medicus, African journals online, and Global Health Data Exchange. The grey literature databases were composed of OAIster/WorldCat, OpenGrey, Centre for Research Libraries Global Resource Network, EU Open Data Portal, and Latin American open Archives Portal. The theses and dissertations databases included Open Access Theses and Dissertations (OATD), EThOS, and DART. In addition, we selected ten highly-relevant studies and additionally conducted forward and backward citation tracking for the first 100 references.

Database searches were conducted with the use of controlled subject terms specific to each database (i.e.caesarean section, maternal mortality and cause of death). We also used key words and word variants for caesarean section (e.g. c?esar?an*, CSection*, C-Section?*, abdominal deliver*, and abdominal birth*) and maternal mortality (e.g. maternal mortal*, maternal death*, pregnan* death*, and wom?n death*). Additionally, word variants along with searches by adjacency for cause of death (e.g. cause* or factor* or contribut* or manor* adjacent mortal* or death*) were combined with the terms for caesarean section and maternal mortality. Subject terms and key words were used in order to limit studies to those that were only conducted on humans. Language or date restrictions were not imposed. The full search strategies for each database are provided in APPENDIX D.

3.1.2 Screening and inclusion criteria

Selection of studies occurred in two levels. In level one, one reviewer screened the titles and abstracts of all citations for potentially relevant papers with the use of Mendeley. We attempted to maximize sensitivity, and only studies that were not related to caesarean section and maternal mortality were excluded during level one screening. In level two, full text articles were assessed by one independent reviewer (AH) who applied the pre-specified inclusion and exclusion criteria. Studies were included in the review if they were randomized controlled trials (RCTs) or observational studies, if the study population included women who underwent or were planned to undergo elective or emergency caesarean section, and if they reported the outcome of maternal mortality. Of the studies that reported maternal mortality, the primary outcome of neonatal mortality was also included. The primary outcome of perioperative maternal mortality (POMMR) was defined as death of a woman from any cause, occurring any time between the start of the procedure or start of anesthesia until hospital discharge or 42 days of follow-up after caesarean section. Perioperative neonatal mortality (PONMR) was also planned as an additional primary outcome, and was defined as death during the first 28 days of life per births by caesarean section.

Studies were excluded if they were case-control studies, ecological studies, book chapters, editorials, if the population was pregnant women only undergoing vaginal delivery, if they examined only maternal mortality unrelated to caesarean section, or if the studies examined mortality more than 42 days after caesarean section. Studies that reported on mixed populations (vaginal delivery and caesarean section) were excluded if the data for the caesarean section subgroup was not reported separately. As the aim of this review was to assess the outcome in all patients undergoing caesarean section, studies that exclusively reported on high-risk groups (i.e. Women with pre-eclampsia, HELLP syndrome, multiple caesarean sections, etc.) were excluded. Studies that provided an estimated number of total caesarean sections rather than an actual denominator and studies that reported adjusted maternal or neonatal mortality rates without crude data were excluded. Non-human studies and simulation studies were excluded.

Due to the epidemiologic nature of our research question, we expected most eligible studies would be descriptive cohorts of caesarean section outcomes with no interventional trials or control-led studies. Comparative studies or randomized controlled trials (RCTs) were eligible for inclusion; however, if the study arm tested a specific intervention that was not considered standard of care, or if there was a differential effect on maternal mortality in the intervention group as compared to the control group, then the intervention arm would be excluded.

3.1.3 Data extraction and critical appraisal

One reviewer (AH) independently extracted data using a data extraction form developed and pilot tested a priori. From the eligible studies, information was extracted on: year of recruitment, study authors, study objective, study design, setting of hospital (urban, rural or both), type of hospital, country of study, observational period, source of sample, data collection method, number of women undergoing caesarean section, total number of maternal deaths during or after caesarean section from any cause, time of death, urgency (elective vs emergency), and maternal characteristics such as: American Society of Anesthesiologists (ASA) physical status score, and any other reported

maternal/obstetric co-morbidity score. Assessment of the quality of the included studies was conducted by one independent reviewer (AH) with the use of the following domains: 1) reporting of the definition of maternal mortality in order to reduce any bias associated with the ascertainment of numerator data (adequate if any published definition was reported vs inadequate if no definition was reported); 2) sample selection was considered acceptable if the population included all consecutive women or a random sample of women who undergo or are planning to undergo a caesarean section, and unacceptable if the population consisted of a certain subgroup of women (i.e. women undergoing emergency caesarean section); 3) adequacy of data sources for outcome assessment to ascertain complete numerator data (registry data such as health records, surgical logbooks, or clinical notes were considered adequate vs verbal autopsies from women or relatives were considered inadequate); 4) A high proportion of cases with cause of death reported (<5% not reported) were deemed adequate. If three of the four domains were met then a study was categorized as high quality.[10,14]

The Human Development Index (HDI) created by the United Nations (UN) was used to assign development status to countries.[13] This index assesses the development of country through the people and their capabilities rather than merely through economic growth; it is a composite index for indicators of per capita income, education and life expectancy.[13] As HDI is an index that changes over time, assignment of HDI was based on the specific time period in which the study was conducted. If a country does not have HDI data available for a required year, then the available HDI closest to that year was used.

3.1.4 Data analysis

Maternal deaths were reported as perioperative maternal mortality ratios (POMMR) per 100,000 caesarean sections, along with their 95% CI. Neonatal deaths were reported as perioperative neonatal mortality ratios (PONMR) per 100,000 caesarean sections, along with their 95% CI. Both a fixed effect model along with a random effects model were run in order to weight the mortality ratios across all the studies. Weighting across studies was addressed in two ways, in order to understand the effect of analytic

choice on effect size estimates. First, ratios were calculated using a fixed effect model for the primary analysis. Then ratios were also calculated using a random effects model as a sensitivity analysis. Meta-regression was conducted with the use of method of moments in order to investigate changes in mortality ratios by time and by HDI. The year in which patients were recruited was used to assess variations in mortality ratio over time. If data were provided over a range of years, then the median year of the time interval was used as the year of recruitment. Subgroup analyses were also performed to report on ratios for each dual-decade era (pre-1970s, 1970-1980s, 1990-2000s, and 2010-2020s). Similarly, subgroup analyses were performed for mortality ratios per 100,000 caesarean sections for HDI categories, defined as high (≥0·8) or low (<0·8) HDI. Additionally, subgroup analysis was also conducted for type of hospital. We used the test for heterogeneity between subgroups to identify if there was a significant difference in the effect sizes between subgroups. We ran sensitivity analyses for prospective versus retrospective data collection, variations in year of recruitment within era groups (i.e. For example, if in pre-1970s majority of studies from 1970s and a few from 1960s) and by excluding studies that investigated specific subgroups of women (e.g. Only regional/general anesthesia or emergency/elective surgeries).

Publication bias and small studies effect were assessed with funnel plots that represented the mortality ratios on a logit scale versus their standard error. Funnel asymmetry was assessed with the Egger's test. Statistical heterogeneity was evaluated with I^2, which represents the percentage of variability between studies that is not solely due to chance.[15] If the I^2 value was greater than 30% than we concluded that there was statistical heterogeneity present between the studies. Analyses were conducted with the use of Stata version 16.

3.2 RESULTS

A total of 10,658 studies were identified from database searches. Additionally, 373 studies were identified from grey literature sources, including thesis and dissertations, and reports from Global Health Data Exchange. After the removal of duplicates, 6052 studies were remaining. 5426 titles and abstracts were excluded as they

were not primary studies, their population was not women who undergo or are planning to undergo a caesarean section, or their outcomes did not include maternal mortality. After title and abstract screening, 626 studies for full-text review remained; of these studies, 489 were excluded as a result of the prespecified inclusion/exclusion criteria. The final sample of 196 studies was included in the systematic review and meta-analysis; this includes 59 studies obtained from forward and backward citation tracking. Please refer to Figure 3.1 PRISMA flow-chart for more details on the screening and study selection process used for this systematic review and meta-analysis.

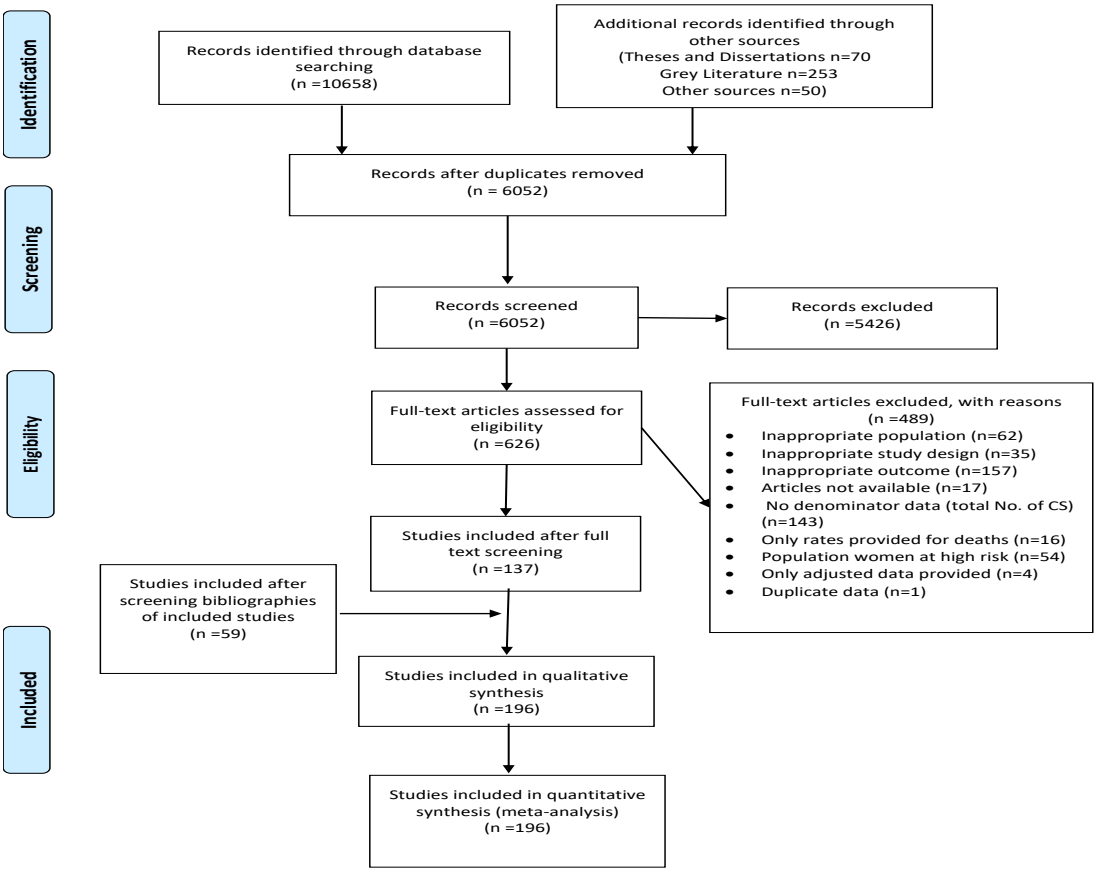


Figure 3.1 PRISMA flow diagram for study identification

3.2.1 Description of studies

Of the 196 studies included in the review, 86.2% (169/196) were from countries with low HDI and 13.8% (27/196) were from countries of high HDI. Of the 196 included

studies, data were provided for 67 countries. Most studies took place in Nigeria (37/196, 18.9%). Eight studies were multi-centre studies. Of the studies that identified type of hospital, 55.4% (93/168) involved tertiary/teaching hospital settings. In total, 22% (43/196) of the included studies also reported neonatal mortality. The timing of maternal death was reported in 39 studies, with 24.6% of studies reporting on intraoperative mortality, 37.7% reporting 24-hour mortality, and 37.7% reporting mortality at 30- to 42-day follow-up. Urgency of caesarean section was identified in 81 studies. In total, 54.3% of the women underwent emergency caesarean section, and 45.7% underwent elective caesarean section. Types of anesthesia used for the obstetric procedure were reported in 45 studies. In total, 56.2% of caesarean sections were conducted under regional anesthesia, and 43.8% were conducted under general anesthesia. APPENDIX E: Table 4 shows the characteristics of the included studies. One randomized controlled trial was included in the analysis however, only the control arm was eligible as the intervention arm showed a differential effect on maternal mortality as compared to the control arm.[8] For subgroup analysis of HDI status, we assumed the HDI category for POMMR data from one study as no information was provided on the countries in which the study was performed.[34] Conversely, we obtained an approximate HDI, given the information on annual per capita income quoted from the study in order to attain an analogous HDI.[34]

3.2.2 Quality assessment

Among the 196 included studies, 54% were of high quality (Figure 3.2). For the domain of ‘outcome assessment’, nearly all the studies were deemed high quality (90%; Figure 3.2). 84% of the studies met the criteria for adequate sample selection and 62% obtained a sufficiently high proportion of cases in which cause of death was established. The definition of maternal mortality was clearly reported in only 20% of studies. Complete details of quality assessment for the included studies are provided in Appendix E: Table 5.

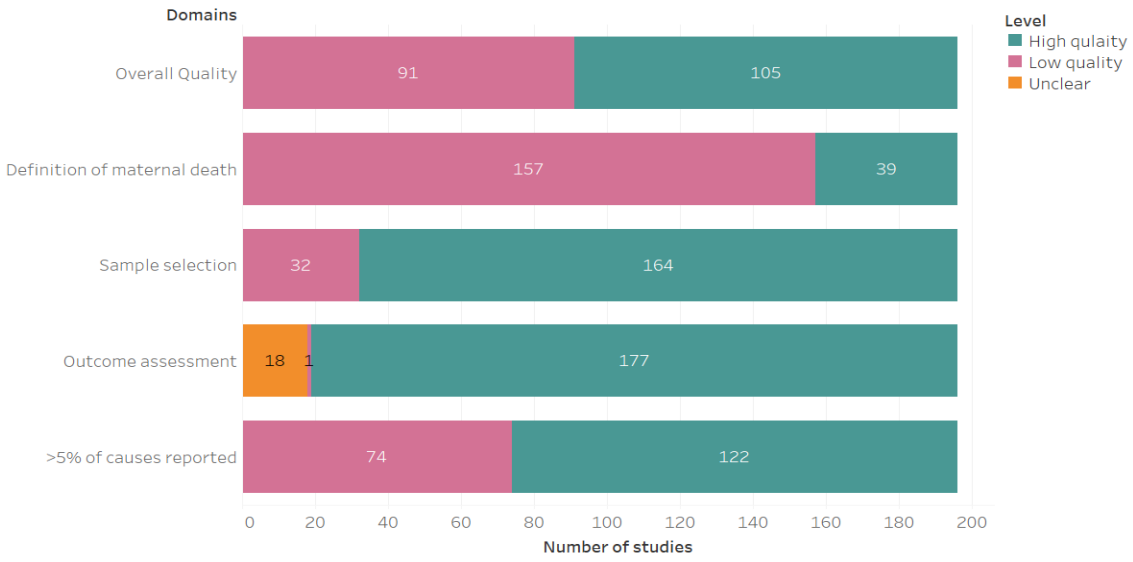


Figure 3.2 Quality of studies on perioperative maternal and neonatal mortality

3.2.3 Perioperative maternal mortality (POMMR)

In total, for every 100,000 women undergoing a caesarean section, 10.82 died (95% CI 9.78-11.89) during follow-up. Statistical heterogeneity for all event ratios was high (I^2 >50%). A gradual decrease in the risk of perioperative maternal mortality associated with caesarean section was identified throughout the decades. Prior to 1970 the risk was 84.92 per 100,000 (95% CI 73.73-96.74), decreasing to 26.68 per 100,000 (95% CI 23.46-30.05) in the 1970s-1980s, 12.49 per 100,000 (95% CI 10.46-14.67) in the 1990s-2000s, and 3.28 per 100,000 (95% CI 2.43-4.24) in the 2010s-2020s (Table 3.1). A statistically significant difference was present between the event ratios for each decade ($p<0.00001$). Although, on meta-regression, the association between year and POMMR was not significant ($p=0.351$; APPENDIX F: Figure 2).

On subgroup analysis, high HDI countries decrease in the risk of perioperative maternal mortality from before the 1970s (41.78 per 100,000 (95% CI 31.50-53.12)) to the 1990s-2000s (14.58 per 100,000 (95% CI 12.45-16.86)). However, this decline was not progressive as there was a slight increase in the risk of perioperative maternal mortality in the 1980s-1990s (47.72 per 100,000 (95% CI 42.58-53.13)) and no data were available for 2010s-2020s. Subgroup analysis of low HDI countries exhibited the same

temporal trend, with a decline from pre-1970s to 2010s-2020s, and a spike in the risk of perioperative maternal mortality in the 1990s-2000s (p<0.00001).

	Number of Studies	Events	POMMR per 100,000 (95% CI)	p value for heterogeneity between sub-groups	
				By HDI	By decade
Pre-1970s	24	572/325422	84.92 (73.73-96.74)		<0.00001
High HDI	11	262/219080	41.78 (31.50-53.12)	<0.00001	
Low HDI	13	310/106342	197.42 (169.86-226.79)		
1970s-1980s	30	894/1472662	26.68 (23.46-30.05)		
High HDI	9	375/709826	47.72 (42.58-53.13)	0.031	
Low HDI	21	519/762836	17.47 (13.60-21.71)		
1990s-2000s	103	3764/2771364	12.49 (10.46-14.67)		
High HDI	7	216/1254932	14.58 (12.45-16.86)	<0.00001	
Low HDI	96	3548/1516432	77.95 (72.24-83.83)		
2010s-2020s	39	3811/4766859	3.28 (2.43-4.24)		
High HDI	NR	NR	NR	N/A	
Low HDI	39	3811/4766859	3.28 (2.43-4.24)		
Overall	196	9041/9336235	10.82 (9.78-11.89)		

HDI=human development index. NR=not reported. N/A=not available.

Table 3.1 Perioperative maternal mortality in women undergoing caesarean section in low and high HDI countries

Type of hospital	Number of Studies	Events	POMMR per 100,000 (95% CI)	p value for heterogeneity between sub-groups
				By hospital type
Teaching/tertiary	93	1372/477452	55.33 (46.59-64.62)	<0.00001
Mixed	40	5999/7759403	27.86 (26.35-29.39)	
Private	3	85/22531	324.53 (248.90-408.78)	
Public	5	230/443861	10.70 (6.43-15.80)	
District	16	260/28501	694.57 (596.78-799.05)	
Referral	10	250/32564	406.60 (330.33-489.10)	
Military	1	0/1339	0.00 (0.00-286.07)	

Table 3.2 Type of hospital and the risk of perioperative maternal mortality in women undergoing caesarean section

After combining the data from all decades, the assessment of the risk of POMMR by HDI through meta-regression identified a progressive decrease in POMMR as HDI increased (p<0.00001; APPENDIX F: Figure 3). The POMMR in low HDI countries was approximately 5 times higher than in high HDI countries (197.42 per 100,000 (95% CI

169.86-226.79) vs 41.78 per 100,000 (95% CI 31.50-53.12)) before the 1970s and in the 1990s-2000s (77.95 per 100,000 (95% CI 72.24-83.83) vs 14.58 per 100,000 (95% CI 12.45-16.86)). During the 1980s-1990s countries of high HDI exhibited approximately a 3 times higher risk of POMMR as compared to low HDI (47.72 per 100,000 (95% CI 42.58-53.13) vs 17.47 per 100,000 (95% CI 13.60-21.71)). Countries of high HDI in the 2010s-2020s were not adequately represented for sub-analysis. The risk of perioperative maternal morality was higher in district hospitals as compared to any other type of hospital (694.57 per 100,000 (95% CI 596.78-799.05); $p<0.00001$ Table 3.2). When we performed sensitivity analysis excluding studies that exclusively evaluated regional/general anesthesia or emergency/elective surgeries, the results did not materially change (APPENDIX F: Table 7). Additionally, in sensitivity analysis, POMMR results were not materially different for prospective versus retrospective studies (APPENDIX F: Table 9). For prospective data collection there were significant differences in terms of the type of hospital and the lack of a statistical significance between HDI categories before 1970s; the other results were not sensitive to this form of data collection as similar conclusions were attained (APPENDIX F: Table 8). As there were only a few studies before 1960 we conducted a sensitively analysis by removing those studies, and the results were not sensitive to the exclusion of these studies (APPENDIX F: Table 10). The event ratios were sensitive to the model used (APPENDIX F, Table 6).

3.2.4 Perioperative neonatal mortality (PONMR)

PONMR was 566.66 per 100,000 caesarean sections (95% CI 533.57-600.60), statistical heterogeneity was high for all event ratios (I^2 >50%). Throughout the decades, the PONMR fluctuated with no progressive decline or incline. Before 1970 the event ratio was 2775.68 per 100,000 (95% CI 2346.03-3239.73) and in the 1970s-1980s there was a decline in the risk (56.84 per 100,000 (95% CI 25.38-97.22)) (Table 3.3). Continuing through the decades in the 1990s-2000s the risk of PONMR increased again (867.10 per 100,000 (95% CI 813.73-921.95)) and decreased in the 2010s to 2020s (292.11 per 100,000 (95% CI 248.73-338.37)). A statistically significant difference between the risks of perioperative neonatal mortality across each decade was present

(p<0.00001). Meta-regression over time indicates a stable PONMR as years increase without statistical significance in the trend over time (p=0.937; APPENDIX F: Figure 4).

Data for high HDI countries was only available before the 1970s, and other decades lacked this information. As a result, the temporal trends for low HDI countries considered alone were the same as the overall trends between the decades.

	Number of studies	Events	PONMR per 100,000 (95% CI)	p value for heterogeneity between sub-groups	
				By HDI	By decade
Pre-1970s	3	157/5271	2775.68 (2346.03-3239.73)		
High HDI	1	100/3500	2857.14 (2354.78-3462.87)	0.738	
Low HDI	2	57/1771	2656.04 (1950.83-3463.90)		
1970s-1980s	3	58/24564	56.84 (25.38-97.22)		
High HDI	NR	NR	NR	N/A	
Low HDI	3	58/24564	56.84 (25.38-97.22)		
1990s-2000s	29	1521/129966	867.10 (813.73-921.95)		
High HDI	NR	NR	NR	N/A	
Low HDI	29	2050/198434	867.10 (813.73-921.95)		
2010s-2020s	8	529/68357	292.11 (248.73-338.37)		
High HDI	NR	NR	NR	N/A	
Low HDI	8	529/68357	292.11 (248.73-338.37)		
Overall	43	2265/228158	566.66 (533.57-600.60)		

HDI=human development index. NR=not reported. N/A=not available.

Table 3.3 Neonatal mortality after caesarean sections in low and high HDI countries

Type of hospital	Number of studies	Events	PONMR per 100,000 (95% CI)	p value for heterogeneity between sub-groups
				By hospital type
Mixed	6	1071/81542	1135.53 (1060.28-1213.10)	
Private	1	16/1140	1403.51 (865.73-2267.69)	
Public	1	2/392	510.20 (140.03-1840.93)	<0·00001
District	4	263/7301	2114.85 (1794.07-2460.82)	
Referral	4	124/18034	471.35 (370.74-582.62)	

Table 3.4 Type of hospital and the risk of neonatal mortality after caesarean section

Meta-regression for the risk of PONMR by HDI indicated that as HDI increased there was a decline in PONMR (p=0.029; APPENDIX F: Figure 5). Before the 1970s the PONMR for both high and low HDI were not significantly different (p=0.738). Due to the inadequate representation of high HDI countries within the remaining decades sub-analysis for the risk of PONMR between the HDI categories could not be conducted. Similar to POMMR, perioperative neonatal mortality was higher in district hospitals (2114.85 per 100,000 (95% CI 1794.07-2460.82)) than other type of hospital (p<0·00001; Table 3.4). Sensitivity analysis for prospective and retrospective data collection produced effect estimates and conclusions that were not similar to the main analysis. Therefore, the results were sensitive to the method of data collection. Since the studies that examined neonatal mortality did not have populations with specific subgroups or studies before the 1960s sensitivity analysis for those two items were not conducted. The event ratios were sensitive to the model used (APPENDIX F, Table 13).

Evidence of small study effect was present for POMMR (Egger's test p=0.002; APPENDIX F: Figure 6), but not for PONMR (Egger's test p=0.802; APPENDIX F: Figure 7).

3.3 DISCUSSION

This systematic review and meta-analysis provides a global view of the risk of perioperative maternal and neonatal mortality, and illustrates how these risks change over time, by HDI countries, and by type of hospital. Over the past 70 years there has been a consistent reduction in the risk of perioperative maternal mortality, whereas the risk of perioperative neonatal mortality has fluctuated with no progressive increase or decrease. Within high HDI countries, the reduction of perioperative maternal mortality throughout the decades was far greater than in low HDI countries, with the exception of the 1970s-1980s in which countries of high HDI had a higher risk of perioperative maternal mortality. Due to the absence of data from high HDI countries for perioperative neonatal mortality, the rate of decline based on low vs high HDI countries could not be analyzed over time.

The pursuit of increased patient safety throughout the years for caesarean deliveries has resulted in various achievements within perioperative care that has allowed for precipitous reduction in POMMR, especially in countries of high HDI in most decades. An example of perioperative improvements includes safer approaches to anesthesia, which has resulted in a 30-fold increase in the safety of anesthesia administered for elective caesarean section relative to the 1960s.[26] Additionally, various preoperative assessments, such as hemoglobin levels of the mother, functionality checks for neonatal recitation equipment, and input from neonatology, have been put into place within obstetric theatres.[4] These practices, along with robust quality control, adequate training of clinicians, and evidence-based guidelines for perioperative care,[16] have likely contributed to the observed trends. Unfortunately, these hypotheses could not be further tested within the analyses as there was insufficient details within the studies.

The rates of caesarean sections have been increasing over time in both low and high HDI countries.[5] In the low HDI regions, the rates of caesarean section as a proportion of births have increased from 1.9% in 1990 to 6.1% in 2014. However, in the high HDI regions, caesarean section rates for 1990 were 14.5%, and in 2014 they had risen to 27.2%.[5] These increasing rates of caesarean section globally have prompted the WHO, along with other medical organizations, to propose interventions to reduce the rates of unnecessary caesarean sections in high-resource settings, and to improve access to medically necessary caesarean sections in low-resource settings. These interventions include continued labour support, attempts to increase trial of labour after a caesarean section, changes in financial incentives, as well as other interventions that are either specifically targeted toward parturients, health care professionals, or organizations.[3,19] These efforts to reduce the rates of caesarean section may have also contributed to the declines in perioperative maternal mortality over the last few decades. During the 1970s-1980s the global rates of caesarean section were increasing, and in high HDI countries the rates were increasing at a more rapid pace than low HDI countries. This is where the concept of too much, too soon comes into play. Within this decade the quality of care, technologies, training, and personnel were not sufficiently advanced and were similar to those in low HDI countries now.[18] Consequently, the increasing surge in caesarean

sections at that time, coupled with the lack of resources and training to allow for safe caesarean sections, may have resulted in the slight increase in perioperative maternal mortality in high HDI countries in the 1970s-1980s. Inappropriate or excessive use of the intervention may have provided more harm than benefit. For example, overuse of caesarean section may lead to uterine rupture, anal sphincter injury, perinatal lacerations and uterine prolapse, particularly when the procedure is medically-unnecessary or unlikely to be life-saving.[18] On the other hand, the increase in perioperative maternal mortality from the 1970s-1980s to the 1990s-2000s may be attributed to the opposing idea of too little, too late.[18] During this time period, the rates of caesarean section within low HDI countries were increasing, but at a slower pace, indicating that there may be inadequate access to caesarean section for life-threatening conditions, or that the women presented too late to benefit from the procedure. Conversely, an absence of resources, skilled providers, and antenatal and perioperative care may have heightened the risk of maternal mortality if caesarean section was available, but was provided unsafely.[19] Furthermore, another rationale for the increasing risk in low HDI countries during the 1990s-2000s may be because most of the research was conducted during this decade, which may have skewed the findings. Although a link is present between maternal and neonatal outcomes, the risk of perioperative neonatal mortality did decrease overall from before the 1970s to the 2010s-2020s. However, this reduction was not progressive, as there were continuous fluctuations throughout the decades. As most of our data for perioperative neonatal mortality was from low HDI countries, these conclusions are mainly geared towards those regions, and may not be applicable to high HDI countries. These findings imply that there may be a lack of continuum of care from the mother to the neonate, and efforts to enhance the safety of newborns may have fallen through the cracks, especially in low HDI countries. The first week of life is the most critical period for a newborn, and yet insufficient efforts to handle specific health issues of newborn babies after caesarean section may still be present.

The consistent decline in perioperative maternal mortality over the years indicates that global efforts to improve safe access and quality of caesarean section through means of improving deficiencies in health systems, which may include: providing sufficient

supplies and drugs to allow healthcare providers to deliver cost-effective and evidence-based interventions, adequate training and number of skilled providers, presence of guidelines for evidence-based care, surgical safety checklists, along with the prevention of postpartum haemorrhage, sepsis, hypertensive disorders and enhanced management of anesthesia, operative techniques, hypothermia, thromboembolism and glucose levels may cooperatively be interpreted as providing improvements in maternal outcomes..[27,29,30,31] On the other hand, the fluctuations and the absence of a reduced progression in perioperative neonatal mortality indicates that in low resource settings there may be a lack of interventions delivered along with low-quality of care during delivery, postpartum and within the postnatal periods. In order to improve survival and enhance the safety of neonates after caesarean section in countries of low HDI deliveries should be conducted in facilities that are well equipped with high-quality of care. Investments geared towards health infrastructure and training of skilled birth attendants are required in order to provide lifesaving interventions during caesarean section and the first week of life. Additionally, improvements in postnatal care interventions should be scaled up. In order to continually observe the results of these efforts for the improvements in patient safety, care and access to caesarean section, updates of this research should be conducted in order to capture more data from the recent decade especially in countries of high HDI. These continued updates will provide a global overview of the trends in maternal and neonatal mortality associated with caesarean section and will provide a measure that represents the global safety efforts for caesarean section.

The rates of decline for perioperative maternal mortality associated with caesarean section vary largely depending on HDI status, and countries with high HDI have lower rates of maternal mortality within most decades. Increases in investments for obstetric health, coupled with the availability of supplies, essential drugs, equipment, referral systems along with skilled prenatal, antenatal and postnatal care are more commonly prevalent in countries that are in higher resource settings. Higher risks of maternal and neonatal mortality during or following caesarean section in low resource settings have been attributed to inadequate technology, insufficient surgical and anesthetic skills, delayed interventions, deficiency of blood transfusion along with

consistent use of general rather than regional anesthesia.[32] Additionally, variations in the composition of patient populations between countries of high and low HDI may contribute to these results – in resource-restricted countries women tend to have predisposing health conditions, complications as a result of delayed diagnosis and interventions, and high-risk pregnancies that require emergency caesarean section.[28] We were unable to further analyze the outcomes based on characteristics of the patient population due to a lack of data. Further research should be conducted in order to test this hypothesis. The increase in perioperative maternal mortality in the 1970s-1980s in countries of high HDI may be a result of increased rates of caesarean section, as compared to countries of low HDI and an inability to cope with the increase due to limitation in the quality of care at the time.[20] For the risk of perioperative neonatal mortality, the presence or absence of discrepancies between countries of low vs high HDI could not be evaluated due to insufficient data.

The risk of maternal and neonatal mortality was higher in district hospitals, and this may be due to the fact that district hospitals are the first point of referral for primary maternity services.[21] Delays in receiving adequate care and treatment at the optimum time for high risk and emergency cases may be detrimental to the health of the mother and neonate, and the risk is increased if the district hospitals have limited resources, which is usually the case in low HDI countries.[22] Conversely, variations in the locations of the district hospitals may have an effect on the results; those located in rural areas or within low HDI settings may have poor infrastructure and vacancy of professional staff along with a patient population that is of higher risk, thereby increasing the risk of maternal and neonatal mortality as compared to urban settings and high HDI countries. Furthermore, in our analysis, all the studies that were conducted in district hospitals were from low HDI countries, this may have skewed the findings.

Caesarean sections are one of the most common surgeries performed worldwide, and may be, life-saving when indications for complications of pregnancy arise. However, this major surgery may also bring maternal and perinatal risks, both in the acute period, and over the longer term.[23,24] Furthermore, caesarean sections may have negative

implications on future pregnancies and deliveries, and may also be associated with long-term risks to both mother and child. Our analysis provides updated results to assist clinicians with evidence-based decision making when weighing the trade-offs, to mitigate potential harms. It will allow them to have a visual representation of the risks of maternal and neonatal mortality within recent decades and in their setting in order to weigh the potential risks and benefits.

At the end of 2015, the Sustainable Development Goals (SDGs) identified a target to reduce the maternal mortality ratio (MMR) below 70 per 100,000 livebirths globally along with an improvement in the health and lives of all individuals by 2030.[25] Despite various global interventions to reduce the impact of maternal and perinatal mortality due to complications of pregnancy and delivery, the magnitude of maternal mortality remains high in low resource settings as compared to high resource settings.[10] As indicated in our analysis, in most decades the risk of perioperative maternal mortality in low HDI countries was 5 times higher than high HDI countries. This implies that throughout various decades there exists gaps in the equity and equality of health care systems and access to safe caesarean sections, despite the efforts from the Millennium Development Goals (MDGs) and the ongoing SDG-3.[1] In 2015, the WHO emphasized that "Every effort should be made to provide caesarean sections to women in need, rather than striving to achieve a specific rate".[25] Providing maternal healthcare services that are evidence-based and high-quality, along with universal access to emergency obstetric procedures, should become a priority on the global health agenda. This will aid in reducing the inequality gap between high and low HDI countries, enhance limiting factors, and expand access to safer and higher-quality obstetric care. In order to enhance the outcome of perioperative neonatal mortality, a focus on the neonatal period also needs to be made a priority. Policy makers should address the causes of neonatal mortality after caesarean section, which differs from stillbirths.

This analysis updated a previous study that examined maternal and perinatal mortality following caesarean section in low- and middle-income countries.[10] Through backward citation tracking, we obtained additional primary studies from this synthesis

that were not captured within our search. We screened the studies to ensure they met our pre-defined inclusion/exclusion criteria. 116 studies were identified from the previous analysis on maternal deaths as a proportion of all caesarean sections,[10] whereas, in our analysis we identified 196 studies in low and high HDI countries. The overall risk of maternal mortality was smaller in our analysis, this may be because we included studies from high HDI countries. Similar to our analysis, this prior review found that the risk of maternal mortality associated with caesarean section was higher in low-income countries than middle-income countries. This review also reported that maternal mortality was higher in tertiary hospitals as compared to other hospitals, however, in our analysis we discovered that the risk of POMMR was higher in district hospitals than in other hospitals.[10] Additionally, they identified that there was no significant difference in the risk of maternal mortality based on year of study; they used year of publication for their analysis. However, within our analysis we reported a significant decrease in POMMR over time.

This synthesis is the first to analyze trends in maternal and neonatal mortality over time, and within high and low HDI countries. We conducted a comprehensive and extensive search within various databases and data sources in order to capture as many relevant studies as possible, both published and unpublished. More than half of the studies that we included in our review were of high quality based on the domains assessed. Clinical heterogeneity was evaluated through subgroup analyses and sensitivity analyses to explore robustness of the results. Patients of different age groups, with differing co-morbidities and indications of caesarean section were included in order to minimize selection bias and the effects of varying patient risk factors from populations in low versus high HDI countries. The trends in perioperative maternal and neonatal mortality were calculated individually in countries of low and high HDI in order to reduce confounding effects between countries within each category. Since patient-level data was generally unavailable, we were only able to obtain crude estimates of mortality and were unable to adjust for co-morbidities, and indications in caesarean section. Therefore, the results may have been subject to bias or confounding that varied throughout the decades. Few studies were identified from high HDI countries, and the

generalizability of our results may be affected considering the distribution of caesarean sections performed globally. The studies that analyzed perioperative maternal mortality before the 1970s may not be as reliable due to the small sample sizes of the studies as compared to the studies from the other decades. Due to inadequate data we were unable to include a domain in our quality assessment that investigated reporting of neonatal mortality. Statistical heterogeneity within our analysis for both maternal and neonatal mortality was high, interpretation of these results should be done with caution. Future research on maternal and neonatal mortality associated with caesarean section should examine the outcomes based on risk groups of patients along with causes of perioperative maternal and neonatal mortality.

3.4 CONCLUSION

The risk of perioperative maternal mortality during or following caesarean section has progressively decreased over the past 70 years, indicating that efforts to enhance patient safety and access to caesarean sections may have been effective. However, in countries with low HDI, a 5-fold higher risk in perioperative maternal mortality remains as compared to high HDI countries, implying that inequalities are still present between low and high resource settings. Evidence-based and high-quality healthcare services, along with universal access to emergency obstetric procedures, should become a priority on the global health agenda, especially in low HDI countries in order to reduce the gap in maternal mortality associated with caesarean section within those regions. The risk of perioperative neonatal mortality has been fluctuating, with no clear decrease over time, though the studies may have been underpowered to test for trends over time, or by HDI setting. Nevertheless, until neonatal mortality approaches zero, there also remains room for improvement through evidence-based interventions to improve neonatal survival.

3.5 BIBLIOGRAPHY

1. The Sustainable Development Goals and Maternal Mortality. (2019). Retrieved 10 July 2020, from https://www.mhtf.org/topics/the-sustainable-development-goals-and-maternal-mortality/
2. Trends in maternal mortality: 2000 to 2017: estimates by WHO, UNICEF, UNFPA, World Bank Group and the United Nations Population Division. Geneva: World

Health Organization. (2019). Retrieved 11 July 2020, from https://www.unfpa.org/featured-publication/trends-maternal-mortality-2000-2017#:~:text=The%20global%20maternal%20mortality%20ratio%20in%202017%20is%20estimated%20at,ratio%20was%202.9%20per%20cent.

3. Chen, I., Opiyo, N., Tavender, E., Mortazhejri, S., Rader, T., Petkovic, J., Yogasingam, S., Taljaard, M., Agarwal, S., Laopaiboon, M., Wasiak, J., Khunpradit, S., Lumbiganon, P., Gruen, R. L., & Betran, A. P. (2018). Non-clinical interventions for reducing unnecessary caesarean section. *The Cochrane database of systematic reviews*, *9*(9), CD005528. https://doi.org/10.1002/14651858.CD005528.pub3
4. Fowler, A. J. (2013). A Review of Recent Advances in Perioperative Patient Safety. *Annals of Medicine and Surgery*, *2*(1), 10-14. doi:10.1016/s2049-0801(13)70020-7
5. Betrán AP, Ye J, Moller A-B, Zhang J, Gülmezoglu AM, Torloni MR (2016) The Increasing Trend in Caesarean Section Rates: Global, Regional and National Estimates: 1990-2014. PLoS ONE 11(2): e0148343. doi:10.1371/journal.pone.0148343
6. World health organisation, UNICEF, UNFPA, Worldbank. Trends in maternal mortality 1990-2010. (2012). Geneva: World health organisation. Retrieved 11 July 2020, from https://www.who.int/reproductivehealth/publications/monitoring/9789241503631/en/
7. World Health Organisation. Coverage of maternity care, a listing of available information. (1996). Geneva: World health organisation. Retrieved 11 July 2020, from https://apps.who.int/iris/handle/10665/63878
8. Zongo, A., Dumont, A., Fournier, P., Traore, M., Kouanda, S., & Sondo, B. (2015). Effect of maternal death reviews and training on maternal mortality among cesarean delivery: post-hoc analysis of a cluster-randomized controlled trial. *European journal of obstetrics, gynecology, and reproductive biology*, *185*, 174–180. https://doi.org/10.1016/j.ejogrb.2014.12.023
9. Luz Gibbons, José M. Belizán, Jeremy A Lauer, Ana P Betrán, Mario Merialdi and Fernando Althabe (2010) 'World Health Report', The Global Numbers and Costs of Additionally Needed and Unnecessary Caesarean Sections Performed per Year: Overuse as a Barrier to Universal Coverage HEALTH SYSTEMS FINANCING, Background Paper, 30.
10. Sobhy, S., Arroyo-Manzano, D., Murugesu, N., Karthikeyan, G., Kumar, V., Kaur, I., Fernandez, E., Gundabattula, S. R., Betran, A. P., Khan, K., Zamora, J., & Thangaratinam, S. (2019). Maternal and perinatal mortality and complications associated with caesarean section in low-income and middle-income countries: a systematic review and meta-analysis. *Lancet (London, England)*, *393*(10184), 1973–1982. https://doi.org/10.1016/S0140-6736(18)32386-9
11. Liberati, A., Altman, D. G., Tetzlaff, J., Mulrow, C., Gøtzsche, P. C., Ioannidis, J. P., Clarke, M., Devereaux, P. J., Kleijnen, J., & Moher, D. (2009). The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ (Clinical research ed.)*, *339*, b2700. https://doi.org/10.1136/bmj.b2700
12. Stroup, D. F., Berlin, J. A., Morton, S. C., Olkin, I., Williamson, G. D., Rennie, D., Moher, D., Becker, B. J., Sipe, T. A., & Thacker, S. B. (2000). Meta-analysis of

observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA*, *283*(15), 2008–2012. https://doi.org/10.1001/jama.283.15.2008

13. Human Development Report 2019— Beyond income, beyond averages, beyond today: Inequalities in human development in the 21st century. (2019). New York: United Nations Development Program. Retrieved 12 July 2020, from http://hdr.undp.org/sites/default/files/hdr2019.pdf
14. Khan, K. S., Wojdyla, D., Say, L., Gülmezoglu, A. M., & Van Look, P. F. (2006). WHO analysis of causes of maternal death: a systematic review. *Lancet (London, England)*, *367*(9516), 1066–1074. https://doi.org/10.1016/S0140-6736(06)68397-9
15. Higgins, J. P., & Thompson, S. G. (2002). Quantifying heterogeneity in a meta-analysis. *Statistics in medicine*, *21*(11), 1539–1558. https://doi.org/10.1002/sim.1186
16. Boerma, T., & Ronsmans, C. (2019). Global epidemiology of use of and disparities in caesarean sections – Authors' reply. *The Lancet*, *394*(10192), 25. doi:10.1016/s0140-6736(19)30698-1
17. *WHO Recommendations Non-Clinical Interventions to Reduce Unnecessary Caesarean Sections*. (2018). World Health Organization. Retrieved 12 July 2020, from https://www.who.int/reproductivehealth/publications/non-clinical-interventions-to-reduce-cs/en/
18. Miller, S., Abalos, E., Chamillard, M., Ciapponi, A., Colaci, D., Comandé, D., Diaz, V., Geller, S., Hanson, C., Langer, A., Manuelli, V., Millar, K., Morhason-Bello, I., Castro, C. P., Pileggi, V. N., Robinson, N., Skaer, M., Souza, J. P., Vogel, J. P., & Althabe, F. (2016). Beyond too little, too late and too much, too soon: a pathway towards evidence-based, respectful maternity care worldwide. *Lancet (London, England)*, *388*(10056), 2176–2192. https://doi.org/10.1016/S0140-6736(16)31472-6
19. Goldenberg, R. L., McClure, E. M., & Saleem, S. (2018). Improving pregnancy outcomes in low- and middle-income countries. *Reproductive health*, *15*(Suppl 1), 88. https://doi.org/10.1186/s12978-018-0524-5
20. Buchsbaum, H. J. (n.d.). *Clinical perspectives in obstetrics and gynecology CP OBGYN*. New York: Springer.
21. Dumont, A., Gaye, A., de Bernis, L., Chaillet, N., Landry, A., Delage, J., & Bouvier-Colle, M. H. (2006). Facility-based maternal death reviews: effects on maternal mortality in a district hospital in Senegal. *Bulletin of the World Health Organization*, *84*(3), 218–224. https://doi-org.proxy1.lib.uwo.ca/10.2471/blt.05.023903
22. Mahmood, M. A., Mufidah, I., Scroggs, S., Siddiqui, A. R., Raheel, H., Wibdarminto, K., Dirgantoro, B., Vercruyssen, J., & Wahabi, H. A. (2018). Root-Cause Analysis of Persistently High Maternal Mortality in a Rural District of Indonesia: Role of Clinical Care Quality and Health Services Organizational Factors. *BioMed research international*, *2018*, 3673265. https://doi-org.proxy1.lib.uwo.ca/10.1155/2018/3673265
23. Keag OE, Norman JE, Stock SJ. Long-term risks and benefits associated with cesarean delivery for mother, baby, and subsequent pregnancies: Systematic review and meta-analysis. *PLoS Med*. 2018;15(1):e1002494. Published 2018 Jan 23. doi:10.1371/journal.pmed.1002494

24. National Institute for Health and Clinical Excellence. (2011). Caesarean Section (NICE Clinical Guideline 132). Retrieved 12 July 2020, from https://www.nice.org.uk/guidance/CG132
25. WHO Statement on Caesarean Section Rates. (2015). Geneva: World Health Organization (WHO/RHR/15.02). Retrieved 12 July 2020, from https://www.who.int/reproductivehealth/publications/maternal_perinatal_health/cs-statement/en/
26. Ngan Kee W. D. (2005). Confidential enquiries into maternal deaths: 50 years of closing the loop. *British journal of anaesthesia*, *94*(4), 413–416. https://doi-org.proxy1.lib.uwo.ca/10.1093/bja/aei069
27. Haider, A., Scott, J. W., Gause, C. D., Meheš, M., Hsiung, G., Prelvukaj, A., Yanocha, D., Baumann, L. M., Ahmed, F., Ahmed, N., Anderson, S., Angate, H., Arfaa, L., Asbun, H., Ashengo, T., Asuman, K., Ayala, R., Bickler, S., Billingsley, S., Bird, P., … Abdullah, F. (2017). Development of a Unifying Target and Consensus Indicators for Global Surgical Systems Strengthening: Proposed by the Global Alliance for Surgery, Obstetric, Trauma, and Anaesthesia Care (The G4 Alliance). *World journal of surgery*, *41*(10), 2426–2434. https://doi.org/10.1007/s00268-017-4028-1
28. Nyamtema, A., Mwakatundu, N., Dominico, S., Mohamed, H., Shayo, A., Rumanyika, R., Kairuki, C., Nzabuhakwa, C., Issa, O., Lyimo, C., Kasiga, I., & van Roosmalen, J. (2016). Increasing the availability and quality of caesarean section in Tanzania. *BJOG : an international journal of obstetrics and gynaecology*, *123*(10), 1676–1682. https://doi.org/10.1111/1471-0528.14223
29. Macones, G., Caughey, A., Wood, S., Wrench, I., Huang, J., & Norman, M. et al. (2019). Guidelines for Postoperative care in Cesarean Delivery: Enhanced Recovery After Surgery (ERAS) Society Recommendations (Part 3). *American Journal Of Obstetrics And Gynecology*. doi: 10.1016/j.ajog.2019.04.012
30. Caughey, A., Wood, S., Macones, G., Wrench, I., Huang, J., & Norman, M. et al. (2018). Guidelines for intraoperative care in cesarean delivery: Enhanced Recovery After Surgery Society Recommendations (Part 2). *American Journal Of Obstetrics And Gynecology*, *219*(6), 533-544.
31. Wilson, R., Caughey, A., Wood, S., Macones, G., Wrench, I., & Huang, J. et al. (2018). Guidelines for Antenatal and Preoperative care in Cesarean Delivery: Enhanced Recovery After Surgery Society Recommendations (Part 1). *American Journal Of Obstetrics And Gynecology*, *219*(6), 523.e1-523.e15.
32. Fenton, P. M., Whitty, C. J., & Reynolds, F. (2003). Caesarean section in Malawi: prospective study of early maternal and perinatal mortality. *BMJ (Clinical research ed.)*, *327*(7415), 587. https://doi.org/10.1136/bmj.327.7415.587
33. Souza, J. P., Gülmezoglu, A., Lumbiganon, P., Laopaiboon, M., Carroli, G., Fawole, B., Ruyan, P., & WHO Global Survey on Maternal and Perinatal Health Research Group (2010). Caesarean section without medical indications is associated with an increased risk of adverse short-term maternal outcomes: the 2004-2008 WHO Global Survey on Maternal and Perinatal Health. *BMC medicine*, *8*, 71. https://doi.org/10.1186/1741-7015-8-71

34. Chi, I. C., Whatley, A., Wilkens, L., & Potts, M. (1986). In-hospital maternal mortality risk by cesarean and vaginal deliveries in two less developed countries--a descriptive study. *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics*, *24*(2), 121–131. http://dx.doi.org/10.1016/0020-7292%2886%2990006-8

Chapter 4 - Reported causes of death during or following caesarean section: a systematic review and meta-analysis

4 INTRODUCTION

Reduction of maternal mortality has been a high priority on the global health agenda, with prominent placement within the UN Sustainable Development Goals (2015-2030) and in the original Millennium Development Goals (2000-2015).[1] The risks associated with pregnancy and labour, along with insufficient access to safe and high quality obstetric care, are conversely related to maternal mortality.[4] A systematic exploration of the distribution of the causes of maternal mortality attributed to caesarean section is vital to allow for evidence-informed development of health policy for maternal health. A description of the causes of caesarean attributed maternal mortality will allow for a better understanding as to why women are dying intraoperatively and postoperatively throughout this obstetric procedure. Furthermore, understanding the global distribution of causes of death attributed to caesarean section will assist in identifying important regional variations. By pinpointing the causes in various regions and income settings, clinicians and policy makers may strategically target specific causes of death through evidence-based interventions.

A 2006 systematic review by the WHO evaluated the distribution of causes of maternal mortality, along with regional variations in the causes and the magnitudes of effect.[2] However, this review mainly focused on overall maternal mortality, and did not independently investigate maternal mortality attributable to caesarean section. Systematic reviews and meta-analyses are an ideal methodology that provide summary estimates that may be used to provide robust evidence on significant issues of public health importance.[3] In this study, we sought to systematically ascertain and map the distribution of causes of maternal mortality during or following caesarean section, and to analyze whether the magnitude of effect for the causes of death changed over time and by country human development index (HDI) status.

4.1 METHODS

A prospective protocol in line with current recommendations was used for this systematic review and meta-analysis. We reported the review as per the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines.[22,23] The study protocol has been registered with PROSPERO, number CRD42020164224.

4.1.1 Search strategy

An extensive search was conducted using multiple sources, including scientific and grey literature databases, from inception until November 21, 2019. The databases searched included EMBASE, MEDLINE, Cochrane Central, Web of science, SCOPUS, CINHAL, WHOLIS, WHO IRIS, WHO Reproductive Health Library, CAB Direct, PAIS Index, Global Index Medicus, African journals online, and Global Health Data Exchange. The grey literature databases were composed of OAIster/WorldCat, OpenGrey, Centre for Research Libraries Global Resource Network, EU Open Data Portal, and Latin American open Archives Portal. The theses and dissertations databases included Open Access Theses and Dissertations (OATD), EThOS, and DART. In addition, we selected ten highly-relevant studies and additionally conducted forward and backward citation tracking for the first 100 references.

Database searches were conducted with the use of controlled subject terms specific to each database (i.e.caesarean section, maternal mortality and cause of death). We also used key words and word variants for caesarean section (e.g. c?esar?an*, CSection*, C-Section?*, abdominal deliver*, and abdominal birth*) and maternal mortality (e.g. maternal mortal*, maternal death*, pregnan* death*, and wom?n death*). Additionally, word variants along with searches by adjacency for cause of death (e.g. cause* or factor* or contribut* or manor* adjacent mortal* or death*) were combined with the terms for caesarean section and maternal mortality. Subject terms and key words were used in order to limit studies to those that were only conducted on humans. Language or date restrictions were not imposed. The full search strategies for each database are provided in APPENDIX D.

4.1.2 Screening and inclusion criteria

Selection of studies occurred in two levels. In level one, one reviewer screened the titles and abstracts of all citations for potentially relevant papers with the use of Mendeley. We attempted to maximize sensitivity, and only studies that were not related to caesarean section and maternal mortality were excluded during level one screening. In level two, full text articles were assessed by one independent reviewer (AH) who applied the pre-specified inclusion and exclusion criteria. Studies were included in the review if they were randomized controlled trials (RCTs) or observational studies, if the study population included women who underwent or were planned to undergo elective or emergency caesarean section, reported the outcome of maternal mortality and reported causes of maternal death. The primary outcome of perioperative maternal mortality (POMMR) was defined as death of a woman from any cause, occurring any time between the start of the procedure or start of anesthesia until hospital discharge or 42 days of follow-up after caesarean section.

Studies were excluded if they were case-control studies, ecological studies, book chapters, editorials, if the population was pregnant women only undergoing vaginal delivery, if they examined only maternal mortality unrelated to caesarean section, studies of mortality more than 42 days after caesarean section, and studies that did not report causes of death. Studies that reported on mixed populations (vaginal delivery and caesarean section) were excluded if the data for the caesarean section subgroup was not reported separately. As the aim of this review was to assess the outcome in all patients undergoing caesarean section, studies that exclusively reported on high-risk groups (i.e. Women with pre-eclampsia, HELLP syndrome, multiple caesarean sections, etc.) were excluded. Studies that provided an estimated number of total caesarean sections rather than an actual denominator, and studies that reported adjusted maternal or neonatal mortality rates without crude data were excluded. Non-human studies and simulation studies were excluded.

Due to the epidemiologic nature of our research question, we expected most eligible studies would be descriptive cohorts of caesarean section outcomes with no

interventional trials or controlled studies. However, comparative studies or randomised controlled trials (RCTs) were eligible for inclusion if the study arm tested a specific intervention that was not considered standard of care or if there was a differential effect on maternal mortality in the intervention group as compared to the control group then the intervention arm would be excluded.

4.1.3 Data extraction and quality assessment

One reviewer (AH) independently extracted data using a data extraction form developed and pilot tested a priori. From the eligible studies, information was extracted on: year of recruitment, study authors, study objective, study design, country of study, observational period, source of sample, data collection method, total number of maternal deaths during or after caesarean section from any cause, maternal deaths during or following caesarean section due to specific causes, urgency (elective vs emergency). Quality assessment of the included studies was performed by one independent reviewer (AH), using similar domains as in prior studies in this area. [2,5] The following domains were used for quality assessment: 1) reporting of the definition of maternal mortality in order to reduce any bias associated with the ascertainment of denominator data (adequate if any published definition was reported vs inadequate if no definition was reported); 2) sample selection was considered acceptable if the population included all consecutive women or a random sample of women who undergo or are planning to undergo a caesarean section, and unacceptable if the population consisted of a certain subgroup of women (i.e. women undergoing emergency caesarean section); 3) adequacy of data sources for outcome assessment to ascertain complete numerator data (registry data such as health records, surgical logbooks, or clinical notes were considered adequate vs verbal autopsies from women or relatives were considered inadequate); 4) A high proportion of cases with cause of death reported (<5% not reported) were deemed adequate; 5) Ascertainment of cause of death through robust approaches indicates whether the cause is a true representation of the underlying condition (autopsies, confidential enquiries, and death certification from multiple sources were considered adequate whereas if no methods were used to confirm cause than it was deemed inadequate). If four of the five domains were met, then a study was categorized as high quality.[2,5]

Human Development Index (HDI), as defined by the United Nations (UN), was used to assign development status to countries.[6] This index assesses the country development through the people and their capabilities rather than merely through economic growth; it is a composite index for indicators of per capita income, education and life expectancy.[6] As HDI is an index that changes over time, assignment of HDI was based on the specific time period in which the study was conducted. If a country does not have HDI data available for a required year, then the available HDI closest to that year was used.

4.1.4 Data analysis

The prevalence of the causes of maternal death during or following caesarean section were reported as a proportion of all maternal deaths during or following caesarean section with 95% CI. The specific causes reported by the individual studies were placed into categories of maternal death according to the International Classification of Diseases-Maternal Mortality (ICD-MM).[7] For studies that reported more than one cause of death for each patient with no further information on the primary cause, we included multiple causes for the same patient into each reported category, depending on the causes provided. When studies reported on causes of death that were considered contributory causes according to the ICD-MM with no further information on any other additional causes, we placed those causes into the unknown/undetermined category. Weighting across studies was addressed in two ways, in order to understand the effect of analytic choice on effect size estimates. First, estimates were calculated using a fixed effect model for the primary analysis. Then, the estimates were also calculated using a random effects model as a sensitivity analysis. Meta-regression was conducted with the use of method of moments in order to investigate changes in the proportion of reported causes of death by time and by HDI. The year in which patients were recruited was used to assess variations in mortality estimates over time. If data were provided over a range of years, then the median year of the time interval was used as the year of recruitment. Subgroup analyses were also performed to report on estimates for each dual-decade era (pre-1970s, 1970-1980s, 1990-2000s, and 2010-2020s). Similarly, subgroup analyses were performed for mortality estimates per 100,000 caesarean sections for HDI subgroups, defined as high

(≥0·8) or low (<0·8) HDI. We used the test for heterogeneity between subgroups to identify if there was a significant difference in the effect sizes across subgroups. In addition, we performed sensitivity analyses for prospective versus retrospective data collection, variations in year of recruitment within era groups (i.e. For example, if in pre-1970s majority of studies from 1970s and a few from 1960s) and by excluding studies that investigated specific subgroups of women (e.g. Only regional/general anesthesia or emergency/elective surgeries).

Publication bias and small studies effect were assessed with funnel plots that represented the cause-specific proportions on a logit scale versus its standard error. Funnel asymmetry was assessed with the Egger's test. Statistical heterogeneity was evaluated with I^2, which represents the percentage of variability between studies that is beyond the expected play of chance.[8] If the I^2 value was greater than 30%, then we concluded that there was statistical heterogeneity present between the studies. Analyses were conducted using Stata version 16.

4.2 RESULTS

From database searches we identified 10,658 studies, a further 373 studies were found from grey literature sources which included theses and dissertations, and reports from Global Health Data Exchange. Once duplicates were removed, 6,052 studies remained. Title and abstract screening removed 5,426 studies as they were not related to caesarean section and maternal mortality. The remaining 626 studies were screened for full-text review; of these, 521 were excluded due to the prespecified inclusion/exclusion criteria. A final sample of 131 studies provided information on causes of maternal deaths during or following caesarean section; this included 26 studies identified from forward and backward citation tracking. Please refer to Figure 4.1 PRISMA flow-chart for more details on the screening and study selection process used for this systematic review and meta-analysis.

4.2.1 Description of studies

We included 131 studies from 54 countries. Of the 5822 cause-specific maternal deaths included in the analysis, 19.1% (25/131) came from countries with high HDI and 80.9% (106/131) were from low HDI countries. Three of the studies were multi-centre studies. The majority (82.6%) of the maternal deaths during or following caesarean section were from obstetric complications, whereas 13.2% of maternal deaths occurred as a result of non-obstetric causes. The remaining 4.2% of maternal deaths during or following caesarean sections were due to unknown or coincidental causes. 36 of the included studies reported timing of death for maternal mortality, with most of the deaths (40.6%) occurring within 24-hours of the caesarean section, 23.4% of the studies reporting intraoperative mortality, and 36% reporting mortality at 30-day to 42-day follow-up. Of the studies that reported on time of death, 19 additionally reported on the cause of death.

For intraoperative mortality, the most common cause of death was unanticipated complications of management accounting for 50% of intraoperative deaths. Obstetric haemorrhage was the most prevalent cause of death for 24-hour mortality with 31.3% of deaths occurring due to this cause among all other causes reported during this time period. Pregnancy-related infections accounted for 55.6% of all reported deaths at 30-day to 42-day follow-up.

From the 131 studies included, 46 reported on the urgency of caesarean section. In total, emergency caesarean section was conducted in 53.6% of women and elective caesarean section was conducted in 46.4% of women. One randomized controlled trial was included into the analysis; however, only the control arm was eligible as the intervention arm showed a differential effect on maternal mortality as compared to the control arm.[9] For subgroup analysis of HDI status we assumed the HDI category from one study as no country-specific information was provided.[10] Conversely, we obtained an approximate HDI, given the information on annual per capita income quoted from the study in order to attain an analogous HDI.[10] APPENDIX G: Table 14 shows the characteristics of the included studies.

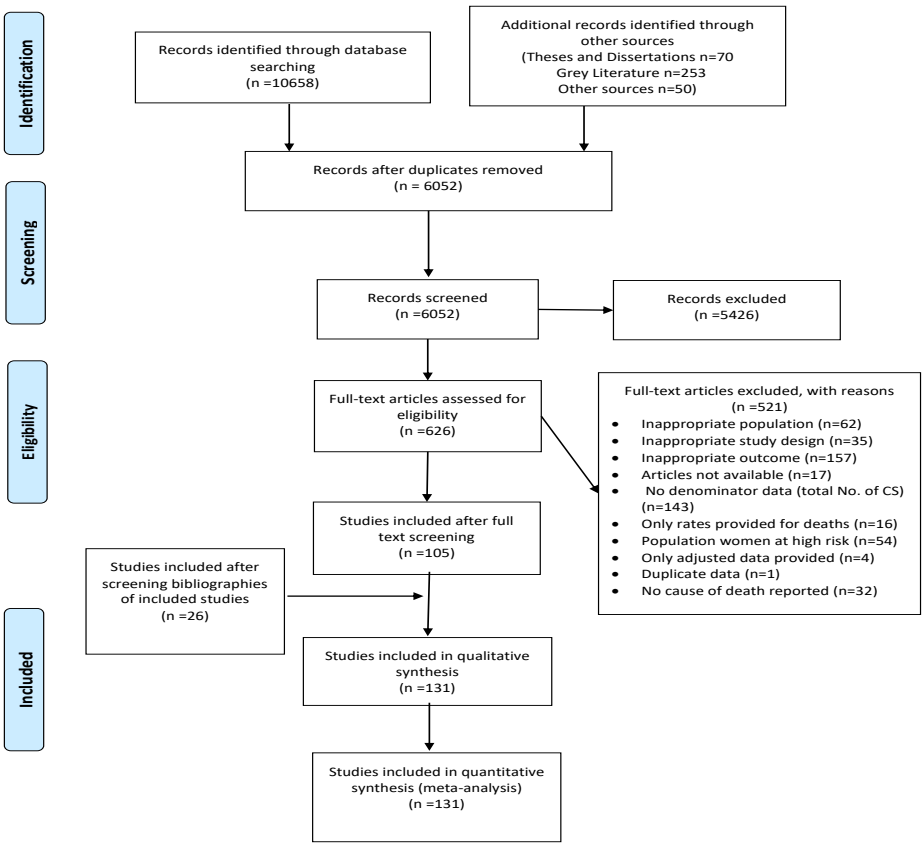


Figure 4.1 PRISMA flow diagram for the study selection process

4.2.2 Quality assessment

From the 131 included studies, 34.4% were of high quality (Figure 4.2). The majority of the studies met criteria for the domain of 'outcome assessment' (88.5%; Figure 4.2). 83.2% of the studies were deemed high quality for sample selection as they included either all women or a random selection of women who have undergone a caesarean section. 80.2% of studies had a sufficiently high proportion of cases in which cause of death was established. 22.1% of studies reported a clear definition of maternal mortality and 39.7% of studies obtained robust methods for the ascertainment of cause of maternal death. Complete details of quality assessment for the included studies are provided in Appendix G: Table 16.

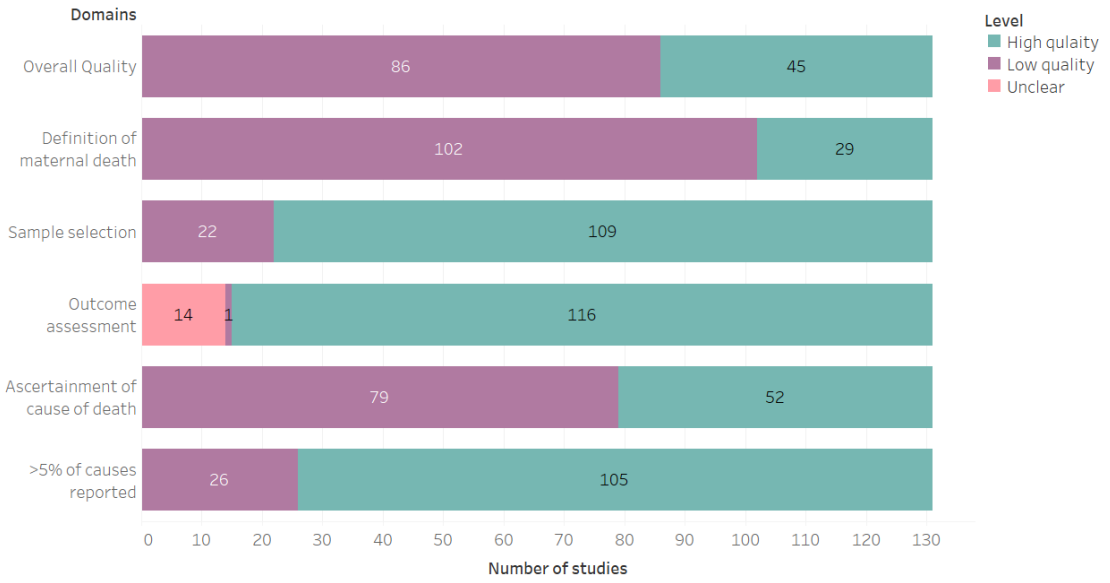


Figure 4.2 Quality of studies reporting on cause of death during or following caesarean section

4.2.3 Variations in causes of caesarean-related death based on HDI status

Globally, obstetric haemorrhage was the leading reported cause of caesarean-related death (29.5%; Figure 4.3). Non-obstetric complications represented 25.9% of the reported proportion of caesarean-related death in countries of high HDI (Figure 4.3), and obstetric haemorrhage was the most common reported cause of caesarean-related death in countries of low HDI (31.2%; Figure 4.3). The distribution for reported causes of caesarean-related death in low-HDI countries was similar to that of the global distribution; this may be due to the fact that most included studies were from those regions. There were differences among the reported causes of death between low and high HDI countries. Obstetric haemorrhage was the cause of 9.3% of caesarean-related deaths in high HDI countries, whereas in low HDI it was the most common reported cause of death (31.2%). Embolism accounted for 18.6% of caesarean associated maternal deaths in high HDI countries, whereas in low-HDI countries, it only accounted for 3.4% of reported deaths. Additionally, non-obstetric complications were the most commonly-reported causes in countries of high HDI, whereas in low HDI countries they only accounted for 12.1% of all reported deaths during or following caesarean section. Unanticipated complications were responsible for 12.7% of caesarean-related death in

low HDI countries, but in high HDI countries these causes only accounted for 4.5% of deaths. Further details on the categorization of the specific causes of death attributable to caesarean section are provided in Appendix G: Table 15.

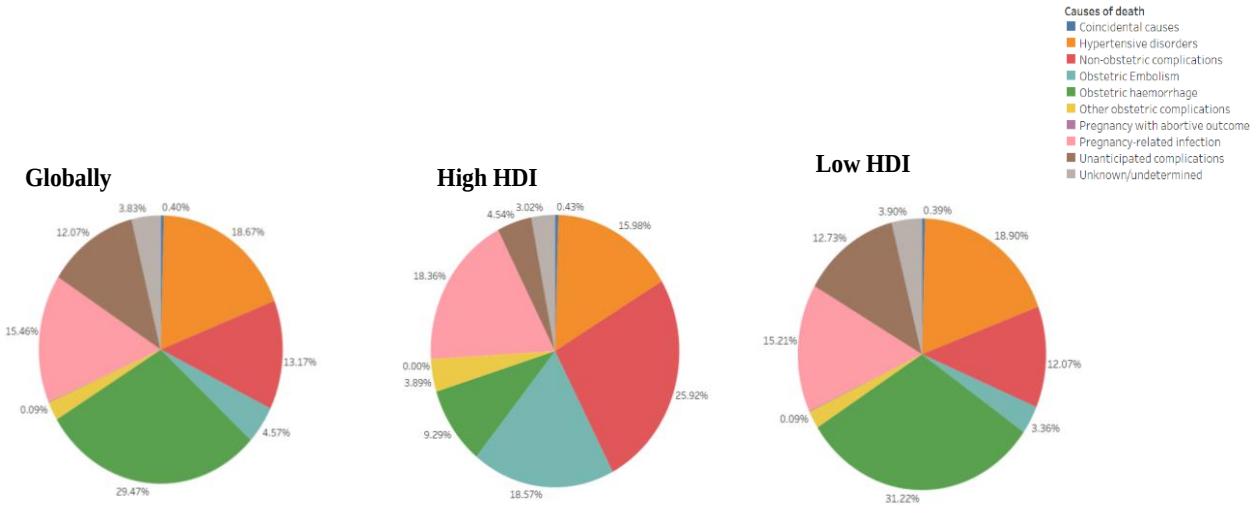


Figure 4.3 Variation in the distribution of causes of death attributed to caesarean section by HDI status with the use of unweighted data

4.2.4 Trends in causes of caesarean-related death by year and HDI

Meta-regression by HDI showed that the proportion of deaths attributed to obstetric haemorrhage declined as HDI increased, whereas, other reported causes of death showed no relationship to HDI status (Figure 4.4).

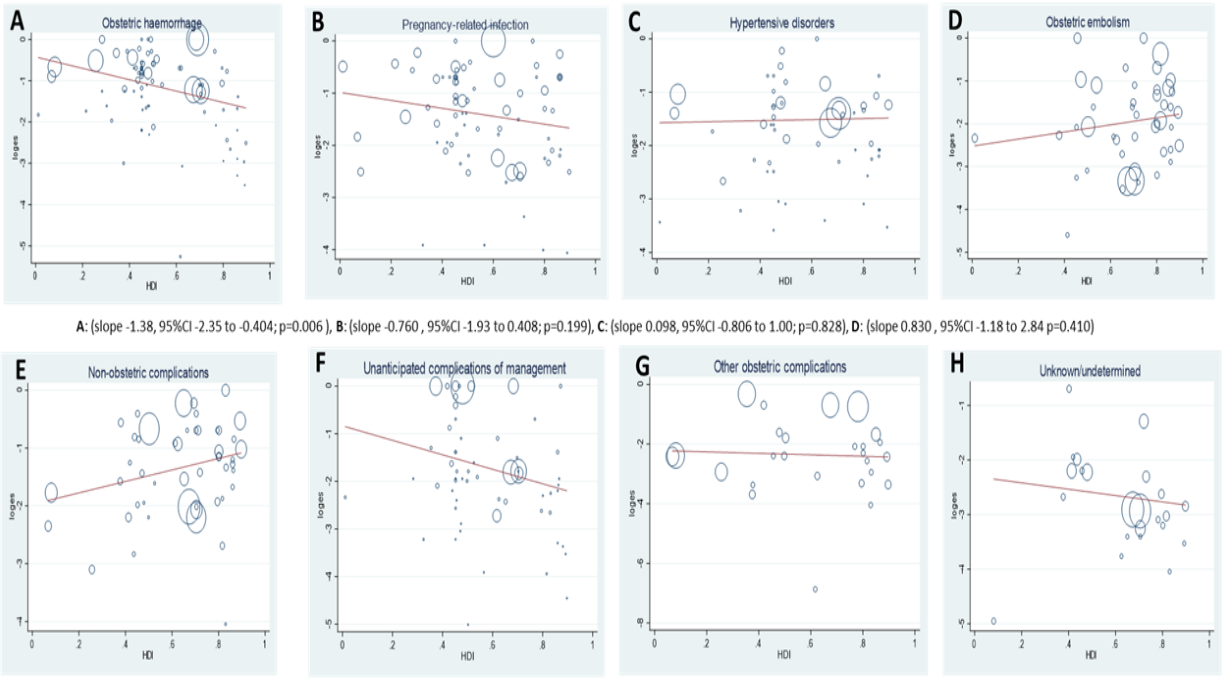


Figure 4.4 Meta-regression for the proportion of reported cause of caesarean-related death by HDI.

Meta-regression by year showed that the proportion of reported deaths attributed to obstetric haemorrhage and hypertensive disorders significantly increased over time (Figure 4.5A, 4.5C), while the proportion of deaths attributed to pregnancy-related infection and non-obstetric complications significantly decreased over time (Figure 4.5B, 4.5E)

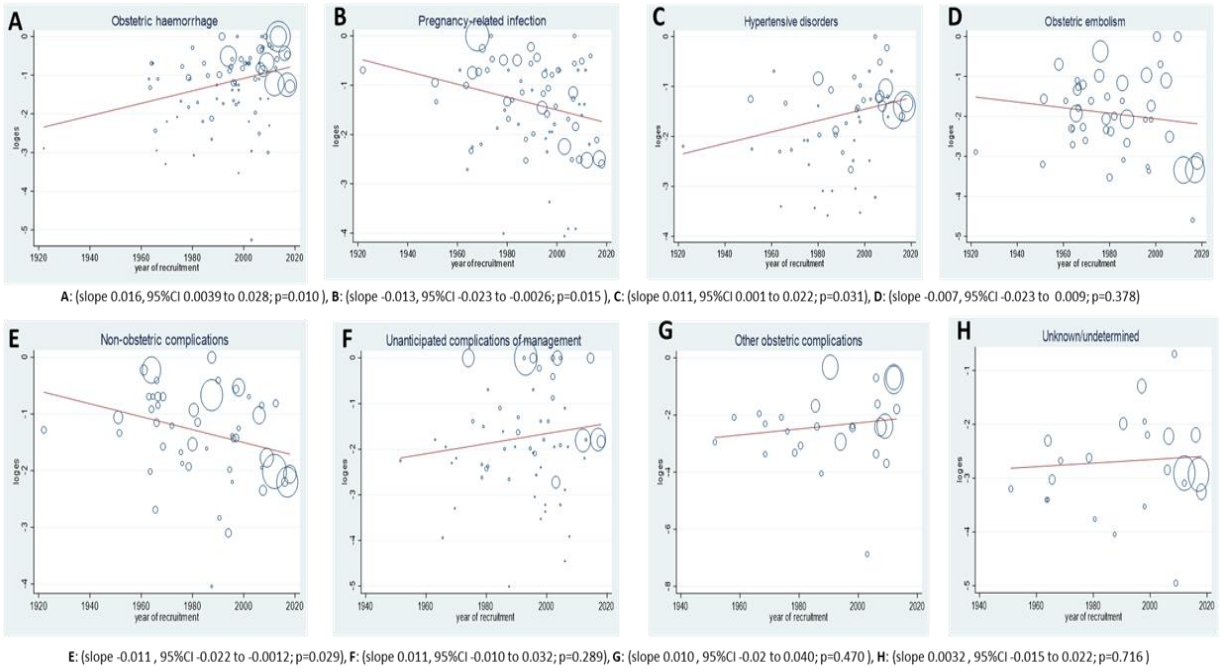


Figure 4.5 Meta-regression for the proportion of reported cause of caesarean-related death by year.

The table below provides numeric estimates for the proportion of all deaths according to specific causes, by HDI subgroup and by decade. Visual representations of the distribution and trends in the reported causes of caesarean-related deaths over time and within low and high HDI countries are provided in Figure 4.6 and Figure 4.7.

	Number of Studies	Events	Proportion of All Deaths (%; 95% CI)	p value for heterogeneity between sub-groups	
				By HDI	By decade
Obstetric haemorrhage					
Pre-1970s	9	33/229	11.01 (6.66-16.06)		
High HDI	4	12/167	6.53 (2.87-11.23)	<0.00001	
Low HDI	5	21/62	32.82 (20.52-46.19)		
1970s-1980s	17	91/504	15.33 (11.96-18.97)		
High HDI	5	18/117	13.30 (7.16-20.67)	0.446	
Low HDI	12	73/387	15.94 (12.03-20.19)		<0.00001
1990s-2000s	44	631/2622	13.80 (12.20-15.45)		
High HDI	4	13/186	5.64 (2.32-9.94)	<0.00001	
Low HDI	40	618/2436	14.62 (12.91-16.38)		
2010s-2020s	12	961/3023	30.65 (28.89-32.44)		
High HDI	NR	NR	NR	N/A	
Low HDI	12	961/3023	30.65 (28.89-32.44)		
Overall	82	1716/6378	21.24 (20.10-22.40)		

Pregnancy-related infection					
Pre-1970s	12	131/422	28.78 (24.22-33.52)		<0.00001
High HDI	7	49/237	16.94 (11.76-22.68)	<0.00001	
Low HDI	5	82/185	44.89 (37.61-52.28)		
1970s-1980s	20	148/604	19.13 (15.55-22.92)		
High HDI	5	27/111	22.03 (14.22-30.80)	0.741	
Low HDI	15	121/493	18.31 (14.33-22.57)		
1990s-2000s	33	369/2449	10.36 (8.90-11.89)		
High HDI	3	9/152	4.16 (1.03-8.61)	0.0005	
Low HDI	30	360/2297	10.85 (9.31-12.47)		
2010s-2020s	10	252/2947	3.74 (2.80-4.77)		
High HDI	NR	NR	NR	N/A	
Low HDI	10	252/2947	3.74 (2.80-4.77)		
Overall	75	900/6422	9.01 (8.15-9.90)		
Hypertensive disorders					
Pre-1970s	8	31/196	12.86 (7.82-18.68)		0.0053
High HDI	5	24/107	19.59 (11.45-28.89)	0.005	
Low HDI	3	7/89	7.55 (2.53-14.42)		
1970s-1980s	13	101/536	16.18 (12.91-19.69)		
High HDI	5	23/140	15.07 (9.22-21.88)	0.611	
Low HDI	8	78/396	16.51 (12.66-20.69)		
1990s-2000s	25	280/1253	18.03 (15.60-20.57)		
High HDI	3	27/128	18.45 (11.72-26.13)	0.720	
Low HDI	22	253/1125	17.97 (15.39-20.67)		
2010s-2020s	7	675/2922	20.22 (18.56-21.92)		
High HDI	NR	NR	NR	N/A	
Low HDI	7	675/2922	20.22 (18.56-21.92)		
Overall	53	1087/4907	19.06 (17.82-20.32)		
Obstetric embolism					
Pre-1970s	16	51/379	10.92 (7.48-14.79)		<0.00001
High HDI	9	38/260	12.32 (8.15-17.07)	0.575	
Low HDI	7	13/119	8.57 (3.19-15.50)		
1970s-1980s	14	74/567	10.52 (7.84-13.47)		
High HDI	6	34/150	20.08 (13.63-27.28)	0.0004	
Low HDI	8	40/417	7.62 (4.90-10.75)		
1990s-2000s	11	37/243	7.34 (3.10-12.64)		
High HDI	3	14/128	9.43 (4.40-15.73)	0.104	
Low HDI	8	23/115	10.27 (3.27-19.40)		
2010s-2020s	4	104/2905	3.45 (2.80-4.17)		
High HDI	NR	NR	NR	N/A	
Low HDI	4	104/2905	3.45 (2.80-4.17)		
Overall	45	266/4094	2.02 (1.42-2.70)		
Unanticipated complications of management					
Pre-1970s	6	8/172	2.03 (0.05-5.72)		<0.00001
High HDI	5	7/166	2.11 (0.07-5.78)	0.196	
Low HDI	1	1/6	16.67 (3.01-56.35)		
1970s-1980s	15	52/530	5.22 (2.99-7.85)		
High HDI	3	9/82	9.19 (3.14-17.26)	0.357	
Low HDI	12	43/448	4.49 (2.21-7.27)		
1990s-2000s	34	171/1630	4.40 (3.05-5.91)		
High HDI	6	5/158	N/A*	N/A	
Low HDI	28	166/1472	5.60 (4.07-7.28)		
2010s-2020s	6	472/2838	14.72 (13.30-16.19)		
High HDI	NR	NR	NR	N/A	
Low HDI	6	472/2838	14.72 (13.30-16.19)		
Overall	61	703/5170	8.81 (7.85-9.80)		
Other obstetric complications					
Pre-1970s	5	5/73	5.48 (0.57-13.26)		<0.00001

High HDI	4	4/44	8.21 (0.81-19.84)	0.279	
Low HDI	1	1/29	3.45 (0.61-17.18)		
1970s-1980s	7	15/230	4.94 (2.08-8.63)		
High HDI	3	8/102	5.76 (1.54-11.74)	0.761	
Low HDI	4	7/128	4.33 (0.92-9.30)		
1990s-2000s	11	75/1917	0.19 (0.00-0.66)		
High HDI	2	6/120	4.58 (1.27-9.38)	0.078	
Low HDI	9	69/1797	0.02 (0.00-0.33)		
2010s-2020s	3	37/88	41.54 (31.18-52.25)		
High HDI	NR	NR	NR	N/A	
Low HDI	3	37/88	41.54 (31.18-52.25)		
Overall	26	132/2308	1.30 (0.69-2.03)		
Non-obstetric complications					
Pre-1970s	16	103/354	25.48 (20.58-30.66)		
High HDI	7	48/225	18.32 (13.13-24.07)	<0.00001	
Low HDI	9	55/129	41.14 (31.87-50.68)		
1970s-1980s	11	144/476	27.02 (22.78-31.46)		
High HDI	6	19/121	10.42 (4.65-17.58)	<0.00001	
Low HDI	5	125/355	33.82 (28.74-39.07)		
1990s-2000s	17	160/983	11.65 (9.33-14.13)		<0.00001
High HDI	3	53/128	41.02 (32.26-50.05)	<0.00001	
Low HDI	14	107/855	8.01 (5.83-10.42)		
2010s-2020s	5	360/2914	11.45 (10.25-12.70)		
High HDI	NR	NR	NR	N/A	
Low HDI	5	360/2914	11.45 (10.25-12.70)		
Overall	49	767/4727	12.46 (11.38-13.58)		
Pregnancy with abortive outcome					
Pre-1970s	NR	NR	NR		
High HDI	NR	NR	NR	N/A	
Low HDI	NR	NR	NR		
1970s-1980s	NR	NR	NR		
High HDI	NR	NR	NR	N/A	
Low HDI	NR	NR	NR		
1990s-2000s	1	3/4	75.00 (30.06-95.44)		0.00005
High HDI	NR	NR	NR	N/A	
Low HDI	1	3/4	75.00 (30.06-95.44)		
2010s-2020s	2	2/2444	0.08 (0.00-0.26)		
High HDI	NR	NR	NR	N/A	
Low HDI	2	2/2444	0.08 (0.00-0.26)		
Overall	3	5/2448	N/A*		
Unknown/undetermined					
Pre-1970s	6	17/301	5.28 (2.81-8.34)		
High HDI	2	7/152	4.52 (1.58-8.63)	0.393	
Low HDI	4	10/149	6.37 (2.67-11.22)		
1970s-1980s	3	6/155	3.55 (0.94-7.35)		
High HDI	1	1/57	1.75 (0.31-9.29)	0.322	
Low HDI	2	5/98	4.84 (1.16-10.33)		
1990s-2000s	9	41/638	2.07 (0.73-3.85)		0.843
High HDI	2	6/120	4.79 (1.40-9.66)	0.821	
Low HDI	7	35/518	1.50 (0.26-3.40)		
2010s-2020s	5	159/2949	5.09 (4.30-5.94)		
High HDI	NR	NR	NR	N/A	
Low HDI	5	159/2949	5.09 (4.30-5.94)		
Overall	23	223/4043	3.59 (2.92-4.32)		
Coincidental causes					
Pre-1970s	NR	NR	NR		
High HDI	NR	NR	NR	N/A	0.321
Low HDI	NR	NR	NR		

1970s-1980s	2	2/65	2.83 (0.00-9.09)	
High HDI	1	1/22	4.55 (0.81-21.80)	0.581
Low HDI	1	1/43	2.33 (0.41-12.06)	
1990s-2000s	1	1/34	2.94 (0.52-14.92)	
High HDI	1	1/34	2.94 (0.52-14.92)	N/A
Low HDI	NR	NR	NR	
2010s-2020s	1	20/1243	1.61 (1.04-2.47)	
High HDI	NR	NR	NR	N/A
Low HDI	1	20/1243	1.61 (1.04-2.47)	
Overall	4	23/1342	0.81 (0.27-1.55)	

***Analysis produced effect estimates with values of zero. HDI=human development index. NR=not reported. N/A=not available.**

Table 4.1 Causes of caesarean-related deaths over time and by HDI status

4.2.5 Sensitivity analyses

The estimates for all causes were not sensitive to the model used (APPENDIX H, Table 17). Similarly, results were similar when sensitivity analysis was performed by excluding studies that exclusively evaluated regional/general anesthesia or emergency/elective surgeries (APPENDIX H: Table 18). Since there were only a few studies before 1960 we conducted a sensitively analysis by removing those studies, and the results were robust to this exclusion (APPENDIX H: Table 21). Additionally, in sensitivity analysis, the proportions for all the causes of death were not materially different for prospective versus retrospective studies (APPENDIX H: Table 19-20). There was insufficient representation of high HDI countries in the 2010s-2020s within all the cause of death categories. In our analysis of the proportion of reported causes of caesarean-related deaths due to obstetric haemorrhage (Egger's test p=0.001; APPENDIX H: Figure 8), pregnancy-related infections (Egger's test p=0.033; APPENDIX H: Figure 9), unanticipated complications of management (Egger's test p=0.005; APPENDIX H: Figure 12), and other obstetric complications (Egger's test p=0.002; APPENDIX H: Figure 13) there was evidence of small study effect. However, evidence of small study effects was not detected for our analysis of deaths during or following caesarean section as a result of hypertensive disorders (Egger's test p=0.050; APPENDIX H: Figure 10), obstetric embolism (Egger's test p=0.333; APPENDIX H: Figure 11), non-obstetric complications (Egger's test p=0.868; APPENDIX H: Figure 14), and unknown or undetermined causes (Egger's test p=0.778; APPENDIX H: Figure 15).

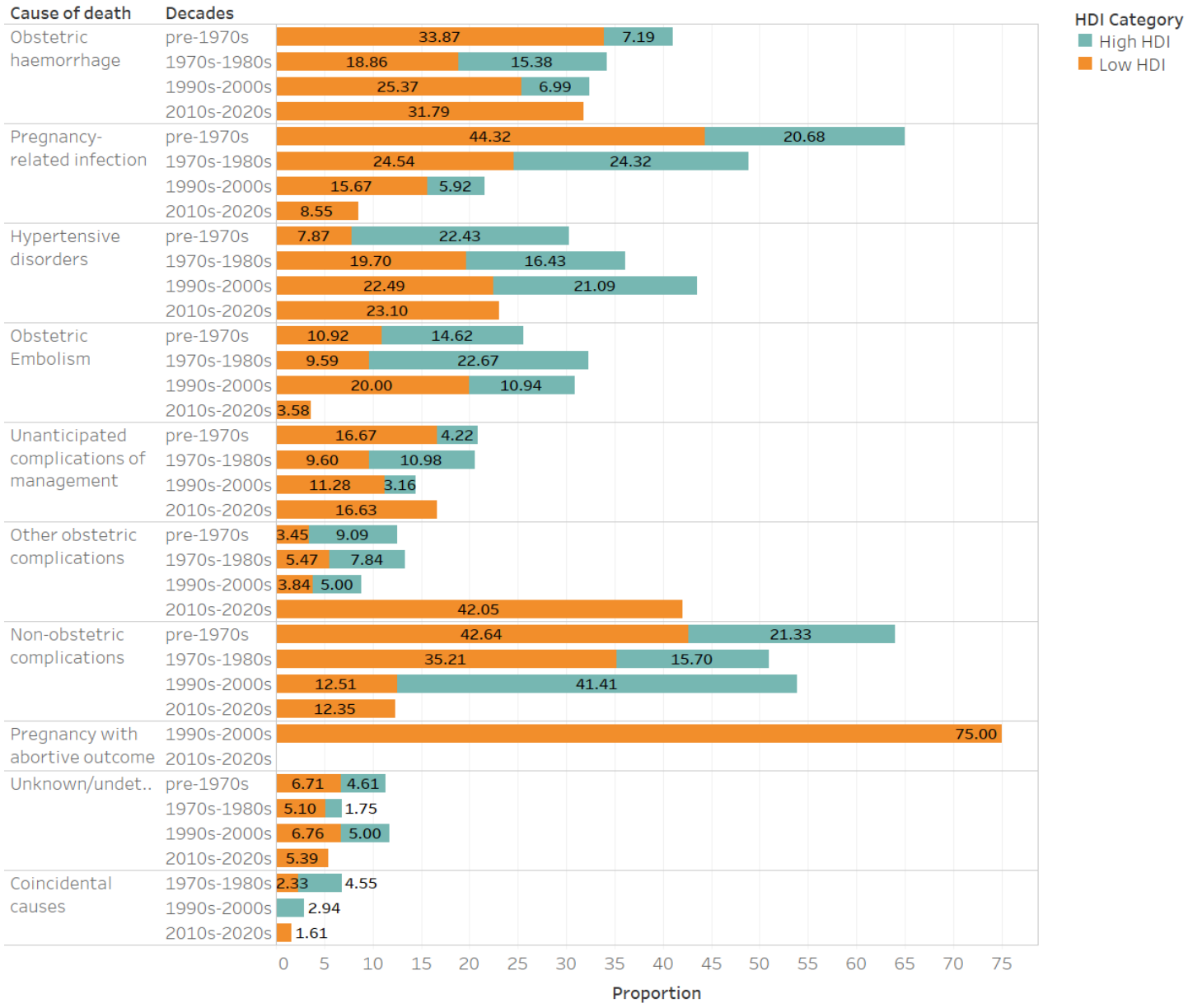
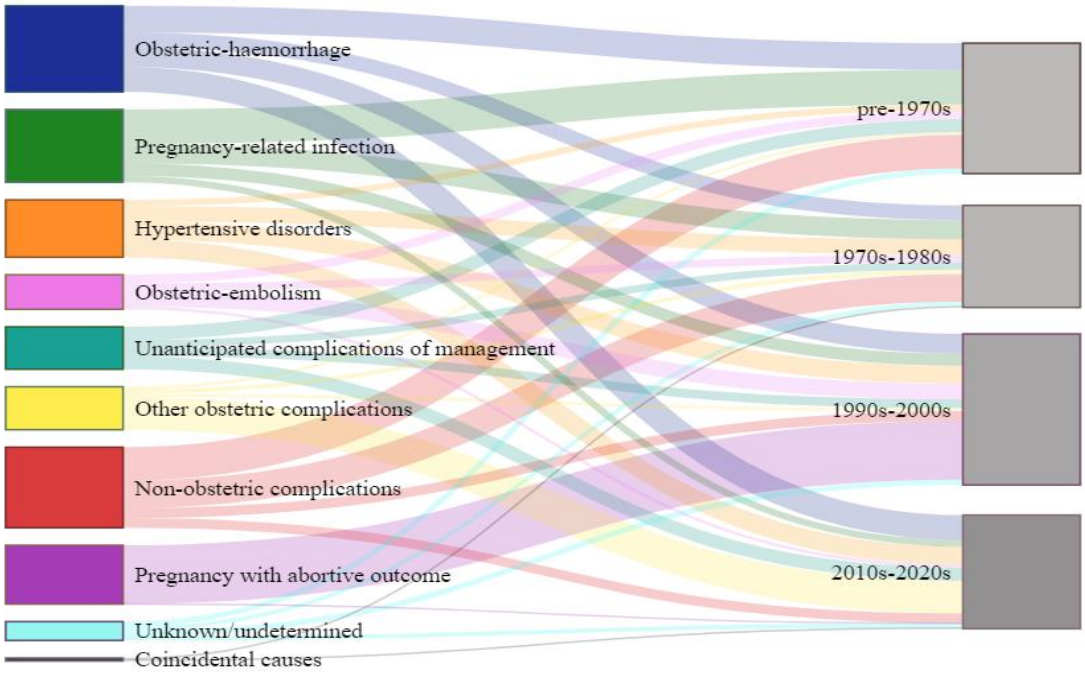
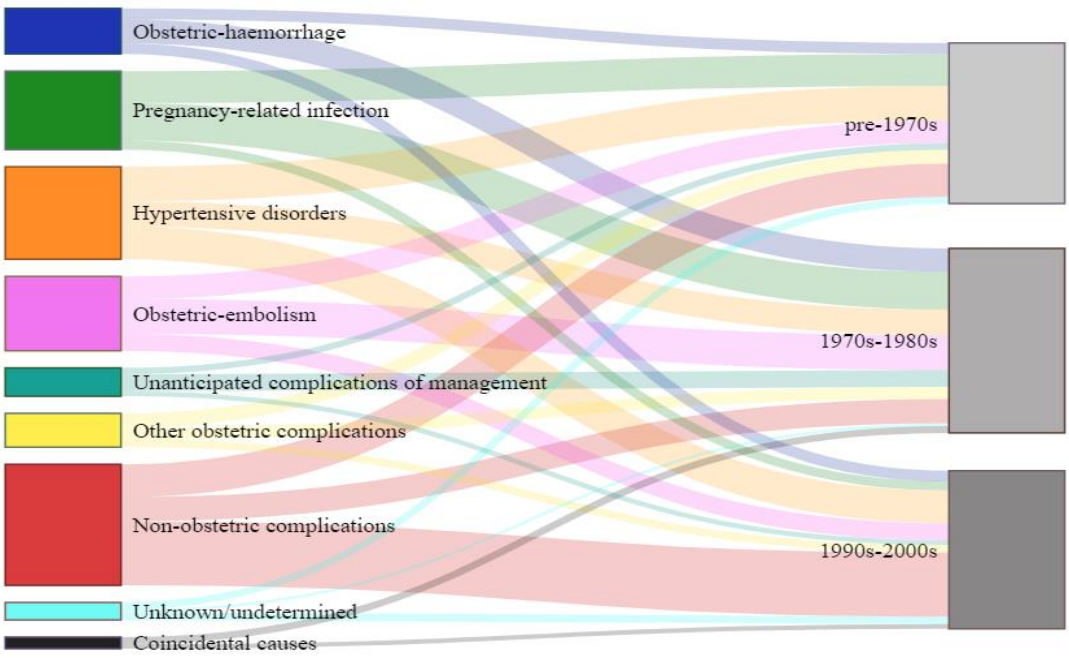


Figure 4.6 Proportion of reported causes of caesarean-related death by time and HDI status, using unweighted data



Low HDI Countries



High HDI Countries

Figure 4.7 Sankey chart demonstrating distribution of categories of reported causes of caesarean-related deaths over time in low and high HDI countries, using unweighted data. The width of the links from causes to decades represent the proportion (%) of cause-specific deaths over the total reported deaths during or following caesarean section.

4.3 DISCUSSION

This systematic review and meta-analysis provides an understating of the global distribution of reported causes of caesarean-related deaths over time, and by HDI status. Changing patterns in the proportions of reported causes of death during or following caesarean section throughout the decades were present. The proportion of reported caesarean-related deaths due to obstetric haemorrhage and hypertensive disorders significantly increased over the past 70 years, whereas the proportion of deaths attributed to pregnancy-related infection and non-obstetric complications significantly reduced over time. A significant relationship was present between HDI status and the proportion of deaths attributed to obstetric haemorrhage, as HDI increased the proportion of deaths due to this causes decreased. The remaining reported causes of death showed no significant relation with HDI.

Although the overall risk of maternal mortality during or following caesarean section has reduced over time, identification of the changes in the specific causes of death provide further insight into why women are dying during or following caesarean section throughout the decades. The increase in the proportion of deaths represented by obstetric haemorrhage may be due to lack of resources for perioperative monitoring and timely treatment of haemorrhage. In addition, late presentation or delays in caesarean section, which lead to more complicated deliveries, may be playing a role. [12] Previous studies on obstetric haemorrhage place emphasis on a proposed timeframe for optimal diagnosis and treatment of haemorrhagic shock. During the onset of haemorrhage, timely resuscitation is essential to enhance safety and reduce risk of death.[13] Survival is lower when the time between the onset of shock and resuscitation is prolonged. In the present study, obstetric haemorrhage was the most commonly reported cause of death for 24-hour mortality, with 31.3% of caesarean attributed deaths occurring due to this cause. To prevent further increase in reported causes of caesarean-related deaths attributed to obstetric haemorrhage, health care systems need to be strengthened through further education and training to enhance the knowledge and skills of clinicians and healthcare workers.[12] Additionally, effective management of obstetric haemorrhage requires recognition of risk

factors, enhanced detection and treatment, mobilization and rapid response of the multi-disciplinary team, and resuscitation of the patient to maintain blood volume.[14]

Reported causes of caesarean-related deaths due to hypertensive disorders have progressively increased over time. As with most causes of death attributable to caesarean section avoidable delays in transport, triage and treatment contribute to a majority of maternal deaths due to hypertensive disorders, especially in low HDI countries.[15] The most common preventable factor for this is a delay in seeking care from the patient along with additional patient-oriented issues, i.e. late presentation of women for antenatal care or a delay in hospital visits when symptoms arise.[16] Additionally, errors in hypertensive disorder management such as a lack of attention to blood pressure control, inappropriate use of magnesium sulphate, along with misidentification of symptoms for pulmonary edema may contribute to the increasing proportion of reported causes of caesarean-related deaths due to hypertensive disorders.[11,17] In high HDI countries, this increase may be a result of more frequent diagnoses of hypertensive disorders, combined with an increasing frequency of women with pre-existing health conditions opting to have children. Hypertensive disorders are one of the most prevalent medical conditions of pregnancy, and the prevention and management of hypertensive disorders is difficult.[16] To reduce hypertensive related maternal deaths during or following caesarean section, improvements in maternal education, evidence-based guidelines for management of severe hypertension, administration of emergency antihypertensive agents, prenatal surveillance, and timely caesarean section are required.[18]

Reported causes of caesarean-related deaths that exhibited a decease over the years, included pregnancy-related infection and non-obstetric complications. The reduction in the proportion of reported deaths attributed to pregnancy-related infection over time may be have been achieved as a result of advancements in antisepsis and prophylactic antibiotics, along with evidence-based recommendations and enhanced sanitation throughout the obstetric procedure.[21] Although the proportion of women having children and undergoing caesarean section continues to rise along with the risk of non-obstetric complications, continuous efforts to enhance patient safety throughout the

years may have allowed for a decrease in the proportion of caesarean- related deaths due to non-obstetric complications. Global patient safety initiatives, including the use of evidence-based interventions, enhanced training of skilled providers, development of guidelines and recommendations, and surgical safety checklists, allowed for a reduction in the proportion of maternal deaths during or following caesarean section due to pregnancy-related infection and non-obstetric complications.[19] Assessment of the hypotheses mentioned above could not be conducted due to insufficient data contained within the studies.

No significant relationship was evident between the reported causes of caesarean-related deaths and HDI, with the exception of obstetric haemorrhage. As HDI increased, the proportion of deaths attributed to obstetric haemorrhage decreased; increased availability of drugs/supplies, advanced technology, and skilled healthcare workers are predominately present in high resource settings. A lack of decline in low resource settings may be attributed to delayed caesarean section, insufficient technology, and an absence of education/training in the management of obstetric haemorrhage. Additionally, the other reported causes of caesarean-related deaths showed no relation with HDI. These findings indicate that when perioperative maternal mortality during or following caesarean section was broken down into specific causes, the gaps in the equity and equality of health care systems and access to safe caesarean sections diminished. From this it may be assumed that efforts targeted towards specific causes along with an absence of initiatives for other causes have resulted in similar effects in low and high HDI countries. This implies that the specific reported causes of caesarean-related deaths assessed may be prevalent to similar degrees globally. When independently looking at the discrepancies of low and high resource settings based on the categories of reported causes of caesarean-related death, efforts to improve global caesarean-related deaths, specifically in low HDI countries, may have allowed for a reduction in the gaps in terms of the access to safe caesarean section and quality of care. Sufficient provisions of equipment and medication in obstetric health units and enhanced performance of obstetric procedures by skilled birth attendants within low HDI countries may be prominent reasons for the nonsignificant relation between the reported causes of caesarean-related deaths and HDI.

This implies that efforts from the Millennium Development Goals (MDGs) and the ongoing SDG-3[20] have provided a reduction in the gaps of cause-specific caesarean deaths between low and high HDI settings for most causes assessed.

Distinguishing between the cause of caesarean-related deaths is essential when planning, monitoring, and evaluating interventions for the improvement of maternal safety. Conversely, it identifies the need for interventions that assess the specific causes of death. Failure to differentiate between the causes, along with implementation of inappropriate interventions, may result in impractical expectations for the effect of the intervention on the cause of death and misallocation of resources. Consequently, when identifying appropriate interventions, clinicians must take into account common causes of caesarean-related deaths in order to tackle those specific complications of pregnancy and delivery using suitable interventions. The results of our analysis will provide policy makers with a representation of the changes in the distribution of caesarean-related deaths over time, globally. This will allow them to implement and enforce certain interventions and guidelines to target causes with increasing frequency, and to continually enhance interventions for causes with declining frequencies. The use of effective cause-specific interventions according to the distribution of causes in resource settings may have large implications for the reduction of the global rate of maternal mortality during or following caesarean section in order to diminish preventable maternal deaths and reach the SDG-3 target.[20] Additionally, the findings may be used by clinicians to assist with evidence-based decision making in order to assess the potential benefits and risks of the individual causes of caesarean-related deaths for patients undergoing caesarean section.

This systematic review and meta-analysis is the first to analyze the trends and distributions in the causes of maternal death during or following caesarean section over time, and within countries of low and high HDI. Our search was extensive and comprehensive as we collected studies from numerous databases, grey literature sources, and other additional data sources to ensure relevant studies were included. We conducted a rigorous quality assessment and attempted to the reduce risk of bias as a result of weaknesses in the methodology by implementing strict inclusion and exclusion criteria.

To assess the robustness of the findings, clinical heterogeneity was explored through subgroup and sensitivity analyses. Selection bias, along with differences in patient risk factors in low and high resource settings, were minimized through the inclusion of patient populations with varying age groups, co-morbidities, and indication for caesarean section. In order to reduce confounding effects within the decades due to HDI status, we individually assessed the trends of the reported causes of caesarean-related deaths within low and high HDI countries. Due to inadequate patient-level data and our inability to adjust for indications of caesarean sections and co-morbidities, only crude estimates for the reported causes of caesarean-related deaths were obtained. This may have caused the results to be subject to confounding and bias that varied over the decades. Due to high levels of statistical heterogeneity and a predominate number of low-quality studies, caution should be taken when interpreting these results. The findings of the analysis can only be as robust as the data obtained from the primary studies. Cause of death data poses difficulty when conducting analyses due to errors in the classification and representation of causes, along with omissions and incorrect entries as a result of pre-existing disorders leading to maternal death. Additionally, inadequate detail in the reporting of caesarean-related causes of death by the included studies, along with the absence of differentiation between primary and contributory causes of death, resulted in difficulty when categorizing the specific causes reported by the studies. ICD-MM provides codes and categories for primary causes of death, however, many of the included studies reported contributory causes that had to be classified as unknown or undetermined as they did not fit into the pre-defined categories by ICD-MM. Conversely, studies that reported on multiple primary causes of caesarean-related deaths were placed into corresponding categories based on the causes reported, and this may have cause inflation in the numerators as single patients were placed in multiple categories. The generalizability of our findings in terms of the global distribution of reported causes of caesarean-related deaths may be affected, as few included studies were from high HDI countries.

Future research on the causes of caesarean-related deaths should further assess the prevalence of each cause within specific regions of the world and attempt to break down the categories into more specific root causes and contributors. Furthermore, efforts to

improve the quality of recording, reporting, and ascertainment of the causes of death within primary studies will increase the robustness of future estimates. This synthesis should be regularly updated in order to report changes in the profile of reported causes of caesarean-related deaths.

4.4 CONCLUSION

The proportion of all caesarean-related deaths due to obstetric haemorrhage and hypertensive disorders have increased over the past 70 years. This indicates that lack of resources for perioperative monitoring and timely treatment of haemorrhage, errors in hypertensive disorder management, along with late presentation or delays in caesarean section may have contributed to the rise in caesarean-related deaths due to these causes over time. However, causes of death during or following caesarean section attributed to pregnancy-related infection and non-obstetric complications have decreased over time. This demonstrates that the initiatives to enhance safe access to caesarean section, which contributed to the reduction of overall perioperative maternal mortality, may be taking effect in reducing maternal mortality due to these specific causes. For most of the reported causes of caesarean-related deaths, no relationship was present between the proportion of these causes and HDI, implying that inequalities may not be present across HDI status when assessing individual cause categories. In order to continually reduce caesarean-related deaths, efforts such as universal access to emergency obstetric procedures and high-quality healthcare services should be reinforced in both low and high HDI countries.

4.5 BIBLIOGRAPHY

1. The Sustainable Development Goals and Maternal Mortality. (2019). Retrieved 10 July 2020, from https://www.mhtf.org/topics/the-sustainable-development-goals-and-maternal-mortality/
2. Khan, K. S., Wojdyla, D., Say, L., Gülmezoglu, A. M., & Van Look, P. F. (2006). WHO analysis of causes of maternal death: a systematic review. *Lancet (London, England)*, *367*(9516), 1066–1074. https://doi.org/10.1016/S0140-6736(06)68397-9
3. Dickersin K. (2002). Systematic reviews in epidemiology: why are we so far behind?. *International journal of epidemiology*, *31*(1), 6–12. https://doi.org/10.1093/ije/31.1.6

4. Freedman, L. P., Waldman, R. J., de Pinho, H., Wirth, M. E., Chowdhury, A. M., & Rosenfield, A. (2005). Transforming health systems to improve the lives of women and children. *Lancet (London, England)*, *365*(9463), 997–1000. https://doi-org.proxy1.lib.uwo.ca/10.1016/S0140-6736(05)71090-4
5. Sobhy, S., Babiker, Z., Zamora, J., Khan, K. S., & Kunst, H. (2017). Maternal and perinatal mortality and morbidity associated with tuberculosis during pregnancy and the postpartum period: a systematic review and meta-analysis. *BJOG : an international journal of obstetrics and gynaecology*, *124*(5), 727–733. https://doi-org.proxy1.lib.uwo.ca/10.1111/1471-0528.14408
6. Human Development Report 2019— Beyond income, beyond averages, beyond today: Inequalities in human development in the 21st century. (2019). New York: United Nations Development Program. Retrieved 12 July 2020, from http://hdr.undp.org/sites/default/files/hdr2019.pdf
7. World Health Organization. (2012). *The WHO application of ICD-10 to deaths during pregnancy, childbirth and the puerperium: ICD-MM*. Geneva: WHO.
8. Higgins, J. P., & Thompson, S. G. (2002). Quantifying heterogeneity in a meta-analysis. *Statistics in medicine*, *21*(11), 1539–1558. https://doi.org/10.1002/sim.1186
9. Zongo, A., Dumont, A., Fournier, P., Traore, M., Kouanda, S., & Sondo, B. (2015). Effect of maternal death reviews and training on maternal mortality among cesarean delivery: post-hoc analysis of a cluster-randomized controlled trial. *European journal of obstetrics, gynecology, and reproductive biology*, *185*, 174–180. https://doi.org/10.1016/j.ejogrb.2014.12.023
10. Chi, I. C., Whatley, A., Wilkens, L., & Potts, M. (1986). In-hospital maternal mortality risk by cesarean and vaginal deliveries in two less developed countries--a descriptive study. *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics*, *24*(2), 121–131. http://dx.doi.org/10.1016/0020-7292%2886%2990006-8
11. Duley, L., Gülmezoglu, A. M., & Chou, D. (2010). Magnesium sulphate versus lytic cocktail for eclampsia. *The Cochrane database of systematic reviews*, *2010*(9), CD002960. https://doi.org/10.1002/14651858.CD002960.pub2
12. Maswime, S., & Buchmann, E. (2016). Causes and avoidable factors in maternal death due to cesarean-related hemorrhage in South Africa. *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics*, *134*(3), 320–323. https://doi-org.proxy1.lib.uwo.ca/10.1016/j.ijgo.2016.03.013
13. Lalonde, A., Daviss, B. A., Acosta, A., & Herschderfer, K. (2006). Postpartum hemorrhage today: ICM/FIGO initiative 2004-2006. *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics*, *94*(3), 243–253. https://doi-org.proxy1.lib.uwo.ca/10.1016/j.ijgo.2006.04.016
14. Sebghati, M., & Chandraharan, E. (2017). An update on the risk factors for and management of obstetric haemorrhage. *Women's health (London, England)*, *13*(2), 34–40. https://doi-org.proxy1.lib.uwo.ca/10.1177/1745505717716860

15. von Dadelszen, P., & Magee, L. A. (2016). Preventing deaths due to the hypertensive disorders of pregnancy. *Best practice & research. Clinical obstetrics & gynaecology*, *36*, 83–102. https://doi-org.proxy1.lib.uwo.ca/10.1016/j.bpobgyn.2016.05.005
16. Moodley J. (2004). Maternal deaths associated with hypertensive disorders of pregnancy: a population-based study. *Hypertension in pregnancy*, *23*(3), 247–256. https://doi.org/10.1081/PRG-200030301
17. Clark, S. L., Belfort, M. A., Dildy, G. A., Herbst, M. A., Meyers, J. A., & Hankins, G. D. (2008). Maternal death in the 21st century: causes, prevention, and relationship to cesarean delivery. *American journal of obstetrics and gynecology*, *199*(1), 36.e1–e11. https://doi-org.proxy1.lib.uwo.ca/10.1016/j.ajog.2008.03.007
18. Keskinkılıç, B., Engin-Üstün, Y., Sanisoğlu, S., Şahin Uygur, D., Keskin, H. L., Karaahmetoğlu, S., Özcan, A., Esen, M., Alkan, A., Kabasakal, A., & Şencan, İ. (2017). Maternal mortality due to hypertensive disorders in pregnancy, childbirth, and the puerperium between 2012 and 2015 in Turkey: A nation-based study. *Journal of the Turkish German Gynecological Association*, *18*(1), 20–25. https://doi.org/10.4274/jtgga.2016.0244
19. Haider, A., Scott, J. W., Gause, C. D., Meheš, M., Hsiung, G., Prelvukaj, A., Yanocha, D., Baumann, L. M., Ahmed, F., Ahmed, N., Anderson, S., Angate, H., Arfaa, L., Asbun, H., Ashengo, T., Asuman, K., Ayala, R., Bickler, S., Billingsley, S., Bird, P., … Abdullah, F. (2017). Development of a Unifying Target and Consensus Indicators for Global Surgical Systems Strengthening: Proposed by the Global Alliance for Surgery, Obstetric, Trauma, and Anaesthesia Care (The G4 Alliance). *World journal of surgery*, *41*(10), 2426–2434. https://doi.org/10.1007/s00268-017-4028-1
20. The Sustainable Development Goals and Maternal Mortality. (2019). Retrieved 10 July 2020, from https://www.mhtf.org/topics/the-sustainable-development-goals-and-maternal-mortality/
21. Halder, A., Vijayselvi, R., & Jose, R. (2015). Changing perspectives of infectious causes of maternal mortality. *Journal of the Turkish German Gynecological Association*, *16*(4), 208–213. https://doi-org.proxy1.lib.uwo.ca/10.5152/jtgga.2015.0134
22. Liberati, A., Altman, D. G., Tetzlaff, J., Mulrow, C., Gøtzsche, P. C., Ioannidis, J. P., Clarke, M., Devereaux, P. J., Kleijnen, J., & Moher, D. (2009). The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ (Clinical research ed.)*, *339*, b2700. https://doi.org/10.1136/bmj.b2700
23. Stroup, D. F., Berlin, J. A., Morton, S. C., Olkin, I., Williamson, G. D., Rennie, D., Moher, D., Becker, B. J., Sipe, T. A., & Thacker, S. B. (2000). Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA*, *283*(15), 2008–2012. https://doi.org/10.1001/jama.283.15.2008

Chapter 5 - The effect of interventions for caesarean section on perioperative maternal mortality

5 OVERVIEW

In our systematic overview, chapter 1 we identified available syntheses on the effect of perioperative interventions for caesarean section on maternal mortality. This was conducted in order to identify gaps in the evidence base and to efficiently examine the effects of individual interventions for caesarean section on maternal mortality. Subsequently, we had intended to update the meta-analyses of interventions identified in Chapter 1 with the added studies identified in Chapter 3 in order to provide updated estimates of the impact of caesarean section-related interventions on maternal and neonatal mortality. However, we were unable to provide updated meta-analyses for specific interventions as most of the studies identified for Chapter 3 were descriptive observational studies that did not specifically study the impact of defined interventions on maternal or neonatal mortality through comparative studies, or if they were comparative, did not provide adequate data to update previous meta-analyses.

From the 196 studies Identified in Chapter 3, only five studies were comparative,[1-5] and one was a randomized controlled trial.[6] Table 5.1 outlines the additional studies of interventions identified, which were considered for potential inclusion, but for which there was inadequate new studies to update previous meta-analyses. The studies that investigated anesthesia were already included in a meta-analysis assessed in Chapter 1.[1,3,7] Similarly, the studies assessing clinical officers as compared to medical officers were include in a previous meta-analysis from Chapter 1.[1,2,5,8] Therefore, we were unable to attain additional studies to update prior findings. The other two intervention and comparator groups had insufficient studies to conduct a meta-analysis.[4,6]

It is notable that all of the additional studies identified in Chapter 3, would only serve to further consolidate the conclusions of prior meta-analyses. For example, the conclusion that clinical officers instead of medical doctors were associated with increased

maternal mortality, and conclusions that general anesthesia instead of regional anesthesia was associated with increased mortality would be further strengthened in the prior meta-analyses, which had already shown these same conclusions given the pre-existing studies on these same questions. This raises the possibility that current research may be redundant on these areas, unless they are adding aspects to prior evidence on this topic. Efficient research requires that existing gaps should be the focus of new research, rather than continuously repeating the same type of research on older questions which may already have an adequate evidence base.

Study	Comparisons	Population	Effect estimate	Main findings
Fenton et al.[1]	Clinical officer surgeon's vs medically qualified surgeons	All caesarean sections	unadjusted OR: 1.8 (1.0 to 3.1), adjusted OR: 1.4 (0.7 to 2.9), p-value=0.4	-
Fenton et al.[1]	Untrained vs trained anaesthetists	All caesarean sections	unadjusted OR: 2.7 (1.6 to 4.6), adjusted OR: 2.9 (1.6 to 5.1), p-value: <0.001	-
Fenton et al.[1]	General vs spinal anaesthesia	All caesarean sections	unadjusted OR: 13.1 (4.7 to 35), adjusted OR: 6.6 (2.3 to 18.7), p-value: <0.001	-
Chilopora et al.[2]	Clinical officer vs medical officers	All women undergoing caesarean section	clinical officers n=22 (1.2%), medical officers n=1 (0.4%) , p-value: 0.292	There were numerically more maternal deaths in the CO group (n = 22/1875; 1.2%) than in the MO group (n = 1/ 256; 0.4%) but the difference is not statistically significant by Fisher's exact test.
Adisso et al.[3]	Regional vs general anesthesia	all women who have undergone a caesarean.	regional anesthesia n=0, general anesthesia n=2 (1.3%), p-value: 0.478	Between control cases, caesarean sections under general anaesthesia, we count 19 cases of difficulty of

				intubations 12, 5% and 2 cases of maternal death operating 1, 3%.
Gessessew et al.[4]	Nonphysician clinician's vs physician	All deliveries	physician n=8 (47.1), NPC n=9 (52.9), p-value: 0.80	No statistical differences in mortality by type of attending staff.
McCord et al.[5]	Assistant medical officer's vs medical officers	major emergency obstetrical surgery/ All emergency caesarean sections	AMO n=16 (1.7%), MO n=5 (3.5%), OR 0.47 95% CI (0.16–1.68), p-value: 0.14	-
Zongo et al.[6]	Interactive workshop and quarterly educational clinically oriented and evidence-based outreach visits vs no intervention from the research team.	All deliveries	Adjusted OR: 0.71 (0.58–0.82), p-value: 0.0034	Compared to the control, the adjusted OR of maternal mortality was 0.71 (95% CI: 0.58–0.82, p = 0.0034) among women with caesarean delivery.

Table 5.1 Summary of comparative studies: Impact on maternal mortality

As there still exists important unaddressed knowledge gaps regarding how to reduce maternal and neonatal mortality when caesarean section is required, we call on further research to be conducted on topics that remain unaddressed, in order to advance the evidence base and provide an umbrella assessment of interventions for caesarean section as effect moderators on perioperative maternal mortality.

5.1 BIBLIOGRAPHY

1. Fenton, P. M., Whitty, C. J., & Reynolds, F. (2003). Caesarean section in Malawi: prospective study of early maternal and perinatal mortality. *BMJ (Clinical research ed.)*, *327*(7415), 587. https://doi.org/10.1136/bmj.327.7415.587
2. Chilopora, G., Pereira, C., Kamwendo, F., Chimbiri, A., Malunga, E., & Bergström, S. (2016). Postoperative outcome of caesarean sections and other major emergency obstetric surgery by clinical officers and medical officers in Malawi. *Malawi Medical Journal*, *28*(3), 94–98. https://doi.org/10.1186/1478-4491-5-17
3. Adisso, S., Takpara, I., Teguete, I., Gbegnide, H., Chobli, M., & Alihonou, E. (2006). Pronostic maternel selon le type d'anesthésie pour la césarienne en milieu urbain au Bénin. *Fondation Genevoise pour la Formation et la Recherche Médicales*.
4. Gessessew, A., Barnabas, G. A., Prata, N., & Weidert, K. (2011). Task shifting and sharing in Tigray, Ethiopia, to achieve comprehensive emergency obstetric care.

International Journal of Gynecology and Obstetrics, *113*(1), 28–31. https://doi.org/10.1016/j.ijgo.2010.10.023

5. McCord, C., Mbaruku, G., Pereira, C., Nzabuhakwa, C., & Bergstrom, S. (2009). The quality of emergency obstetrical surgery by assistant medical officers in Tanzanian district hospitals. *Health Affairs*, *28*(5), w876–w885. https://doi.org/10.1377/hlthaff.28.5.w876
6. Zongo, A., Dumont, A., Fournier, P., Traore, M., Kouanda, S., & Sondo, B. (2015). Effect of maternal death reviews and training on maternal mortality among cesarean delivery: post-hoc analysis of a cluster-randomized controlled trial. *European journal of obstetrics, gynecology, and reproductive biology*, *185*, 174–180. https://doi.org/10.1016/j.ejogrb.2014.12.023
7. Sobhy, S., Zamora, J., Dharmarajah, K., Arroyo-Manzano, D., Wilson, M., Navaratnarajah, R., et al (2016). Anaesthesia-related maternal mortality in low-income and middle-income countries: A systematic review and meta-analysis. *The Lancet Global Health*, *4*, e320-e327. https://doi-org.proxy1.lib.uwo.ca/10.1016/S2214-109X(16)30003-1
8. Wilson, A., Lissauer, D., Thangaratinam, S., Khan, K.S., MacArthur, C., & Coomarasamy, A. (2011). A comparison of clinical officers with medical doctors on outcomes of caesarean section in the developing world: Meta-analysis of controlled studies. *BMJ*, *342*, d2600. https://doi-org.proxy1.lib.uwo.ca/10.1136/bmj.d2600

Chapter 6 – Discussion

6 GENERAL DISCUSSION

This thesis provides a collection of successive stages of enquiry on maternal mortality during or following caesarean section. This final chapters aims to bring together all the individual research objectives by presenting a discussion on the topic of maternal mortality during or following caesarean section.

The overall goal of this thesis was to provide additional insight into the magnitude of risk of maternal and neonatal death to inform patient safety during or following caesarean section. In order to achieve these objectives, we introduced concepts and new definitions for perioperative maternal and neonatal mortality, created frameworks for caesarean-related intervention categories and evidence gap maps, and proposed methodologies for visually representing the flow of reported causes of caesarean-related deaths over time through Sankey diagrams. First, in Chapter 2, we provided an overview of mortality effects of interventions for caesarean section summarized from previous systematic reviews in order to identify gaps in the evidence base for future research. In Chapter 3, we systematically updated a previous study[1] to provide contemporary estimates of the risk of perioperative maternal and neonatal mortality over time and by HDI status in order to inform whether global efforts to reduce caesarean attributed maternal deaths have been successful. In Chapter 4, we sought to explore reasons why women die during or after caesarean section and whether these reported causes of death have changed over time and by country HDI status. In Chapter 5, we further assessed the effect of various intervention and comparator groups on the outcome of caesarean attributed maternal deaths in order to fill in the gaps that were identified in Chapter 2.

Through this thesis we identified that, none of the interventions studied in meta-analyses resulted in a significantly *lower* risk in all-cause maternal mortality or neonatal mortality. In contrast, two interventions were associated with a significantly *higher* risk of mortality: the use of general anaesthesia instead of regional anaesthesia; and, delivery

of caesarean section by clinical officers instead of medical officers. These results need to be interpreted in light of important caveats. In particular, since we limited our assessment of interventions for this section to meta-analyses assessing death related to caesarean section, there will be a number of interventions with benefits other than a proven reduction in mortality which were not included in our review in Chapter 2 due to the fact that they either did not assess mortality, or were singular trials which have not yet been included in a meta-analysis. Furthermore, this chapter needed to be interpreted in light of the fact that a number of meta-analyses of interventions found no difference in mortality, but were still underpowered to rule out significant impacts on mortality given the relatively few studies which have been done with mortality as an outcome.

Our analysis of epidemiologic trends showed that POMMR progressively decreased over the decades, whereas PONMR fluctuated over time. Analysis of causes of death showed that the proportion of caesarean-related deaths due to obstetric haemorrhage and hypertensive disorders significantly increased over the past 70 years. However, reported causes of maternal death during or following caesarean section from pregnancy-related infection and non-obstetric complications have significantly decreased over time. Meta-regression by HDI showed that the proportion of deaths attributed to obstetric haemorrhage declined as HDI increased, whereas, other reported causes of death showed no relationship to HDI status.

6.1 IMPACT AND IMPORTANCE

Assessment of the magnitude of maternal mortality associated with caesarean section along with the identification of probable causes over time has important implications for the field of evidence-based medicine and as per our knowledge has not been previously conducted. The reviews performed within this thesis were the largest reviews of caesarean attributed maternal mortality and significantly expanded on analyses of this outcome over time and within low and high resource settings. The findings of our analyses may be used as a tool by researchers to fill in further gaps and expand on the evidence of maternal mortality during or following caesarean section as this area is not research replete. Additionally, for clinicians and policy makers the results may be utilized

as a guide for decisions related to implementation (or de-implementation) of interventions, allocation of resources, and access to caesarean section.

6.2 IMPLICATIONS

The findings and conclusions of this thesis have implications for decision making, prioritization and allocation of resources, monitoring the integration of services and quality of care, and identifying areas for future potential research. Continuous global efforts to improve deficiencies in health care systems and provide access to caesarean section through the availability of supplies and drugs, adequate training and number of skilled providers, presence of guidelines for evidence-based care, surgical safety checklists along with access to prenatal care and management of pregnancy-related complications have contributed to the progressive decline in perioperative maternal mortality during or following caesarean section.[2] These initiatives should continually be reinforced in order to additionally reduce caesarean associated maternal deaths in the upcoming decades. For the overall assessment of perioperative maternal mortality, discrepancies were present for the risk of mortality among high and low HDI countries, however, these variations in maternal mortality were not present among most of the causes of death. Causes of caesarean-related deaths due to obstetric haemorrhage indicate potential gaps in the equity of access to safe and high-quality caesarean section. This category of death was the most commonly reported cause of caesarean associated death globally; obstetric haemorrhage accounted for 29.47% of reported deaths within our analysis. In light of this, global resources should be allocated to low HDI countries to provide focused research and interventions to improve caesarean-related bleeding. Routine availability of blood products, early identification of patients at risk of bleeding through enhanced monitoring, and implementation of recommended strategies from evidence-based guidelines should be further evaluated for contextually-relevant research and implementation within low HDI countries.[3,4] While a number of these interventions have not yet proven to reduce overall mortality, they have been shown to provide other benefits such as reduced risk of hemorrhage. Whether studies have been underpowered to show a significant reduction in all-cause mortality, or whether these interventions have net benefits without affecting mortality remains to be proven through continued large

clinical trials across low HDI contexts, with adequate power and follow-up, as indicated in our systematic overview of interventions in Chapter 2. Additionally, as seen in our evidence gap map there remains an absence of evidence syntheses to guide decision making regarding net impact on caesarean-related mortality for antifibrinolytic drugs within low income countries. Future research should focus on studies with adequate power to detect net impact on mortality, and should be incorporated into existing systematic reviews and meta-analyses to assess the effect of these interventions on caesarean-related maternal mortality in low income countries.

In order to further enhance the safety of caesarean section, efforts to reduce caesarean-related deaths due to obstetric haemorrhage and hypertensive disorders through prevention and treatment should also be prioritized on the global health agenda. Current research suggests promising results for the following interventions, further research should be focused on conducting studies of adequate size and duration to assess the net benefit and overall impact on maternal and neonatal mortality for the following: appropriate strategies for management of third stage of labour, accessibility and use of oxytocin for prevention of obstetric haemorrhage, use of cord traction for placental delivery, timing of caesarean section, antepartum surveillance of patients with preeclampsia for early identification, availability and administration of antihypertensive therapy, strategies for early access and patient transfer to reduce late presentation for caesarean.[3,5] Furthermore, protocols should be established in hospitals to allow optimal monitoring and response when maternal clinical conditions and vital signs change. Initiatives to reduce the risk of neonatal mortality following caesarean section and improvements in postnatal care interventions need to be made a priority globally in order to enhance the safety of the newborn.

Consistent updates on the magnitude of perioperative maternal and neonatal mortality and causes of caesarean-related deaths is necessary to monitor national and global commitments to improve maternal and neonatal health.

6.3 NEXT STEPS AND FUTURE DIRECTIONS

This research has provided a comprehensive global analysis of maternal and neonatal mortality during or following caesarean section. Through systematic reviews and meta-analyses, we have presented the first assessment of maternal mortality during or following caesarean section and causes of caesarean-related deaths over time and by HDI. However, the findings of this thesis are only the initial step in understanding the trends in caesarean attributed maternal deaths and being able to enhance maternal safety globally in an effort to save the lives of women undergoing this obstetric procedure.

Throughout the synthesis process we identified that the evidence base on this topic is less replete than expected. Within our systematic overview, there were various gaps in perioperative interventions for caesarean section and their impact on maternal mortality, especially in low income countries. This framework may be used by researchers in order to identify areas in which evidence is required in terms of interventions and country income settings. Various promising interventions at the most preliminary stages have not yet been adequately evaluated, demonstrating that there is more to be discovered within this research area as the evidence is deficient. Future studies on current and upcoming interventions must be of adequate size and duration for assessing mortality alongside other patient-relevant outcomes to provide meaningful guidance for evidence-based decision making, formulation of recommendations, programs and policies along with evidence-based care.

Further assessment of perioperative interventions for caesarean section should aim to add to the knowledge attained from Chapter 2 by expanding the inclusion criteria to all studies reporting on patient-relevant outcomes, including those that did not analyze maternal mortality. In addition, future studies should analyze costs and resource-related outcomes along with the health outcomes of the perioperative interventions for caesarean section. A comparison of the various interventions on the basis of costs and effectiveness, and formal economic evaluation would allow for informed priority-setting.

Investigations into maternal and neonatal mortality associated with caesarean section should examine the outcomes based on risk groups of patients. In order to obtain

a better understanding of the distribution of the causes of caesarean-related deaths, future research should further assess the prevalence of each cause within specific regions of the world. Additionally, efforts to improve the quality of recording, reporting, ascertainment of the causes of death, and uniformity of definitions and timing of causes of death within primary studies will allow for improved utility and comparability of future estimates. This will be exceedingly important to better inform global metrics for maternal and neonatal mortality in alignment with tracking progress toward effective and safe universal access to caesarean sections, in line with the 2030 sustainable development goals.

6.4 BIBLIOGRAPHY

1. Sobhy, S., Arroyo-Manzano, D., Murugesu, N., Karthikeyan, G., Kumar, V., Kaur, I., Fernandez, E., Gundabattula, S. R., Betran, A. P., Khan, K., Zamora, J., & Thangaratinam, S. (2019). Maternal and perinatal mortality and complications associated with caesarean section in low-income and middle-income countries: a systematic review and meta-analysis. *Lancet (London, England)*, *393*(10184), 1973–1982. https://doi.org/10.1016/S0140-6736(18)32386-9
2. Haider, A., Scott, J. W., Gause, C. D., Meheš, M., Hsiung, G., Prelvukaj, A., Yanocha, D., Baumann, L. M., Ahmed, F., Ahmed, N., Anderson, S., Angate, H., Arfaa, L., Asbun, H., Ashengo, T., Asuman, K., Ayala, R., Bickler, S., Billingsley, S., Bird, P., … Abdullah, F. (2017). Development of a Unifying Target and Consensus Indicators for Global Surgical Systems Strengthening: Proposed by the Global Alliance for Surgery, Obstetric, Trauma, and Anaesthesia Care (The G4 Alliance). *World journal of surgery*, *41*(10), 2426–2434. https://doi.org/10.1007/s00268-017-4028-1
3. *WHO Recommendations for the Prevention and Treatment of Postpartum Haemorrhage*. (2012). World Health Organization.
4. Bishop, D., Dyer, R. A., Maswime, S., Rodseth, R. N., van Dyk, D., Kluyts, H. L., Tumukunde, J. T., Madzimbamuto, F. D., Elkhogia, A. M., Ndonga, A., Ngumi, Z., Omigbodun, A. O., Amanor-Boadu, S. D., Zoumenou, E., Basenero, A., Munlemvo, D. M., Youssouf, C., Ndayisaba, G., Antwi-Kusi, A., Gobin, V., … ASOS investigators (2019). Maternal and neonatal outcomes after caesarean delivery in the African Surgical Outcomes Study: a 7-day prospective observational cohort study. *The Lancet. Global health*, *7*(4), e513–e522. https://doi-org.proxy1.lib.uwo.ca/10.1016/S2214-109X(19)30036-1
5. Magee, L. A., Pels, A., Helewa, M., Rey, E., von Dadelszen, P., & Canadian Hypertensive Disorders of Pregnancy Working Group (2014). Diagnosis, evaluation, and management of the hypertensive disorders of pregnancy: executive summary. *Journal of obstetrics and gynaecology Canada : JOGC = Journal d'obstetrique et gynecologie du Canada : JOGC*, *36*(5), 416–441. https://doi-org.proxy1.lib.uwo.ca/10.1016/s1701-2163(15)30588-0

Appendices

APPENDIX A: SYSTEMATIC OVERVIEW METHODOLOGY

DATABASE SEARCH STRATEGIES

EMBASE Search Strategy Conducted on July 25, 2019

1. exp cesarean section/ ; 100370 results
2. c?esar?an*.mp. ; 117930 results
3. CSection*.ti,ab,tw. ; 121 results
4. C-Section*.ti,ab,tw. ; 3446 results
5. (abdominal* adj2 (deliver* or birth*)).ti,ab.; 1056 results
6. or/1-5 ; 120147 results
7. exp maternal mortality/ ; 23365 results
8. exp Maternal death/; 2142 results
9. (maternal adj4 (mortal* or death*)).mp. ; 36744 results
10. ((pregnan* or wom?n) adj4 (mortal* or death*)).mp. ; 29538 results
11. or/7-10 ; 62541 results
12. exp meta analysis/ ; 174079 results
13. exp "systematic review"/ ; 222884 results
14. (meta-analy* or metaanaly*).mp. ; 279859 results
15. (systematic* adj (review* or overview*)).mp. ; 299859 results
16. or/12-15; 442690 results
17. 6 and 11 and 16; 436 results

Total: 436 results

MEDLINE Search Strategy Conducted on July 25, 2019

1. Exp cesarean section/; 43757 results
2. C?esar?an*.mp.; 71733 results
3. CSection*.mp. ; 2 results
4. C-Section*.mp. ; 1267 results
5. (abdominal* adj2 (deliver* or birth*)).ti,ab.; 742 results
6. or/1-5 ; 72468 results
7. exp maternal mortality/ ; 9980 results
8. exp Maternal death/. ; 707 results
9. (maternal adj4 (mortal* or death*)).mp. ; 23308 results
10. ((pregnan* or wom?n) adj4 (mortal* or death*)).mp. ; 20138 results
11. or/7-10 ; 40850 results
12. exp meta-analysis/ ; 105818 results
13. exp "systematic review"/ ; 114059 results
14. (meta-analy* or metaanaly*).mp. ; 186928 results
15. (systematic* adj (review* or overview*)).mp. ; 175996 results
16. or/12-15 ; 281729 results
17. 6 and 11 and 16 ; 240 results

Total: 240 results

Cochrane (CDSR) Search Strategy Conducted on July 25, 2019

1. MeSH descriptor: [Cesarean Section] explode all trees ; 2925 results
2. ("cesarean section"):ti,ab,kw (Word variations have been searched) ; 10365 results
3. ("cesarean delivery"):ti,ab,kw (Word variations have been searched) ; 3263 results
4. ("cesarean birth"):ti,ab,kw (Word variations have been searched) ; 211 results
5. ("Caesarean section"):ti,ab,kw (Word variations have been searched) ; 10179 results
6. ("Caesarean delivery"):ti,ab,kw (Word variations have been searched) ; 3082 results
7. ("Caesarean birth"):ti,ab,kw (Word variations have been searched) ;174 results
8. ("abdominal delivery"):ti,ab,kw (Word variations have been searched); 36 results
9. ("abdominal birth"):ti,ab,kw (Word variations have been searched) ; 1 result
10. #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 ; 11302 results
11. MeSH descriptor: [Maternal Mortality] explode all trees ; 107 results
12. ("maternal mortality"):ti,ab,kw (Word variations have been searched) ; 691 results
13. ("maternal death"):ti,ab,kw (Word variations have been searched) ; 470 results
14. ("pregnancy death"):ti,ab,kw (Word variations have been searched) ; 14 results
15. ("pregnancy mortality"):ti,ab,kw (Word variations have been searched) ; 4 results
16. ("women death"):ti,ab,kw (Word variations have been searched); 8 results
17. ("women mortality"):ti,ab,kw ; 8 results
18. #11 OR #12 OR #13 OR #14 OR #15 OR #16 #17 ; 999 results
19. #10 AND #18 (in Cochrane Reviews and Cochrane Protocols); 36 results

Total: 36 results

Web of Science Search Strategy Conducted on July 25, 2019

1. TS=("C$esarean section*" OR "C$esarian section*" OR "C$esarean birth*" OR "C$esarean deliver*" OR "C$esarian birth*" OR "C$esarian deliver*" OR "CSection*" OR "C-Section*" OR "abdominal deliver*" OR "abdominal birth*")Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years ; 50,605 results
2. TS=("maternal mortal*" OR "maternal death*" OR "pregnan* mortal*" OR "pregnan* death*" OR "wom$n death*" OR "wom$n mortal*")Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years ; 12,569 results
3. #2 AND #1
   Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI
   Timespan=All years ; 1,917 results
4. TS=("Meta analys*" OR "Metaanaly*" OR "systematic review*" OR "systematic overview*")
   Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI
   Timespan=All years ; 534,513 results
5. #3 AND #4

Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI
Timespan=All years ; 141 results

Total: 141 results

SCOPUS Search Strategy Conducted on July 25, 2019

(((TITLE-ABS-KEY("C?esarean Section*")) OR (TITLE-ABS-KEY("C?esarian section*")) OR (TITLE-ABS-KEY("C?esarean deliver*")) OR (TITLE-ABS-KEY("C?esarean birth*")) OR (TITLE-ABS-KEY("C?esarian birth*")) OR (TITLE-ABS-KEY("C?esarian deliver*")) OR (TITLE-ABS-KEY("CSection?")) OR (TITLE-ABS-KEY("C Section?")) OR (TITLE-ABS-KEY("abdominal deliver*")) OR (TITLE-ABS-KEY("abdominal birth*"))) AND ((TITLE-ABS-KEY("maternal mortal*")) OR (TITLE-ABS-KEY("maternal death*")) OR (TITLE-ABS-KEY("pregnan* death*")) OR (TITLE-ABS-KEY("pregnan*mortal*")) OR (TITLE-ABS-KEY("wom?n death*")) OR (TITLE-ABS-KEY("wom?n mortal*")))) AND (((TITLE-ABS-KEY("Meta analys*")) OR (TITLE-ABS-KEY("Metaanaly*")) OR (TITLE-ABS-KEY("Literature review*")) OR (TITLE-ABS-KEY("systematic review*")) OR (TITLE-ABS-KEY("systematic overview*"))))

Total: 361 results

CINAHL Search Strategy Conducted on July 25, 2019

S1 (MH "Cesarean Section+") ; 16,315 results
S2 "C#esarean Section*" ; 20,333 results
S3 "C#esarian section*" ; 183 results
S4 "C#esarean birth*" ; 926 results
S5 "C#esarean deliver*" ; 6,630 results
S6 "C#esarian deliver*" ; 30 results
S7 "C#esarian birth*" ; 9 results
S8 "CSection*" ; 16 results
S9 "C-Section*" ; 8,991 results
S10 "abdominal deliver*" ; 49 results
S11 "abdominal birth*" ; 3 results
S12 (S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11) ; 23,006 results
S13 (MH "Maternal Mortality +") ; 5,407 results
S14 "maternal mortal*" ; 6,901 results
S15 "maternal death*" ; 2,443 results
S16 "pregnan* death*" ; 18 results
S17 "pregnan* mortal*" ; 52 results
S18 "wom#n death*" ; 36 results
S19 "wom#n mortal*" ; 58 results
S20 (MH "Meta Analysis+") ; 40,477 results
S21 "Meta analys*" ; 72,595 results
S22 "Metaanaly*" ; 1,139 results

S23 (MH "Literature Review+") ; 83,221 results
S24 (MH "Systematic Review+") OR (MH "Cochrane Library+") ; 80,745 results
S25 "systematic review*" ; 129,208 results
S26 “systematic overview*” ; 303 results
S27 (S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19) ; 7,765 results
S28 (S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26) ; 156,108 results
S29 (S12 AND S27 AND S28) ; 66 results

Total: 66 results

Global Index Medicus Search Strategy Conducted on July 25, 2019

((tw:(cesarean section*)) OR (tw:(caesarean section*)) OR (tw:(cesarian section*)) OR (tw:(caesarian section*)) OR (tw:(cesarean birth*)) OR (tw:(caesarean birth*)) OR (tw:(cesarian birth*)) OR (tw:(caesarian birth*)) OR (tw:(cesarean deliver*)) OR (tw:(caesarean deliver*)) OR (tw:(cesarian deliver*)) OR (tw:(caesarian deliver*)) OR (tw:(csection*)) OR (tw:(c section*)) OR (tw:(abdominal deliver*)) OR (tw:(abdominal birth*))) AND ((tw:(maternal mortal*)) OR (tw:(maternal death*)) OR (tw:(pregnan* death*)) OR (tw:(pregnan* mortal*)) OR (tw:(women death*)) OR (tw:(woman death*)) OR (tw:(women mortal*)) OR (tw:(woman mortal*)))) AND (instance:"ghl") AND (type_of_study:("systematic_reviews" OR "overview"))

Total: 23 results

African Journals Online Search Strategy Conducted on July 25, 2019

("maternal Mortality" OR "maternal mortal*" OR "maternal death*" OR "pregnan* death*" OR "pregnan* mortal*") AND ("Cesarean Section*" OR "Caesarean Section*" OR "Cesarian section*" OR "Cesarean deliver*" OR "Cesarean birth*" OR "Cesarian birth*")

Keywords: ("Caesarian section*" OR "Caesarean deliver*" OR "Caesarean birth*" OR "Caesarian birth*" OR "Caesarian deliver*" OR "CSection" OR "C Section" OR "abdominal deliver*" OR "abdominal birth*")

Total: 25 results

CADTH Search Strategy Conducted on July 25, 2019
Keywords: caesarean section AND maternal mortality – 11 results
Keywords: cesarean section AND maternal mortality – 9 results
Keywords: caesarian section AND maternal mortality – 8 results
Keywords: caesarean delivery AND maternal mortality – 12 results
Keywords: cesarean delivery AND maternal mortality – 11 results
Keywords: caesarian delivery AND maternal mortality – 8 results
Keywords: caesarean birth AND maternal mortality – 11 results
Keywords: cesarean birth AND maternal mortality – 9 results
Keywords: caesarian birth AND maternal mortality – 7 results

Keywords: c section AND maternal mortality – 34 results
Keywords: abdominal delivery AND maternal mortality – 8 results
Keywords: abdominal birth AND maternal mortality – 7 results

Total: 135 results

NICE Search Strategy Conducted on July 25, 2019
Keywords: "cesarean section" and "maternal mortality" – filtered by systematic reviews – 17 results
Keywords: "caesarean section" and "maternal mortality" - filtered by systematic reviews – 42 results
Keywords: "cesarean delivery" and "maternal mortality" – filtered by systematic reviews – 12 results
Keywords: "caesarean delivery" and "maternal mortality" – filtered by systematic reviews – 14 results
Keywords: "caesarian delivery" and "maternal mortality" – filtered by SR – 1 result
Keywords: "caesarean birth" and "maternal mortality" - filtered by SR – 4 result
Keywords: "cesarean section" and "maternal death" – filtered by systematic reviews – 14 results
Keywords: "caesarean section" and "maternal death" – filtered by systematic reviews – 36 results
"cesarean delivery" and "maternal death"– filtered by systematic reviews – 9 results
Keywords: "caesarean delivery" and "maternal death"– filtered by systematic reviews – 7 results
Keywords: "caesarean birth" and "maternal death"– filtered by systematic reviews – 6 results

Total: 159 results

WHO IRIS Search Strategy Conducted on July 25, 2019

Keywords: caesarean and "maternal mortality" and "systematic review" and "meta analysis"

Total:166 results

THESES AND DISSERTATIONS

Open access theses and dissertations (OATD) Search Strategy Conducted on July 25, 2019
Keywords: "caesarean section" and "maternal mortality"
Total: 42 results
Keywords: "cesarean section" and "maternal mortality"
Total: 17 results
Keywords: "caesarian section" and "maternal mortality"
Total: 4 results
Keywords: "cesarian section" and "maternal mortality"

Total: 1 result
Keywords: "caesarean delivery" and "maternal mortality"
Total: 3 results
Keywords: "cesarean delivery" and "maternal mortality"
Total :1 result
Keywords: "caesarian delivery" and "maternal mortality"
Total: 1 result
Keywords: "caesarean section" and "maternal death"
Total: 15 results
Keywords: "cesarean section" and "maternal death"
Total: 3 results
Keywords: "cesarian section" and "maternal death"
Total: 1 result
Keywords: "caesarean birth" and "maternal mortality"
Total: 1 result
Keywords: "cesarean birth" and "maternal mortality"
Total: 1 result

EThOS Search Strategy Conducted on July 25, 2019
Keywords: "caesarean section" AND "Maternal mortality"
Total: 7 results
Keywords: "caesarean section" AND "Maternal death"
Total: 4 results

DART Search Strategy Conducted on July 25, 2019
Keywords: "cesarean section" and "Maternal mortality"
Total: 2 results
Keywords: "caesarean section" AND "Maternal mortality"
Total: 8 results

GREY LITERATURE DATABASES

OAIster/WorldCat Search Strategy Conducted on July 25, 2019
Keywords: "caesarean section" and "maternal mortality"
Total: 174 results
Keywords: "cesarean section" and "maternal mortality"
Total: 81 results
Keywords: "caesarian section" and "maternal mortality"
Total: 9 results
Keywords: "caesarean section" and "maternal death"
Total: 57 results
Keywords: "cesarean section" and "maternal death"
Total: 14 results
Keywords: "caesarean delivery" and "maternal mortality"
Total: 22 results
Keywords: "caesarean delivery" and "maternal death"

Total: 11 results
Keywords: "cesarean delivery" and "maternal mortality"
Total: 23 results
Keywords: "cesarean delivery" and "maternal death"
Total: 6 results

OpenGrey Search Strategy Conducted on July 25, 2019
Keywords: "caesarean section" and "maternal mortality"
Total: 2 results
Keywords: "caesarean section" and "maternal death"
Total: 1 result

Centre for Research Libraries Global Resource Network Search Strategy Conducted on July 25, 2019
Methods: (caesarean) and (mortality)
Total: 1 result
Methods: (cesarean) and (mortality)
Total: 1 result

ABSTRACTS

List of conferences from major obstetrics and gynecology societies in which abstracts were obtained, conducted on July 25, 2019

- ACOG 2019
- ACOG 2018
- ACOG 2017
- ACOG 2016
- ACOG 2015
- ACOG 2014
- NGOF 2002
- NFOG 2008
- NFOG 2010
- NFOG 2012
- NFOG 2014
- NFOG 2018
- FIGO 2012
- FIGO 2015
- FIGO 2018
- AOFOG 2015
- AOFOG 2017
- AOFOG 2018
- RCOG 2013
- RCOG 2014
- RCOG 2016
- RCOG 2017

- RCOG 2019

Total: 181 results

APPENDIX B: SUMMARY OF STUDY CHARACTESTICS AND FINDINGS FOR 20 INCLUDED ARTICLES

Table 1: Characteristics of included systematic reviews and meta-analyses

Review Year	Review objective	Search Strategy	Search Period	No. Studies Included	Population		Intervention			Outcomes	Setting	
					Description	Sample size (n)	Comparisons	Intervention category	Details of administration/ timing of intervention		Income setting	Countries
Ferrer et al.[18] 2009	To assess the effectiveness and safety of anti-fibrinolytic agents in post partum bleeding.	MEDLINE, PubMed, EMBASE, Cochrane Central Register of Controlled Trials, Web of Science SCI/ISI, metaRegister of Controlled Trials, Reproductive Health Library, LILACS, African healthline, CINAHL, POPLINE, Med-Carib and Clinicaltrials.gov. and the reference lists of eligible trials.	Until Novembe r 2008	3 RCTs	Women with any type of bleeding from the genital tract during the postpartum period.	Total n=461 women (caesarean section n=280 women, spontaneous vaginal delivery n= 181 women)	Anti-fibrinolytic agent (aprotinin, tranexamic acid and epsilon-aminocaproic acid) vs placebo or no treatment.	Preoperative	For CS studies one dose of 1 gram tranexamic acid was administered intravenously 10 and 20 minutes, respectively, before incision. The trial for spontaneous vaginal birth compared four groups. All participants received oxytocin, 10 UI IV, immediately after delivery of the fetal shoulders in the second stage of labour.	Maternal Mortality	High- and middle-income countries	China and Japan, India
Shakur et al.[25] 2018	To determine the effectiveness and safety of antifibrinolytic drugs for treating primary PPH.	Cochrane Pregnancy and Childbirth's Trials Register, ClinicalTrials.gov, the WHO International Clinical Trials Registry Platform (ICTRP) and reference lists of retrieved studies.	28-May-17	3 RCTs	Women after birth following a pregnancy of at least 24 weeks' gestation with a diagnosis of primary postpartum haemorrhage (PPH), regardless of mode of birth (vaginal or caesarean section) or other aspects of third stage	Total n= 20,412 women (vaginal delivery n=14191 women, caesarean section n= 5825 women)	The interventions considered were antifibrinolytic drugs: aprotinin, tranexamic acid (TXA), epsilon-aminocaproic acid (EACA) and aminomethylbenzoic acid administered by whatever route (e.g. intravenous, oral). Comparisons: • Aprotinin plus standard care versus placebo, or standard care alone • TXA plus standard care versus placebo, or standard care alone	Postoperative	Intervention given to women diagnosed with PPH after delivery. Women receiving treatment with TXA after delivery. Administration included a loading dose of 4 g TXA mixed with 50 mL saline, administered intravenously (IV) over one hour followed	• Mortality due to bleeding • All-cause mortality • Mortality from causes other than bleeding	High, middle- and low-income countries	high income: UK, and low- and middle-income countries: Nigeria, Pakistan, Uganda, Kenya, Cameroon, Sudan, Tanzania, Nepal, Zambia, Albania, Democratic Republic of Congo, Bangladesh, Ethiopia, Burkina Faso, Jamaica, Ghana, Papua New Guinea, Egypt, Colombia, Cote d'Ivoire,

					management .		• EACA plus standard care versus placebo, or standard care alone •Aminomethylbenzoic acid plus standard care versus placebo, or standard care alone • Standard care plus systemic aprotinin, TXA, EACA and aminomethylbenzoic acid versus standard care plus topical antifibrinolytic • Standard care plus one antifibrinolytic drug therapy versus another		by a maintenance dose of 1 g/hour for six hours, the intervention group were given IV TXA 1 g as an IV bolus over 10 minutes; if after 30 minutes bleeding continued, or had stopped and restarted within 24 hours of the first dose, women were given a second dose, and 1 g IV TXA repeated after 30 minutes.			France, Iran
Su et al.[15] 2012	To determine if the use of oxytocin agonist is as effective as conventional uterotonic agents for the prevention of PPH and assess the best routes of administration and optimal doses of oxytocin agonist.	Cochrane Pregnancy and Childbirth Group's Trials Register (1 March 2011), the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library 2011, Issue 1 of 4), MEDLINE (1966 to 1 March 2011) and EMBASE (1974 to 1 March 2011). Checked references of articles and communicated with authors and pharmaceutical industry contacts.	1 March 2011	11 RCTs	Women who undergo caesarean or vaginal births.	Total n= 2635 women (caesarean section n=1354 women)	1. Carbetocin versus other uterotonic agents at any route or doses.(A standard dose of 100 µg carbetocin as an intravenous bolus is administered across all trials, but the dose of the comparator drug, oxytocin, varies across the trials.) 2. Carbetocin versus placebo or no treatment. comparisons that subgrouped based on caesarean section included (carbetocin vs oxytocin and carbetocin vs placebo).	Intraoperative	Intervention given to women in the third stage of labour.	Maternal death or severe morbidity (e.g. major surgery, organ failure, intensive care unit admission, hyperpyrexia or as defined by trial authors).	High-income countries	Canada (2), UK, Finland, (last study was in the form of an abstract so could not find information, Barton 1996)
Walsh et al.[14] 2009	Caesarean section delivery is a commonly performed surgical procedure, and	Pubmed, Medline, and Cochrane databases. In addition, the Current Controlled Trials register	1958-June 2008	11 RCTs	Women undergoing uterine repair at caesarean section delivery.	n= 3183 women	Extraabdominal (exteriorized) vs intraabdominal (in situ) uterine repair.	Intraoperative	Uterine repair is conducted after delivery of the infant(s) and placenta.	Postoperative complications (wound infection and	High and middle-income countries	USA (4), UK (2), Nigeria, Turkey, Iran, Canada, Brazil

	rates of caesarean delivery are increasing. Previous randomized trials that compared extraabdominal and intraabdominal uterine repair at caesarean section delivery have yielded conflicting results.	(www.controlled-trials.com) was searched.								maternal death).		
Paranjothy et al.[17] 2014	To determine whether interventions given prior to caesarean section reduce the risk of aspiration pneumonitis in women with an uncomplicated pregnancy.	Cochrane Pregnancy and Childbirth Group's Trials Register.	30-Apr-13	32 RCTs - only 22 RCTs provided quantitative data	Pregnant women undergoing elective or emergency caesarean section under general or regional anaesthesia.	2658 women	Any pharmacological or non-pharmacological intervention given specifically to prevent aspiration pneumonitis at caesarean section, this includes: 1. Particulate or non-particulate antacids. 2. H2 antagonists (e.g. ranitidine). 3. Proton pump antagonists (e.g. omeprazole). 4. Prokinetic drugs (e.g. metoclopramide). 5. Non-pharmacological interventions. Comparisons were any of the above interventions versus any other, placebo or no intervention.	Preoperative	Administered prior to induction of anaesthesia.	Incidence of mortality due to aspiration pneumonitis.	High and middle-income countries	Italy (2), Canada (3), USA (3), Egypt (2), China (3), UK (3), Taiwan, France (2), Turkey (2), South Africa (2), India, Germany (2). 6 studies could not find country
Wilson et al.[13] 2011	To review the effectiveness and safety of clinical officers (healthcare providers trained to perform tasks usually undertaken by doctors) carrying out caesarean	Medline, Embase, Cochrane Central Register of Controlled Trials, CINAHL, BioMed Central, the Reproductive Health Library, and the Science Citation Index (from inception to August 2010). Hand searches	Inception to Aug-10	6 non-randomised controlled cohort studies	Caesarean section in the developing world.	16,018 women	Clinical officers vs medically trained doctors.	Intraoperative	Clinical officers are authorised to provide obstetric care and carry out caesarean sections and other emergency obstetric surgery.	maternal mortality and wound infection.	Low-income countries	Zaire/Congo, Mozambique, Malawi (2), Burkina Faso, Tanzania

	section in developing countries compared with doctors.	complemented electronic searches, and they checked reference lists.										
Cluver et al.[27] 2013	To determine, from the best available evidence, the optimal positioning of the mother during a caesarean section to improve outcomes for both the mother and the baby.	Cochrane Pregnancy and Childbirth Group's Trials Register (20 August 2012), PubMed (1966 to 20 August 2012) and manually searched the references of retrieved articles.	1966 - 20-Aug-12	11 RCTs	Women undergoing caesarean section.	857 women	Various positions of the mother compared with a neutral supine position or alternative positions, including: 1. lateral tilt; 2. head raised; 3. head lowered; 4. table flexed; 5. wedges and cushions.	Intraoperative	During a CS the mother can be placed in a number of positions.	• Maternal mortality. • Neonatal mortality.	High and middle-income countries	South Africa, Colombia, Canada, UK, Singapore, USA, Spain, Japan, UK, China (2)
Alam et al.[30] 2015	To determine if the prophylactic administration of TXA is associated with an improvement in peripartum hemorrhage rates, morbidity, and mortality and whether there are any adverse events associated with its use.	MEDLINE (1946–January 2015), (ii) EMBASE (1947–January 2015), and (iii) Cochrane Central Register of Controlled Trials (2005–January 2015), The references of all retrieved articles were manually searched, abstracts from major obstetrics societies searched. Published protocols on www.clinicaltrials.gov were also searched.	1946-January 2015	21 RCTs - 18 RCTs included for quantitative analysis	Caesarean section (CS) or spontaneous vaginal deliveries (SVDs), and (iii) adult (N18 years) patients.	Total n= 3846 women (caesarean section n=3287, vaginal delivery n=559)	Prophylactic use of TXA vs placebo or no treatment.	Perioperative	TXA dose of either 1 g or 10mg/kg administered prior to incision or anesthesia during CS or at delivery of anterior shoulder in SVD or after delivery of anterior shoulder.	Maternal mortality.	Middle-income countries	China and Japan, India (5), Iran (3), Turkey (3), China, Egypt (3), Pakistan, one study could not find country
Bain et al.[28] 2014	To assess the effects of thromboprophylaxis in women who are pregnant or have recently given birth and are at increased risk of VTE on the incidence of VTE and adverse effects of treatment.	Cochrane Pregnancy and Childbirth Group's Trials Register.	27 November 2013	19 RCTs - 16 RCTs included for quantitative analysis	Women who were pregnant or had given birth in the previous six weeks and were at increased risk of VTE. This includes women who had a caesarean section, had previously	2592 women (caesarean section = 2011 women)	Any intervention that may reduce VTE compared with placebo or with no treatment: or other listed intervention. The interventions include the following: 1. <u>Pharmacological interventions</u> • Unfractionated heparin (UFH); • low molecular weight (LMWH); • aspirin; • warfarin;	Perioperative	Trials had various administrations of the intervention either pre- or post- caesarean section or antenatally.	• Maternal death • post-caesarean infection	High-income countries	Australia, United States (3), Belgium, Spain, United Kingdom (6), Germany (3), Ireland, Finland, Israel, Switzerland

					had VTE, had an acquired or inherited thrombophilia, and other risk factors for VTE.		• hydroxyethyl starch (HES); • other. 2. Non-pharmacological interventions • Graduated compression stockings; • intermitted pneumatic compression (intermittent compression of the calves during surgery); • early mobilisation; • surveillance (screening for asymptomatic thromboembolic events to prevent symptomatic deep venous thrombosis (DVT) or pulmonary embolism (PE).				
Afolabi et al.[29] 2012	To compare the effects of regional anaesthesia with those of general anaesthesia on the outcomes of caesarean section.	Cochrane Pregnancy and Childbirth Group's Trials Register.	30 November 2011 (updated the search on 20 August 2012)	29 RCTs - 22 RCTs included for quantitative analysis	Mothers having elective or emergency caesarean section for any indication, with the various definitions of elective and emergency taken into consideration.	1793 women	Intervention: regional anaesthesia, whether spinal, epidural or any combination of both. Control: general anaesthesia using any combination of anaesthetic drugs and muscle relaxants.	Intraoperative	Intravenous anaesthetic agents provided right before caesarean section.	• Maternal death • Incidence of postoperative wound infection • Neonatal death	High and middle-income countries	Turkey (9), South Africa (2), USA (3), Greece (3), Germany, Finland, South Korea (2), India (3), Thailand, Italy, Jordan, Iran, Egypt,
Hadiati et al.[24] 2018	To compare the effects of different antiseptic agents, different methods of application, or different forms of antiseptic used for preoperative skin preparation	Cochrane Pregnancy and Childbirth's Trials Register, ClinicalTrials.gov, the WHO International Clinical Trials Registry Platform (ICTRP), and reference lists of retrieved studies.	27 November 2017	11 RCTs	Pregnant women undergoing elective or emergency caesarean section.	6237 women	different antiseptic agents used for caesarean section skin preparation (e.g. alcohol, povidone iodine), different methods of antiseptic application (e.g. scrub, paint, drape),	Preoperative	Antiseptics are provided before caesarean section.	• Surgical site infection (SSI) (as defined by trialists) • Maternal mortality	High and middle-income countries	Nigeria, Denmark, Indonesia, USA (6), France, South Africa

	for preventing post-caesarean infection.						or different forms of antiseptic (e.g. powder, liquid).				
Hofmeyr et al.[23] 2008	To compare the effects of complete methods of CS not covered in previous reviews of individual aspects of CS technique.	Cochrane Pregnancy and Childbirth Group's Trials Register, the Cochrane Central Register of Controlled Trials, search of the reference lists of all identified articles.	August 2007 (updated February 15, 2012)	14 RCTs	Pregnant women due for delivery by elective or emergency caesarean section.	2950 women	Interventions: Different techniques of CS: (1) Pfannenstiel; (2) Pelosi type; (3) Joel-Cohen and its modifications; (4) Misgav-Ladach; and (5) extraperitoneal. Comparisons: Joel-Cohen– based CS compared with Pfannenstiel CS, Misgav-Ladach compared with the traditional method, Misgav-Ladach vs modified Misgav-Ladach methods, Extraperitoneal vs intraperitoneal CS	Intraoperative	Various techniques for performing a caesarean section.	• Maternal death. • Wound infection, as defined by trial authors	High, middle- and low-income countries	Tanzania, Italy (4), Sweden (2), Germany (2), China, India, South Africa, Senegal, Portugal.
Mackeen et al.[21] 2014	To compare the effects of caesarean antibiotic prophylaxis administered preoperatively versus after neonatal cord clamp on postoperative infectious complications for both the mother and the neonate.	Cochrane Pregnancy and Childbirth Group's Trials Register and reference lists of retrieved papers.	1 March 2014	Ten RCTs (12 trial reports)	Pregnant women who have undergone caesarean delivery and received prophylactic antibiotics.	5041 women	Prophylactic intravenous (IV) antibiotic administration for caesarean birth 0 to 30 and 30 to 60 minutes prior to skin incision vs prophylactic antibiotic administration for caesarean birth after neonatal umbilical cord clamping.	Perioperative	Antibiotics for prophylaxis were administered intravenously either before the incision versus after clamping of the neonatal umbilical cord. Studies administered antibiotics before incision at various time frames with the vast majority ranging from15 to 60 minutes.	• Maternal mortality • wound infection • Neonatal mortality.	High and middle-income countries	India (2), USA (5), Egypt, Austria, Turkey.
Novikova et al.[19] 2015	To determine, from the best available evidence, whether TA is effective and safe for preventing PPH in	We searched the Cochrane Pregnancy and Childbirth Group's Trials Register and reference lists of retrieved studies.	28 January 2015	12 RCTs	Women undergoing vaginal or CS birth who received TA for prophylaxis of PPH.	Total n= 3285 (caesarean section n=2453 women, vaginal delivery n=832 women)	Comparisons of TA dosages or routes of administration. Comparisons: 1. TA versus placebo/no treatment 2. TA versus	Perioperative	TA was administered at different times in the trials: • before commencement of CS. • at the time of	•Maternal death or severe maternal morbidity such as seizure, thromboem	Middle-income countries	Egypt (2), China (3), India, Turkey (3), Iran (2), Pakistan

	comparison to placebo or no treatment (with or without uterotonic co-treatment), or to uterotonic agents.						uterotonics 3. Different dosages of TA 4. Different routes of administration of TA		induction of anaesthesia. • 10 minutes before skin incision. • 20 minutes before commencement of spinal anaesthesia. • 10 minutes before anaesthesia. • 20 minutes after beginning of anaesthesia.	bolic events, need for intensive care unit admission, hysterectomy, organ failure.		
Sobhy et al.[32] 2017	To compare the rates of maternal and perinatal complications in pregnant women who were administered general vs. regional anesthesia in LMICs.	MEDLINE, Embase, Scopus, CINAHL, Web of Science, and WHO Library and Medicus. Reference lists of the included studies and relevant reviews and articles for eligible papers were searched.	Inception until February 2017	14 studies (retrospective and observational studies, randomized studies.)	Pre-eclamptic women undergoing CS exposed to general or regional anesthesia in LMICs as defined by the World Bank.	10411 women	General vs. regional anesthesia	Intraoperative	Anesthetic management of these mothers is a crucial part of intrapartum care.	maternal death	High and middle-income countries	Nigeria (5), South Africa (3), India (2), Iran, Pakistan, Thailand, and Taiwan.
Gates et al.[31] 2013	To compare the effects of using a wound drain with not using a wound drain at caesarean section, and of different types of drain, on maternal health and healthcare resource use.	Cochrane Wounds Group Specialised Register; The Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library); Ovid Medline; Ovid Medline - In-Process & Other Non-Indexed Citations; Ovid Embase; and EBSCO CINAHL. They scrutinised the reference lists of relevant reviews and trials to identify additional studies.	Until November 2013	10 RCTs	Women undergoing caesarean section.	5248 women	Any type of wound drain compared with no drain or compared with any other type of drain. Types of drain that could be included: suction drains, corrugated drains, wide-bore tube drains.	Intraoperative	Sub-rectus sheath drains or drains between the sheath and the skin (subcutaneous) are sometimes used after caesarean section operations.	•Wound infection (as defined by trial authors) •Maternal death or admission to intensive care unit.	High and middle-income countries	Egypt, USA (3), UK and Italy(multicentre), China, South Africa, Switzerland, UK, India
Gallos et al.[26] 2018	To identify the most effective uterotonic agent(s) to prevent PPH with the least side effects and	Cochrane Pregnancy and Childbirth's Trials Register, ClinicalTrials.gov, the World Health Organization (WHO) International Clinical	24-May-18	196 RCTs	Women in the third stage of labour following a vaginal or caesarean	total n= 135,559 (caesarean section n= 9530 women)	Uterotonic agents of any dosage, route or regimen systemically at birth for preventing PPH, vs other uterotonic agents, placebo or no	Intraoperative	The administration of uterotonic agents to prevent PPH is part of the active	• Maternal deaths	High, middle- and low-income countries	53 countries (including high-, middle- and low-income countries)

	generate a ranking according to their effectiveness and side-effect profile.	Trials Registry Platform (ICTRP), and reference lists of retrieved studies.			birth in hospital or community settings.		treatment.		management of the third stage of labour. The active management of the third stage of labour refers to the administration of a uterotonic agent, early cord clamping, and controlled cord traction until delivery of the placenta.			
Moramarco et al.[20] 2019	The objectives of this study were to review the following systematically: first, the short-term maternal and infant risks with preterm classical compared with low transverse Caesarean sections; and second, the risk of spontaneous or early labour uterine rupture.	Medline, EMBASE, Cochrane Central Register of Controlled Trials, and ClinicalTrials.gov. References of included studies were hand searched for additional articles.	January 1980 to July 2018	23 cohort studies and case series	Women who were delivered preterm by Caesarean section.	39043 caesarean sections	classical versus low transverse Caesarean section	Intraoperative	Vertical or classical incision conducted at the time of Caesarean section	• Maternal mortality before discharge and intensive care unit (ICU) admission • Neonatal death. • Wound infection or dehiscence • Sepsis	High and middle-income countries	USA (14), Canada (4), Ireland, UK, Australia, Nigeria, India
Mathai et al.[22] 2013	To determine the benefits and risks of alternative methods of abdominal surgical incisions for caesarean section.	Cochrane Pregnancy and Childbirth Group's Trials Register.	28-Feb-13	4 RCTs	Pregnant women due for delivery by caesarean section.	666 women	Abdominal incisions for caesarean section performed according to a prespecified technique. (Joel-Cohen incision versus Pfannenstiel incision, Joel-Cohen incision versus vertical incision, Muscle cutting incision versus Pfannenstiel incision).	Intraoperative	Various abdominal incisions are conducted during caesarean section.	•Operative complications (death) • Wound infection	High and middle-income countries	France (2), Italy and Switzerland, India
Sobhy et al.[16] 2016	To obtain precise estimates of anaesthesia-attributed deaths in pregnant	MEDLINE, Embase, Scopus, the Cumulative Index to Nursing and Allied Health Literature	Inception until Oct 1, 2015	140 observational studies and RCTs	Pregnant women exposed to anaesthesia for an	44 studies (632,556 pregnancies) provided data for risk of death from	Anaesthesia no comparator (one arm study).	Intraoperative	Anesthesia is conducted at the start of the procedure.	Anaesthesia-attributed maternal mortality.	Low and middle-income countries	Low-income and middle-income countries

women exposed to anaesthesia and to identify the factors linked to adverse outcomes in pregnant women exposed to anaesthesia in low-income and middle-income countries.	(CINAHL), Web of Science, and the WHO Library and Global Index Medicus. we searched the reference lists of the included studies and relevant reviews for eligible studies.	obstetric procedure in countries categorised as low-income and middle-income countries by the World Bank.	anaesthesia in women undergoing obstetric surgical procedures, and 95 studies (32,149,636 pregnancies, 36,144 deaths) reported anaesthesia-attributed maternal mortality as a proportion of maternal deaths. 25 studies (414,069 pregnancies) assessed the association between anaesthesia-related risk factors and complications in women undergoing obstetric procedure. 611,291 caesarean section.		

Abbreviations:
RCTs= Randomized controlled trials, ICU= Intensive care unit, LMIC= low and middle-income countries, CS= Caesarean section, PPH= Postpartum haemorrhage, TA/TXA= Tranexamic acid, WHO= World Health Organization, VTE= Venous thromboembolism

Table 2: Summary of study findings

INTERVENTION AND COMPARISON	OUTCOME	NO. STUDIES (NO. PARTICIPANTS)	STUDY TYPES	DETAILS OF META-ANALYSIS	RESULTS	P-VALUE	I^2 OR COCHRAN'S Q TEST (P-VALUE)
			PREOPERATIVE				
PREANESTHETIC MEDICATION							
ANY PHARMACOLOGICAL OR NON-PHARMACOLOGICAL INTERVENTION[17]	Maternal Mortality	-	-	-	None of the included studies reported maternal death.	-	-

SKIN WASH/ VAGINAL CLEANSING

DIFFERENT ANTISEPTIC AGENTS USED FOR CAESAREAN SECTION SKIN PREPARATION (E.G. ALCOHOL, POVIDONE IODINE), DIFFERENT METHODS OF ANTISEPTIC APPLICATION (E.G. SCRUB, PAINT, DRAPE), OR DIFFERENT FORMS OF ANTISEPTIC (E.G. POWDER, LIQUID).[24]	Maternal Mortality	-	-	-	No data were reported for maternal mortality in either of the included studies.	-	-
DRAPE VS NO DRAPE[24]	Surgical site infection (subgroup Iodine)	1 (691 women)	RCT	RR (M-H, fixed, 95% CI)	1.42 (0.98, 2.04)	P = 0.061	N/A
	Surgical site infection (subgroup Chlorhexidine)	1 (603 women)	RCT	RR (M-H, fixed, 95% CI)	1.11 (0.70, 1.76)	P = 0.67	N/A
	Surgical site infection or wound infection (overall)	2 (1294 women)	RCTs	RR (M-H, fixed, 95% CI)	1.29 (0.97, 1.71)	P = 0.084	I^2 =0.0%
ONE-MINUTE ALCOHOL SCRUB WITH IODOPHOR DRAPE VERSUS FIVE-MINUTE IODOPHOR SCRUB WITHOUT DRAPE[24]	Surgical site infection	1 (79 women)	RCT	RR (M-H, fixed, 95% CI)	0.0 (0.0, 0.0)	N/A	N/A
PARACHLOROMETAXYLENOL WITH IODINE VS IODINE ALONE[24]	Surgical site infection	1 (50 women)	RCT	RR (M-H, fixed, 95% CI)	0.33 (0.04, 2.99)	P = 0.33	N/A
CHLORHEXIDINE GLUCONATE VERSUS POVIDONE IODINE[24]	Surgical site infection	6 (3607 women)	RCTs	RR (M-H, Fixed, 95% CI)	0.80 (0.62, 1.02)	P = 0.076	I^2 =0.0%

ANTI-FIBRINOLYTIC DRUGS							
TRANEXAMIC ACID VS NO TREATMENT[18]	Maternal Mortality	1 (100 women)	RCT	N/A	0.0 (0.0, 0.0)	N/A	N/A
			INTRAOPERATIVE				
ANESTHETIC MANAGEMENT							
REGIONAL ANAESTHESIA VS GENERAL ANAESTHESIA[29]	Maternal Mortality	-	-	-	The included studies did not report on maternal death.	-	-
	Wound infection	-	-	-	The included studies did not report on wound infection.	-	-
	Neonatal Mortality	-	-	-	The included studies did not report on neonatal death.	-	-
GENERAL ANESTHESIA VS REGIONAL ANESTHESIA[32]	Maternal Mortality	7 (1301 women)	Observational studies and RCTs	OR (random effects, 95% CI)	7.70 (1.9, 31.02)	p=0.026	I^2=58%
ANESTHESIA[16]	Anaesthesia-attributed maternal deaths	31 (1028 CS deaths)	Observational studies and RCTs	Meta-regression, rate (%)	13.8 (9.0, 20.7)	N.R.	I^2=84%
UTEROTONIC DRUGS							
CARBETOCIN VERSUS OTHER UTEROTONIC AGENTS AT ANY ROUTE OR DOSES OR	Maternal Mortality	-	-	-	The identified trials did not report the	-	-

PLACEBO/NO TREATMENT[15]					outcome of maternal death.		
MISOPROSTOL VS OXYTOCIN[26]	Maternal Mortality	3 (565 women)	RCTs	Risk Ratio (IV, Random, 95% CI)	0.33 (0.01, 8.09)	P = 0.50	N/A
CARBETOCIN VS OXYTOCIN[26]	Maternal Mortality	4 (788 women)	RCTs	Risk Ratio (IV, Random, 95% CI)	0.0 (0.0, 0.0)	N/A	N/A
MISOPROSTOL PLUS OXYTOCIN VS OXYTOCIN[26]	Maternal Mortality	4 (935 women)	RCTs	Risk Ratio (IV, Random, 95% CI)	0.0 (0.0, 0.0)	N/A	N/A
MISOPROSTOL VS CARBETOCIN[26]	Maternal Mortality	1 (177 women)	RCTs	Risk Ratio (IV, Random, 95% CI)	0.0 (0.0, 0.0)	N/A	N/A
MISOPROSTOL PLUS OXYTOCIN VS CARBETOCIN[26]	Maternal Mortality	1 (380 women)	RCT	Risk Ratio (IV, Random, 95% CI)	0.0 (0.0, 0.0)	N/A	N/A
OXYTOCIN VS PLACEBO OR NO TREATMENT[26]	Maternal Mortality	0	N/A	Risk Ratio (IV, Random, 95% CI)	0.0 (0.0, 0.0)	N/A	N/A
CARBETOCIN VS PLACEBO OR NO TREATMENT[26]	Maternal Mortality	0	N/A	Risk Ratio (IV, Random, 95% CI)	0.0 (0.0, 0.0)	N/A	N/A
MISOPROSTOL VS PLACEBO OR NO TREATMENT[26]	Maternal Mortality	0	N/A	Risk Ratio (IV, Random, 95% CI)	0.0 (0.0, 0.0)	N/A	N/A
INJECTABLE PROSTAGLANDINS VS	Maternal Mortality	0	N/A	Risk Ratio (IV, Random, 95%	0.0 (0.0, 0.0)	N/A	N/A

PLACEBO OR NO TREATMENT[26]				CI)			
ERGOMETRINE VS PLACEBO OR NO TREATMENT[26]	Maternal Mortality	0	N/A	Risk Ratio (IV, Random, 95% CI)	0.0 (0.0, 0.0)	N/A	N/A
ERGOMETRINE PLUS OXYTOCIN VS PLACEBO OR NO TREATMENT[26]	Maternal Mortality	0	N/A	Risk Ratio (IV, Random, 95% CI)	0.0 (0.0, 0.0)	N/A	N/A
MISOPROSTOL PLUS OXYTOCIN VS PLACEBO OR NO TREATMENT[26]	Maternal Mortality	0	N/A	Risk Ratio (IV, Random, 95% CI)	0.0 (0.0, 0.0)	N/A	N/A
INJECTABLE PROSTAGLANDINS VS OXYTOCIN[26]	Maternal Mortality	0	N/A	Risk Ratio (IV, Random, 95% CI)	0.0 (0.0, 0.0)	N/A	N/A
ERGOMETRINE VS OXYTOCIN[26]	Maternal Mortality	0	N/A	Risk Ratio (IV, Random, 95% CI)	0.0 (0.0, 0.0)	N/A	N/A
ERGOMETINE PLUS OXYTOCIN VS OXYTOCIN[26]	Maternal Mortality	0	N/A	Risk Ratio (IV, Random, 95% CI)	0.0 (0.0, 0.0)	N/A	N/A
INJECTABLE PROSTAGLANDINS VS MISOPROSTOL[26]	Maternal Mortality	0	N/A	Risk Ratio (IV, Random, 95% CI)	0.0 (0.0, 0.0)	N/A	N/A
ERGOMETRINE VS MISOPROSTOL[26]	Maternal Mortality	0	N/A	Risk Ratio (IV, Random, 95% CI)	0.0 (0.0, 0.0)	N/A	N/A
MISOPROSTOL VS ERGOMETRINE PLUS OXYTOCIN[26]	Maternal Mortality	0	N/A	Risk Ratio (IV, Random, 95% CI)	0.0 (0.0, 0.0)	N/A	N/A

MISOPROSTOL VS MISOPROSTOL PLUS OXYTOCIN[26]	Maternal Mortality	0	N/A	Risk Ratio (IV, Random, 95% CI)	0.0 (0.0, 0.0)	N/A	N/A
CARBETOCIN VS INJECTABLE PROSTAGLANDINS[26]	Maternal Mortality	0	N/A	Risk Ratio (IV, Random, 95% CI)	0.0 (0.0, 0.0)	N/A	N/A
INJECTABLE PROSTAGLANDINS VS ERGOMETRINE[26]	Maternal Mortality	0	N/A	Risk Ratio (IV, Random, 95% CI)	0.0 (0.0, 0.0)	N/A	N/A
INJECTABLE PROSTAGLANDINS VS ERGOMETRINE PLUS OXYTOCIN[26]	Maternal Mortality	0	N/A	Risk Ratio (IV, Random, 95% CI)	0.0 (0.0, 0.0)	N/A	N/A
MISOPROSTOL PLUS OXYTOCIN VS INJECTABLE PROSTAGLANDINS[26]	Maternal Mortality	0	N/A	Risk Ratio (IV, Random, 95% CI)	0.0 (0.0, 0.0)	N/A	N/A
ERGOMETRINE VS CARBETOCIN[26]	Maternal Mortality	0	N/A	Risk Ratio (IV, Random, 95% CI)	0.0 (0.0, 0.0)	N/A	N/A
CARBETOCIN VS ERGOMETRINE PLUS OXYTOCIN[26]	Maternal Mortality	0	N/A	Risk Ratio (IV, Random, 95% CI)	0.0 (0.0, 0.0)	N/A	N/A
ERGOMETRINE VS ERGOMETRINE PLUS OXYTOCIN[26]	Maternal Mortality	0	N/A	Risk Ratio (IV, Random, 95% CI)	0.0 (0.0, 0.0)	N/A	N/A
MISOPROSTOL PLUS OXYTOCIN VS ERGOMETRINE[26]	Maternal Mortality	0	N/A	Risk Ratio (IV, Random, 95% CI)	0.0 (0.0, 0.0)	N/A	N/A
MISOPROSTOL PLUS OXYTOCIN VS	Maternal Morality	0	N/A	Risk Ratio (IV, Random, 95%	0.0 (0.0, 0.0)	N/A	N/A

ERGOMETRINE PLUS OXYTOCIN[26]				CI)			
MATERNAL POSITION							
MANUAL DISPLACER VS 15º LEFT LATERAL TILT[27]	Maternal Mortality	1 (90 women)	RCT	RR (M-H, fixed, 95% CI)	0.0 (0.0, 0.0)	N/A	N/A
	neonatal mortality	-	-	-	No studies reported on neonatal mortality.	N/A	N/A
OPERATIVE TECHNIQUES							
EXTRAPERITONEAL VS INTRAPERITONEAL[23]	Maternal Mortality	1 (412 women)	RCT	RR (M-H, fixed, 95% CI)	0.17 (0.02, 1.37)	P = 0.096	N/A
JOEL-COHEN TYPE VS PFANNENSTIEL[23]	wound infection (Joel-Cohen subgroup)	1 (72 women)	RCT	RR (M-H, random, 95% CI)	1 (0.07, 15.38)	P = 1.0	N/A
	wound infection (Misgav-Ladach subgroup)	1 (158 women)	RCT	RR (M-H, random, 95% CI)	3.61 (0.79, 16.49)	P = 0.097	N/A
	wound infection (Modified Misgav-Ladach subgroup)	4 (841 women)	RCTs	RR (M-H, random, 95% CI)	1.21 (0.33, 4.51)	P = 0.77	I^2=72%
	wound infection (overall)	6 (1071 women)	RCTs	RR (M-H, random, 95% CI)	1.43 (0.52, 3.91)	P = 0.49	I^2=61%
MISGAV-LADACH VS LOWER MIDLINE[23]	Wound infection	1 (339 women)	RCT	RR (M-H, fixed, 95% CI)	1.14 (0.68, 1.91)	P = 0.63	N/A
CLASSICAL CESAREAN SECTION VS LOW	Maternal Mortality	2 (2069 CS)	cohort studies and case series	OR (IV, random, 95%	2.38 (0.15, 38.07)	P=0.44	N.R.

TRANSVERSE INCISION[20]				CI)			
	Wound Infection or dehiscence	2 (1190 CS)	cohort studies and case series	OR (IV, random, 95% CI)	0.84 (0.39, 1.80)	P=0.65	I^2=0%
	Sepsis	2 (1190 CS)	cohort studies and case series	OR (IV, random, 95% CI)	2.39 (1.03, 5.52)	P=0.04	I^2=0%
ABDOMINAL INCISIONS FOR CAESAREAN SECTION PERFORMED ACCORDING TO A PRESPECIFIED TECHNIQUE. (JOEL-COHEN INCISION VERSUS PFANNENSTIEL INCISION, JOEL-COHEN INCISION VERSUS VERTICAL INCISION, MUSCLE CUTTING INCISION VERSUS PFANNENSTIEL INCISION)[22]	Maternal Mortality	-	-	-	Maternal death was not reported by any of the included trials.	-	-
JOEL-COHEN VS PFANNENSTIEL INCISION[22]	Wound infection	1 (310 women)	RCT	RR (M-H, random, 95% CI)	1.56 (0.45, 5.42)	P = 0.48	N/A
MUSCLE-CUTTING/MAYLARD CUTTING VS PFANNENSTIEL INCISION[22]	Wound infection	1 (97 women)	RCT	RR (M-H, fixed, 95% CI)	1.26 (0.27, 5.91)	P = 0.77	N/A
EXTERIORIZED VS. IN SITU[14]	Maternal Mortality	2 (945 women)	RCTs	OR (random, 95% CI)	2.61 (0.24, 28.90)	P = 0.43	P=0.51
	Wound infection	6 (1760 women)	RCTs	OR (random, 95% CI)	0.81 (0.52, 1.26)	P= 0.35	P=0.77
SURGICAL PERSONNEL							

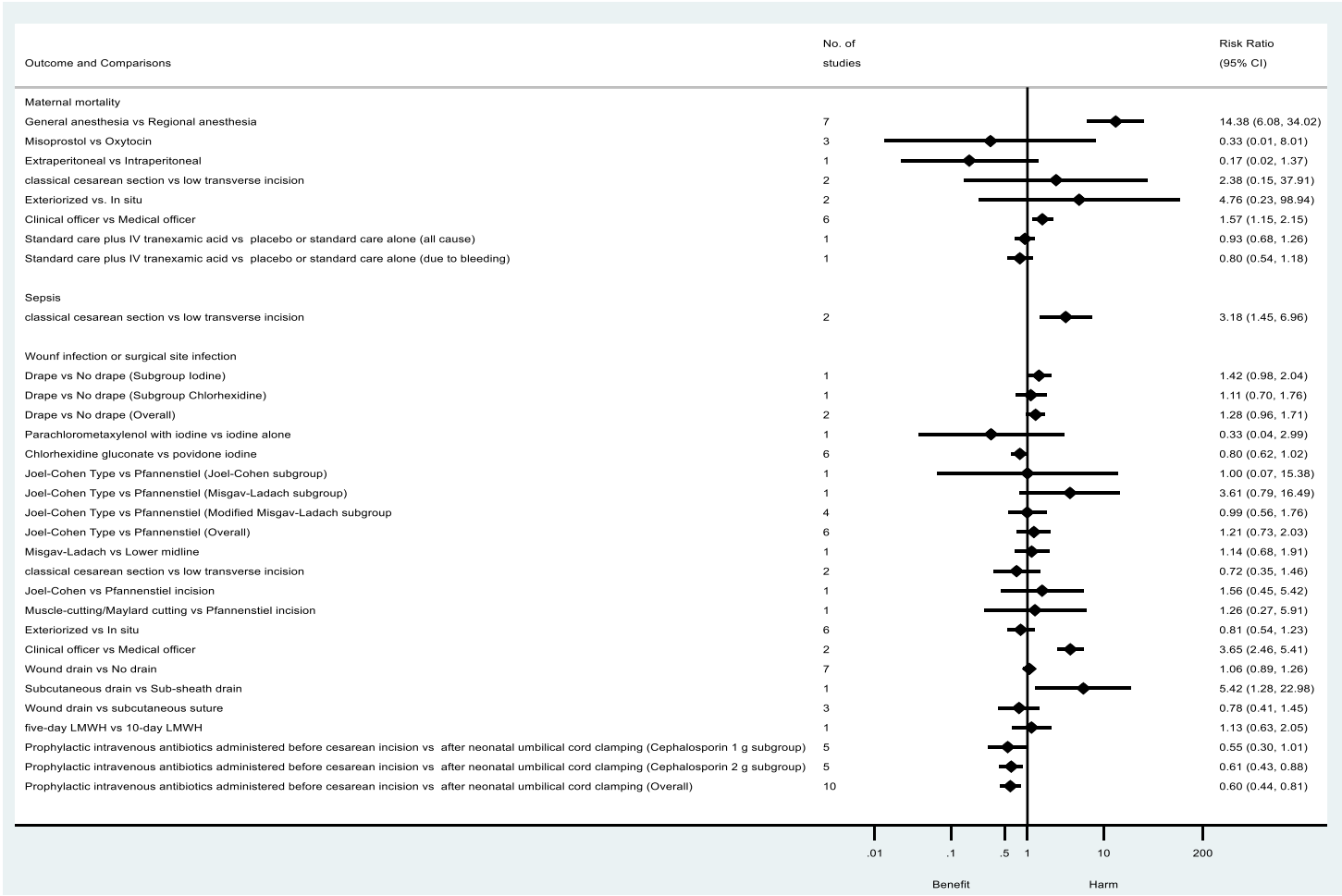
CLINICAL OFFICER VS MEDICAL OFFICER[13]	Maternal Mortality	6 (16018 women)	non-randomised controlled cohort studies	OR (M-H, random, 95% CI)	1.46 (0.78 to 2.75)	P=0.24	I^2=60%
	Wound infection	2 (4436 women)	non-randomised controlled cohort studies	OR (M-H, random, 95% CI)	1.58 (1.01 to 2.47)	P=0.05	I^2=0%
WOUND DRAINAGE							
ANY TYPE OF WOUND DRAIN COMPARED WITH NO DRAIN, OR COMPARED WITH ANY OTHER TYPE OF DRAIN. TYPES OF DRAIN THAT COULD BE INCLUDED: SUCTION DRAINS, CORRUGATED DRAINS, WIDE-BORE TUBE DRAINS. [31]	Maternal Mortality	-	-	-	Maternal death was not reported.	-	-
WOUND DRAIN VS NO DRAIN[31]	Wound infection	7 (4377 women)	RCTs	RR (M-H, fixed, 95% CI)	1.02 (0.85, 1.21)	P = 0.85	I^2=0%
SUBCUTANEOUS DRAIN VS SUB-SHEATH DRAIN[31]	Wound infection	1 (121 women)	RCT	RR (M-H, fixed, 95% CI)	5.42 (1.28, 22.98)	N.R.	N.R.
WOUND DRAIN VERSUS SUBCUTANEOUS SUTURE[31]	Wound infection	3 (533 women)	RCTs	RR (M-H, fixed, 95% CI)	0.77 (0.42, 1.44)	P = 0.42	I^2=0%
			POSTOPERATIVE				
ANTI-FIBRINOLYTIC DRUGS							
STANDARD CARE PLUS IV TRANEXAMIC ACID VS PLACEBO OR STANDARD CARE ALONE[25]	Maternal mortality due to bleeding	1 (5823 women)	RCT	RR (M-H, fixed, 95% CI)	0.8 (0.54, 1.18)	P = 0.25	N/A
	Maternal Mortality (all	1 (5825 women)	RCT	RR (M-H, fixed,	0.93 (0.68, 1.26)	P = 0.62	N/A

	cause)			95% CI)			
			PERIOPERATIVE				
THROMBOEMBOLISM PREVENTION							
FIVE-DAY LMWH VS 10-DAY LMWH[28]	Maternal mortality	1 (646 women)	RCT	RR (M-H, fixed, 95% CI)	0.0 (0.0, 0.0)	N/A	N/A
	Post-caesarean infection	1 (646 women)	RCT	RR (M-H, fixed, 95% CI)	1.13 (0.63, 2.05)	P = 0.68	N/A
ANTIMICROBIAL PROPHYLAXIS							
PROPHYLACTIC INTRAVENOUS (IV) ANTIBIOTIC ADMINISTRATION FOR CESAREAN BIRTH 0 TO 30 AND 30 TO 60 MINUTES PRIOR TO SKIN INCISION VS PROPHYLACTIC ANTIBIOTIC ADMINISTRATION FOR CESAREAN BIRTH AFTER NEONATAL UMBILICAL CORD CLAMPING[21]	Maternal mortality	-	-	-	There were no occurrences of maternal deaths.	-	-
	Neonatal mortality	-	-	-	No studies reported on neonatal mortality.	-	-
PROPHYLACTIC INTRAVENOUS ANTIBIOTICS ADMINISTERED BEFORE CESAREAN INCISION VS AFTER NEONATAL UMBILICAL CORD CLAMPING [21]	Wound infection (Cephalosporin 1 g subgroup)	5 (2144 women)	RCTs	RR (M-H, fixed, 95% CI)	0.55 (0.30, 1.01)	P = 0.054	I^2=0%
	Wound infection (Cephalosporin 2 g subgroup)	5 (2897 women)	RCTs	RR (M-H, fixed, 95% CI)	0.61 (0.43, 0.88)	P = 0.0074	I^2=0%
	Wound infection (overall)	10 (5041 women)	RCTs	RR (M-H, fixed, 95% CI)	0.59 (0.44, 0.81)	P = 0.00099	I^2=0%

ANTI-FIBRINOLYTIC DRUGS							
PROPHYLACTIC USE OF TXA VS PLACEBO OR NO TREATMENT[30]	Maternal Mortality	-	RCTS	-	None of the included studies specifically assessed mortality, except to indicate that no participants in the study died.	-	-
TRANEXAMIC ACID VS PLACEBO/NO TREATMENT[19]	Maternal death and severe maternal morbidity	2 (952 women)	RCTs	RR (M-H, fixed, 95% CI)	0.0 (0.0, 0.0)	N/A	N/A

Abbreviations:
RCTs= Randomized controlled trials, RR=Risk ratio, OR= Odds ratio, P=p-value, N/A= not applicable, M-H= Mantel-Haenszel, CI= Confidence interval

Figure 1: Forest plot of the results reported from individual meta-analyses with the use of a common effect estimate (RR) on perioperative interventions for caesarean section stratified by outcome



APPENDIX C: AMSTAR 2 QUALITY ASSESSMENT FOR 20 INCLUDED ARTICLES

Table 3: AMSTAR 2 ratings of included systematic reviews and meta-analyses

Author	1. Question and Inclusion	2. Protocol	3. Study Design	4. Comprehensive Search	5. Study Selection	6. Data Extraction	7. Excluded Studies Justification	8. Included Studies Details	9. Risk of Bias (RoB)	10. Funding Sources	11. Statistical Methods	12. RoB on meta-analysis	13. RoB in individual Studies	14.Explanation for Heterogeneity	15. Publication Bias	16. Conflict of Interest	Overall Rating
Ferrer et al.[18]	Yes	No	No	Partial yes	Yes	Yes	Yes	Partial Yes	No	No	Yes	No	Yes	Yes	No	No	Low quality
Shakur et al.[25]	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Moderate quality
Su et al.[15]	Yes	Yes	No	Yes	Yes	Yes	Yes	Partial Yes	Yes	Yes	Yes	No	Yes	No	No	Yes	Moderate quality
Walsh et al.[14]	No	No	No	No	No	No	Yes	No	No	No	No	Yes	No	Yes	No	No	Critically Low quality
Paranjothy et al.[17]	Yes	Yes	No	Partial Yes	Yes	Yes	Yes	Partial Yes	Yes	No	No	No	No	Yes	No	Yes	Critically Low quality
wilson et al.[13]	Yes	No	No	Partial Yes	Yes	Yes	Yes	Partial Yes	Yes	No	Yes	No	Yes	Yes	No	Yes	Moderate quality
Cluver et al.[27]	Yes	Yes	No	Partial yes	Yes	Yes	Yes	Partial yes	Yes	No	No	No	No	No	No	No	Critically Low quality
Alam et al.[30]	Yes	No	No	Partial yes	Yes	Yes	Yes	Partial Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Moderate quality
Bain et al.[28]	Yes	No	No	Partial Yes	Yes	Yes	Yes	Partial Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Moderate quality

Afolabi et al.[29]	Yes	Yes	No	Partial Yes	Yes	Yes	Yes	Partial Yes	Yes	No	Yes	No	No	No	No	No	Low quality
Hadiati et al.[24]	Yes	Yes	No	Yes	Yes	Yes	Yes	Partial Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Moderate quality
Hofmeyr et al.[23]	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	No	No	No	Yes	Low quality
Mackeen et al.[21]	Yes	Yes	No	Partial Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Moderate quality
Novikova et al.[19]	Yes	Yes	No	Yes	Yes	Yes	Yes	Partial Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Moderate quality
Sobhy et al.[32]	Yes	No	No	Partial Yes	Yes	Yes	Yes	Yes	No	No	No	No	No	No	No	Yes	Critically Low quality
Gates et al.[31]	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	Moderate quality
Gallos et al.[26]	Yes	Yes	No	Yes	Yes	Yes	Yes	Partial Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Moderate quality
Moramarco et al.[20]	Yes	Yes	Yes	Partial Yes	Yes	Yes	Yes	Partial Yes	Yes	No	No	Yes	No	No	No	Yes	Critically Low quality
Mathai et al.[22]	Yes	Yes	No	Partial Yes	Yes	Yes	Yes	Partial Yes	Yes	No	Yes	No	No	Yes	No	Yes	Low quality
Sobhy et al.[16]	Yes	Yes	No	Partial Yes	Yes	Yes	Yes	Partial Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Moderate quality

APPENDIX D: SYSTEMATIC REVIEW METHODOLOGY

DATABASE SEARCH STRATEGIES

EMBASE

1. exp cesarean section/ ; 99949 results
2. c?esar?an*.mp. ; 117570 results
3. CSection*.ti,ab,tw. ; 123 results
4. C-Section*.ti,ab,tw. ; 3417 results
5. (abdominal* adj2 (deliver* or birth*)).ti,ab.; 1046 results
6. or/1-5 ; 119802 results
7. maternal mortality/ ; 23235 results
8. Maternal death/; 2188 results
9. ((maternal or mother* or pregnan* or wom?n) adj4 (mortal* or death* or fatal* or expir*)).mp. ; 65940 results
10. "cause of death"/ ; 116067 results
11. exp cesarean section/co [Complication] ; 11 results
12. ((cause* or factor* or contribut* or manner*) adj7 (mortal* or death* or fatal* or expir*)).mp. ; 559224 results
13. or/7-9 ; 65940 results
14. or/10-12 ; 559235 results
15. exp human/; 21653347 results
16. exp animal/; 26994942 results
17. 15 and 16; 21653347 results
18. 16 not 17 ; 5341595 results
19. 15 not 18 ; 21653347 results
20. 6 and 13 and 14 and 19 ; 1981 results

Total: 1981

MEDLINE

1. exp cesarean section/; 44050 results
2. C?esar?an*.mp.; 72341 results
3. CSection*.mp. ; 2 results

4. C-Section*.mp. ; 1292 results
5. (abdominal* adj2 (deliver* or birth*)).ti,ab.; 743 results
6. or/1-5 ; 73088 results
7. maternal mortality/ ; 10026 results
8. Maternal death/ ; 718 results
9. ((maternal or mother* or pregnan* or wom?n) adj4 (mortal* or death* or fatal* or expir*)).mp. ; 43738 results
10. or/7-9 ; 43738 results
11. "Cause of Death"/ ; 47054 results
12. exp Cesarean Section/mo [Mortality] ; 493 results
13. ((cause* or factor* or contribut* or manner*) adj7 (mortal* or death* or fatal* or expir*)).mp. ; 350404 results
14. or/11-13 ; 350799 results
15. exp human/; 18147917 results
16. exp animal/; 22796825 results
17. 15 and 16; 18147917 results
18. 16 not 17 ; 4648908 results
19. 15 not 18 ; 18147917 results
20. 6 and 10 and 14 and 19 ; 1064 results

Total: 1064

Cochrane (CDSR)

1. MeSH descriptor: [Cesarean Section] explode all trees ; 2973 results
2. ("Cesarean"):ti,ab,kw (Word variations have been searched) ; 12010 results
3. ("abdominal delivery"):ti,ab,kw (Word variations have been searched); 36 results
4. ("abdominal birth"):ti,ab,kw (Word variations have been searched) ; 1 result
5. #1 OR #2 OR #3 OR #4; 12017 results
6. MeSH descriptor: [Maternal Mortality] this term only ;110 results
7. ("maternal mortality"):ti,ab,kw (Word variations have been searched) ; 682 results
8. (maternal or mother* or woman or pregnan* near/3 mortal* or death* or fatal* or expir*):ti,ab,kw (Word variations have been searched)) ; 240951 results
9. #6 OR #7 OR #8 ; 240951 results
10. MeSH descriptor: [Cause of Death] this term only; 1582 results
11. (cause* or factor* or contribut* or manner* near/7 mortal* or death* or fatal* or expir*):ti,ab,kw ; 405240 results

12. #10 OR #11; 405232 results
13. #5 AND #9 AND #12 ; 2462 results total – 2263 Cochrane trial results

Total: 2263

Web of Science

1. TS=("C$esarean*" OR "C$esarian*" OR "CSection*" OR "C-Section*" OR "abdominal deliver*" OR "abdominal birth*") Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years ; 54,492 results
2. TS=((maternal or mother* or pregnan* or wom?n) NEAR/4 (mortal* or death* or fatal* or expir*))Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years; 40,438 results
3. TS=(("cause*" OR "factor*" OR "contribut*" OR "manner") NEAR/7 ("mortal*" or "death*" or "fatal*" or "expir*")) Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years; 317,716 results
4. #3 AND #2 AND #1Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years ; 807 results
   Total: 807

SCOPUS

(((TITLE-ABS-KEY (cause* OR factor* OR contribut* OR manner*) W/7 (mortal* OR death*)))) AND ((TITLE-ABS-KEY ("C?esarean*" OR "C?esarian*" OR "CSection?" OR "C Section?" OR "abdominal deliver*" OR "abdominal birth*"))) AND ((TITLE-ABS-KEY ("maternal mortal*" OR "maternal death*" OR "maternal fatal*" OR "maternal expir*" OR "pregnan* death*" OR "pregnan* mortal*" OR "pregnan* fatal*" OR "pregnan* expir*" OR "wom?n death*" OR "wom?n mortal*" OR " wom?n fatal*" OR " wom?n expir*")))

Total: 1,341

CINAHL

S1 (MH "Cesarean Section+") ; 16,518 results
S2 c#esar#an* ; 24,382 results
S3 "CSection*" ; 1 results
S4 "C-Section*" ; 9,022 results
S5 "abdominal deliver*" ; 46 results

S6 "abdominal birth*" ; 3 results
S7 (MH "Maternal Mortality") ; 5,474 results
S8 (maternal or mother* or woman or pregnan*) N5 (mortal* or death* or fatal* or expir*) ; 59,552 results
S9 (MH "Cause of Death"); 12,979 results
S10 (MH "Cesarean Section/MO") ; 80 results
S11 (cause* or factor* or contribut* or manner*) N5 (mortal* or death* or fatal* or expir*); 82,187 results
S12 S1 OR S2 OR S3 OR S4 OR S5 OR S6; 24,531 results
S13 S7 OR S8; 59,552 results
S14 S9 OR S10 OR S11; 82,251 results
S15 S12 AND S13 AND S14; 585 results
Total: 585

Global Index Medicus

tw:(((tw:(cesarean section*)) OR (tw:(caesarean section*)) OR (tw:(cesarian section*)) OR (tw:(caesarian section*)) OR (tw:(cesarean birth*)) OR (tw:(caesarean birth*)) OR (tw:(cesarian birth*)) OR (tw:(caesarian birth*)) OR (tw:(cesarean deliver*)) OR (tw:(cesarian deliver*)) OR (tw:(caesarian deliver*)) OR (tw:(csection*)) OR (tw:(c section*)) OR (tw:(abdominal deliver*)) OR (tw:(abdominal birth*))) AND ((tw:(maternal mortal*)) OR (tw:(maternal death*)) OR (tw:(pregnan* death*)) OR (tw:(pregnan* mortal*)) OR (tw:(women death*)) OR (tw:(woman death*)) OR (tw:(women mortal*)) OR (tw:(woman mortal*))) AND (type_of_study:("clinical_trials" OR "cohort" OR "case_control" OR "evaluation_studies")))

Total: 120 results

WHO IRIS
Method: caesarean and "maternal mortality"
Total: 819 results
Method: caesarean and "maternal death"
Total: 656 results

WHO Reproductive Health Library

Methods: caesarean and "maternal mortality"
Total: 62 results

CAB Direct
("cesarean section" or "Caesarean Section" or "Cesarian section" or "Caesarian section" or "csection" or "c section") AND ("maternal mortality" or "maternal death" or "pregnancy death" or "pregnancy mortality" or "women death" or "women mortality")
Total: 35 results
PAIS Index

("C$esarean section*" OR "C$esarian section*" OR "C$esarean birth*" OR "C$esarean deliver*" OR "C$esarian birth*" OR "C$esarian deliver*" OR "CSection*" OR "C-Section*" OR "abdominal deliver*" OR "abdominal birth*") AND ("maternal mortal*" OR "maternal death*" OR "pregnan* mortal*" OR "pregnan* death*" OR "wom$n death*" OR "wom$n mortal*")

Total: 20 results

African Journals Online

(("maternal mortality" OR "maternal death" OR "pregnancy death" OR "pregnancy mortality" OR “woman mortality” OR “woman death” OR “women mortality” OR “women death”) AND (("Cesarean Section" OR "Cesarean delivery" OR "Cesarean birth" OR "Caesarean Section" OR "Caesarean delivery" OR "Caesarean birth" OR "Cesarian section" OR “Cesarian delivery” OR "Cesarian birth" OR "Caesarian section" OR "Caesarian birth" OR "Caesarian delivery" OR "CSection" OR "C Section" OR "abdominal delivery" OR "abdominal birth"))

Total: 905 results

THESES AND DISSERTATIONS

Open access theses and dissertations (OATD)
Keywords: "caesarean section" and "maternal mortality"
Total: 42 results
Keywords: "cesarean section" and "maternal mortality"

Total: 17 results
Keywords: "caesarian section" and "maternal mortality"
Total: 4 results
Keywords: "cesarian section" and "maternal mortality"
Total: 1 result
Keywords: "caesarean delivery" and "maternal mortality"
Total: 3 results
Keywords: "cesarean delivery" and "maternal mortality"
Total :1 result
Keywords: "caesarian delivery" and "maternal mortality"
Total: 1 result
Keywords: "caesarean section" and "maternal death"
Total: 15 results
Keywords: "cesarean section" and "maternal death"
Total: 3 results
Keywords: "cesarian section" and "maternal death"
Total: 1 result
Keywords: "caesarean birth" and "maternal mortality"
Total: 1 result
Keywords: "cesarean birth" and "maternal mortality"
Total: 1 result

EThOS

Keywords: "caesarean section" AND "Maternal mortality"
Total: 7 results
Keywords: "caesarean section" AND "Maternal death"
Total: 4 results

DART

Keywords: "cesarean section" and "Maternal mortality"
Total: 2 results
Keywords: "caesarean section" AND "Maternal mortality"
Total: 8 results

GREY LITERATURE DATABASES

OAIster/WorldCat

Keywords: "caesarean section" and "maternal mortality"
Total: 174 results
Keywords: "cesarean section" and "maternal mortality"
Total: 81 results
Keywords: "caesarian section" and "maternal mortality"
Total: 9 results
Keywords: "caesarean section" and "maternal death"
Total: 57 results
Keywords: "cesarean section" and "maternal death"
Total: 14 results
Keywords: "caesarean delivery" and "maternal mortality"
Total: 22 results
Keywords: "caesarean delivery" and "maternal death"
Total: 11 results
Keywords: "cesarean delivery" and "maternal mortality"
Total: 23 results
Keywords: "cesarean delivery" and "maternal death"
Total: 6 results
OpenGrey

Keywords: "caesarean section" and "maternal mortality"

Total: 2 results
Keywords: "caesarean section" and "maternal death"
Total: 1 result

Centre for Research Libraries Global Resource Network

Methods: (caesarean) and (mortality)
Total: 1 result
Methods: (cesarean) and (mortality)
Total: 1 result

APPENDIX E: CHARACTERISTICS OF INCLUDED STUDIES, QUALITY ASSESSMENT AND BIBLIOGRAPHY OF INCLUDED STUDIES

Table 4: Description of the 196 studies included in the systematic review and meta-analysis

Author	Year of publication	Country	Start year	End year	HDI	Type of study	Population	Urgency (n)	Primary outcomes	Types of hospitals	Number of caesarean sections (n)	Source of Data
Okafor et al.[122]	2009	Nigeria	2003	2006	0.467	Retrospective survey	patients that had caesarean delivery	elective n=319, emergency n=410	maternal mortality	Teaching hospital	729	The hospital records case notes, labour ward and theatre records of patients that had caesarean delivery at the University of Nigeria Teaching hospital (UNTH).
Lilford et al.[26]	1990	South Africa	1975	1986	0.625	Retrospective review	108 deaths from each method of delivery	emergency n=23045 CS, elective n= 8524 CS	maternal mortality	an integrated perinatal service composed of primary, secondary and tertiary facilities in Cape Town (mixed)	31564	case-notes of women who died after delivery.
Holmer et al.[128]	2019	Sierra Leone	2016	2016	0.413	retrospective study	all caesarean sections and all reported in-facility maternal deaths	N.R.	In-facility maternal mortality	mixed	7357	All Sierra Leonean health facilities performing caesarean sections in 2016 were visited and numbers of caesarean

												sections, deliveries and maternal deaths reported in facility logbooks were recorded. The Sierra Leone MoHS provided access to the MDSR database, containing patient-level information on all maternal deaths notified through its system in 2016. Every maternal death after caesarean section was validated through on-site facility logbook review (including all available patient files, hospital logbooks, operating room logbooks and blood bank logbooks).
Crichton et al.[30]	1973	South Africa	1961	1971	0.625	N.R.	deliveries conducted in the unit over a period of 19 years. patients were Bantu and Indians from Durban, its suburb. and remote areas of Natal and Zululand. Unbooked patients admitted as emergencies with advanced sequelae of complications, produced the majority of the maternal deaths.	N.R.	maternal death	private hospital	21000	N.R.
Shorunmu et al.[62]	2015	Nigeria	2011	2013	0.512	retrospective study	cases of emergency caesarean delivery	emergency n=608, elective n=122	maternal death	Teaching Hospital	577	case notes from medical records. Data were obtained from the labour ward records,

							performed					theatre records and parturient case files.
Anger et al.[73]	2018	Uganda	2016	2018	0.516	N.R.	all maternal deaths	N.R.	maternal death	mixed	4908	Data was extracted from narrative reports of all maternal deaths that occurred among women delivering at 6 rural hospitals in Uganda
Kim et al.[129]	2012	Afghanistan	<2012	N.R.	0.463	Retrospective cohort (cross-sectional, descriptive assessment)	All caesarean sections	emergency n=151, elective n=18	maternal death and early neonatal death	78 government health facilities (mixed)	173	patient medical records, facility logbooks, and registers
Harfouche et al.[32]	2015	Malawi	2012	2012	0.455	N.R.	all caesarean deliveries	N.R.	maternal and neonatal death	district-level public hospital	513	Comprehensive maternity data at Bwaila Maternity Hospital is collected by Bwaila staff using logbooks.
Nolens et al.[107]	2018	Uganda	207	2015	0.515	prospective observational cohort study	Women with a term singleton pregnancy in vertex presentation who delivered by vacuum extraction or SSCD (second-stage caesarean delivery)	N.R.	maternal death	Teaching hospital	425	Data were extracted from medical records and the admission, discharge, and mortality registers.
Huda et al.[82]	2012	Bangladesh	2007	2008	0.524	N.R.	all pregnant women in the International Centre for Diarrhoeal Disease Research, Bangladesh service area in Matlab, who gave birth during 2007-2008.	N.R.	maternal death	public and private hospitals	591	A physician searched the hospital-records for any Matlab woman admitted during labour or postpartum to the Matlab Hospital, or any of the public or private hospitals in Matlab or Chandpur, including the admission registers and individual patient-records. The hospital-records were reviewed every two weeks, using a structured data-extraction form. Maternal deaths were noted by the CHRWs and matched with maternal

												death reporting from the Matlab's Health and Demographic Surveillance System (HDSS).
Fawole et al.[70]	2012	Nigeria	2004	2005	0.467	analytical cross-sectional survey	All women who delivered in the selected health facilities	Elective n=282, emergency n=1062	maternal death	secondary hospital n=16, tertiary hospital n=5 (mixed)	1344	Medical records of all study participants were reviewed and abstracted by the midwife. Incomplete data in medical records were updated by liaising with attending staff before the patient's discharge.
Ekanem et al. [56]	2008	Nigeria	2000	2001	0.452	N.R.	All emergency caesarean sections	n= 349 emergency CS	maternal mortality	Teaching hospital	349	ward and obstetric theatre registers including case notes of women who had caesarean section in UCTH.
Idoko et al.[102]	2018	Gambia	2014	2014	0.449	retrospective review	all caesarean sections carried out at the Edward Francis Small Teaching Hospital	emergency n= 1024, elective n= 153	maternal mortality	Teaching hospital	1177	The labour ward register, operating room register and patient's record.
McKenzie[118]	1998	Zimbabwe	1992	1994	0.480	A prospective review	Major obstetric procedures	N.R.	anaesthetic-associated maternal deaths	District hospital	8502	Data were obtained from theatre registers, post-mortem reports and (in all but four cases) the case notes.
Kuzma[11]	2016	Ethiopia	2009	2014	0.429	retrospective cohort study	all deliveries of gestational age ≥ 28 weeks	Emergency n= 574, elective n= 839	maternal death	public / teaching hospitals	1413	Patient medical records.
Sultan et al.[97]	2017	Egypt	2014	2014	0.683	prospective study	All women admitted to the ICU in the study period were included.	N.R.	maternal death	university hospital	313	Data were collected using an interview questionnaire. The admission and medical records of the women were also reviewed.
Rutgers et al. [83]	2008	Zimbabwe	1998	2000	0.457	Retrospective cross-sectional.	all caesarean deliveries	n=168 elective CS, n= 925 emergency CS	maternal death related to a CS	district hospitals	1093	Delivery registers, admission books, hospital medical records, maternal mortality notification forms and monthly mortality reporting form.

Remy et al.[22]	1993	Germany	1975	1989	0.801	retrospective	all maternal deaths	N.R.	maternal death	mixed	29257	All intra- and postpartum maternal deaths could be recorded via the Senate Department for Health and Social Affairs of West Berlin and the gynecological clinics or departments. The medical chief's consent could be obtained from the medical records.
Kalisa et al.[121]	2016	Rwanda	2013	2014	0.509	prospective cohort study	All pregnant women admitted for delivery or pregnancy related complications, and who sustained severe acute maternal morbidity	N.R.	maternal death	district hospital	1442	captured relevant data for every woman who presented with severe acute maternal morbidity or died during admission, by using available medical records.
Loh et al.[47]	1994	Singapore	1986	1992	0.718	N.R.	all deliveries	N.R.	maternal death	University Hospital (NUH)	3,288	N.R.
Andrade et al.[84]	2006	Brazil	1927	2001	0.613	retrospective study	deaths that occurred in the hospital during the study period, considering only deaths from direct and indirect obstetric causes. Patients who were transferred to the ICU of other hospitals and died there were excluded	N.R.	maternal death	Teaching hospital	35,365	Patient records regarding their clinical history and data from death certificates.
Chattopadhyay et al.[98]	1983	Saudi Arabia	1978	1980	0.698	N.R.	All maternal deaths	N.R.	maternal death	N.R.	2924	N.R.
Krone et al.[4]	1975	Germany	1963	1974	0.801	N.R.	all deliveries	N.R.	maternal mortality	N.R.	1350	Examined the obstetrics of the clinic.
Zahran et	2017	Egypt	2012	2012	0.675	retrospective	All maternal	N.R.	maternal	university	9,908	Medical records of cases

al.[17]						cohort	deaths		death	hospital		that fulfilled the WHO definition of maternal mortality. The registers of the hospital admissions and Intensive care unit were also reviewed to collect the data required to calculate the indices in our study.
Aboyeji et al.[90]	2007	Nigeria	1997	2002	0.452	retrospective review	All maternal deaths	N.R.	maternal death	Teaching hospital	2016	case-note and records in the labour wards, emergency unit and ward admission registers.
Rasul et al.[71]	2016	Pakistan	2015	2015	0.551	audit	All maternal deaths	N.R.	maternal death	tertiary care hospital	2165	N.R.
Muylder[125]	1990	Zimbabwe	1985	1987	0.498	N.R.	All the delivery deaths occurring in all the health facilities, Exclusions: deaths due to abortion, ectopic pregnancy or choriocarcinoma	N.R.	maternal death	All health facilities in Midlands Province in Zimbabwe	3,602	the Maternal Child Health (MCH) National Committee strongly recommended a post-mortem examination for every maternal death. All these cases were regularly discussed with the consultant, the physicians and the nursing staff involved: the clinical data, medical chart and autopsy findings were reviewed.
Rojas et al.[27]	1974	Colombia	1966	1970	0.600	clinical study	deaths in patients who were pregnant, shuffled or were in the postpartum period.	N.R.	maternal death	teaching hospital	5,003	statistical and pathological anatomy files were reviewed. autopsy study and anatomopathological study (biopsy or surgical specimen) were conducted.
Campbell[9]	1974	Papua New Guinea	1964	1973	0.377	N.R.	all maternal deaths due to pregnancy and childbirth	N.R.	maternal death	District General Hospital	709	Death certificates for the 10-year period, were reviewed. The case notes of all females dying in the child-bearing age were studied.
Kamilya et al.[114]	2010	India	2003	2006	0.539	retrospective cohort study	All deliveries without	N.R.	maternal death	Teaching hospital	13627	hospital records, admission and treatment

							significant maternal disease or complications					records
Schuitemaker et al.[109]	1997	Netherlands	1983	1992	0.830	A nationwide confidential enquiry (retrospective cross-check)	all cases of maternal death.	N.R.	maternal death following caesarean section	nationwide/ mixed	108,587	information on maternal deaths is collected MMC, the National Bureau of Statistics (CBS) and the Dutch Perinatal Database (DPD). All obstetric departments in The Netherlands were asked for additional cases.
Kallianidis et al.[3]	2018	Netherlands	1999	2013	0.897	nationwide retrospective cohort study	all maternal deaths reported to the Dutch Maternal Mortality and Severe Morbidity Audit Committee (MMSMAC).	N.R.	maternal death following caesarean section	nationwide/ mixed	393,443	All available medical records of cases reported to the Dutch Maternal Mortality and Severe Morbidity Audit Committee were assessed by two researchers, and one or two additional experts in case of contradicting opinions, based on a set of pre-identified clinical criteria.
Anaya-Prado et al.[12]	2008	Mexico	2006	2006	0.737	descriptive cross-sectional study (case series type)	all patients operated on by CS between January and December 2006	emergency n=2285, elective n=542	maternal mortality	N.R.	2827	Hospital records.
Oladapo et al.[115]	2007	Nigeria	1990	2005	0.452	Retrospective analysis	all elective Caesarean deliveries	164 elective Caesarean sections	maternal death	Teaching hospital	164	Information was obtained from a combination of theatre records, labour ward registers and case files retrieved from the Medical Record Department of the hospital.
Armon[86]	1979	Tanzania	1971	1977	0.373	survey	All deaths occurring within the hospital during pregnancy or the first six weeks of the	N.R.	maternal death	referral hospital	1,271	Post-mortem examination was performed in 35 % of the cases. In the remaining cases the diagnosis was made on clinical grounds (including the findings of

							puerperium					laparotomy).
Ozumba et al.[117]	2002	Nigeria	1994	1999	0.452	N.R.	All maternal deaths associated with caesarean section	n= 1153 emergency caesarean n= 531 elective	Maternal deaths associated with caesarean section	Teaching hospital	1684	N.R.
Clark et al.[124]	2008	United States	2000	2006	0.889	retrospective study	all maternal deaths	N.R.	maternal death	within 124 hospitals (mixed)	458,097	medical records and augmented when necessary by interviews with involved health care providers.
Gebhardt et al.[80]	2015	South Africa	2011	2013	0.673	N.R.	all maternal deaths	N.R.	maternal death during or after CS	nationwide (mixed)	655686	Data from the completed 2011 - 2013 triennial review.
Gessessew[59]	2007	Ethiopia	1993	2003	0.283	A retrospective review	all labouring mothers	N.R.	maternal death	district hospital	609	Collection of information for all variables was obtained from the delivery registration book. The registration book was regularly checked for its completeness by the physician working in the ward.
Briand et al.[105]	2012	Mali and Senegal	2007	2008	0.068	Cross-sectional survey nested in a randomised cluster trial	All singleton pregnancies, without immediate life-threatening complication.	N.R.	in-hospital maternal mortality, early neonatal mortality	referral hospitals	11,255	Data was collected from medical records by trained midwives who were supervised by the national coordinators of the survey. To avoid under-reporting of in-hospital maternal mortality, a complementary procedure was carried out to identify the eligible maternal deaths among all the female deaths that occurred in the facility using the various registries available (admissions, hospitalizations, operating theatres and morgues).
Wirakusumah[54]	1995	Indonesia	1981-1983 and 1988-		0.525	Retrospective cohort	Maternal deaths	N.R.	in-hospital maternal	Referral/teaching	1424	Maternity Care Monitoring Records of

			1990				associated with caesarean section		mortality, early neonatal death	hospital		Hasan Sadikin Hospital Bandung. To study the maternal mortality in detail in data were collected independently from the following sources: abstracts from the delivery room registry and the medical records of the Department; daily case reports recorded by residents who contain information about the patients (characteristics as well as detailed diagnoses and procedures).
Bishop et al.[48]	2019	22 countries (Benin, Burundi, Republic of the Congo, Democratic Republic of the Congo, Ethiopia, The Gambia, Madagascar, Mali, Niger, Tanzania, Uganda, Zimbabwe, Algeria, Cameroon, Ghana, Kenya, Libya, Mauritius, Namibia, Nigeria, South Africa, Zambia	2016	2016	0.437	A 7-day, international, prospective, observational cohort study	all consecutive patients (aged ≥18 years) admitted to participating centres having elective and non-elective caesarean delivery during the 7-day study cohort period.	elective n=801 emergency n=2867	in-hospital maternal mortality, in-hospital neonatal mortality	183 hospitals (mixed)	3684	hospital's lead investigator to submit the total number of eligible patients during the recruitment week and required that each participating hospital provide complete data for at least 90% of the eligible surgical patients during the recruitment week. Preoperative recruitment and follow-up until discharge was performed by local investigators.
Chi et al.[19]	1986	2 less	1977	1980	0.011	N.R.	women	N.R.	In-hospital	N.R.	857	Maternity Record

		developed countries: The annual per capita income was about US$ I 05 for Country A in 1980 and US$ 560 for Country B in 1982					consecutively admitted to the five hospitals for delivery and for problems associated with late pregnancy, labor and/or delivery.		maternal deaths			
Petitti et al.[40]	1982	United States	1970, 1974, and 1978		0.860	N.R.	all deliveries	N.R.	In-hospital maternal deaths	mixed	350,892	Information was derived from the computerized hospital discharge records of the Professional Activities Study of the Commission on Professional and Hospital Activities.
Buowari et al.[25]	2012	Nigeria	2005	2006	0.452	retrospective study	all patients who had caesarean section	elective n=4, emergency n=151	maternal mortality	District hospital	155	The maternity ward and theatre registers were the sources of data while other clinical records were retrieved from the records department.
Utuk et al.[14]	2010	Nigeria	2004	2006	0.467	retrospective study	all the patients that were delivered by CS	Elective n=192 , Emergency n=508	maternal death	Tertiary/teaching Hospital	700	The case files of all the patients that were delivered by CS between 1 January 2004 and 31 December 2006 were reviewed. The labour ward and theatre registers were also analysed.
Nyamtema et al.[37]	2016	Tanzania	2012	2014	0.503	Before-after intervention study design	All caesarean sections	N.R.	maternal death	health centres (HC)	5868	delivery logbooks, case files and operation records.
Mukherji et al.[69]	1995	India	1988	1993	0.436	retrospective analysis	maternal deaths following caesarean section	N.R.	maternal death following CS	Teaching hospital	8,017	hospital records.
Igberase et al.[77]	2009	Nigeria	1995	2004	0.452	retrospective review	all patients who had caesarean delivery	Emergency n=1124, Elective n=653	maternal death	tertiary hospital	1,777	The data from case notes, antenatal and theatre records of patients who had caesarean delivery over a ten year period in the

												Baptist medical center, Ekuwere extracted and analysed.
Tsen et al.[123]	1998	United States	1990	1995	0.872	N.R.	all parturient who underwent general anesthesia for caesarean section (includes data of patients undergoing all types of anesthesia)	N.R.	maternal mortality	tertiary	12040	the hospital's database and medical records.
Palanisamy et al.[88]	2011	United States	2000	2005	0.889	retrospective analysis	all caesarean deliveries under general anesthesia	N.R.	anesthesia-related maternal mortality	Tertiary hospital	15468	the obstetric database at the institution and medical records.
Enohumah et al.[2]	2006	Nigeria	1991	2000	0.452	retrospective study	patients who had undergone surgical procedures in pregnancy or puerperium	N.R.	anesthesia-related maternal mortality	Tertiary hospital	2323	Information was assessed from available records: the master register in the Labour and Delivery Operating Room, Labour and Delivery records, Intensive Care Unit records and patient charts and maternal mortality database.
Nwobodo et al.[108]	2011	Nigeria	2002	2010	0.474	retrospective analysis	all the patients that had caesarean section	emergency n=1784, elective n= 498	maternal deaths	Tertiary hospital	2284	The records from the labor room and operating theater were retrieved and checked for caesarean deliveries. The delivery records of patients that had elective caesarean sections were obtained and relevant variables extracted.
Swende et al.[104]	2007	Nigeria	2004	2006	0.467	retrospective analysis	all the patients that had caesarean section	emergency n=351, elective n=69	maternal death	Tertiary hospital	420	The case files of all patients that had caesarean section during the period of review were retrieved from medical, theatre and labour ward records.
Zongo et	2015	Senegal and	2007	2011	0.081	cluster-	All deliveries	N.R.	hospital-	mixed	40,975	hospital-based maternal

al.[100]		Mali				randomized controlled trial			based maternal death			death, was measured as the vital status of the mother (dead or alive) at hospital discharge
Talebi Doluee et al.[93]	2018	Iran	2010	2014	0.781	retrospective cross-sectional study	all maternal deaths	N.R.	maternal mortality	N.R.	280957	Data was collected from the reports of Maternal Mortality Committee of Mashhad University of Medical Sciences, Mashhad, Iran. The Committee was consisted of trained professionals in this field including a gynecologist, an anesthesiologist, a hospital director, a representative of the Deputy Minister of Health, a midwife, a nurse, and a forensics expert. The number of live births per year was obtained from the Statistics Center of Mashhad University of Medical Sciences, Mashhad, Iran.
Löfgren et al.[60]	2015	Uganda	2011	2011	0.494	A prospective, questionnaire -based study	all major and minor operative procedures	N.R.	perioperative mortality	district hospitals	496	using 2 pretested questionnaires, one for data collection in the operating room and one for data collection on the ward. Forms filled in the operation room were cross- checked with the operating room registers and the forms filled in on the ward. If required, clinical notes from the wards and registers at the time of admission were checked to correct any inconsistency.
Maaløe et al.[29]	2012	Tanzania	2009	2010	0.479	retrospective criterion-based audit.	All emergency caesarean sections	emergency n=303, elective n=35	maternal death, Early neonatal deaths	Two rural hospitals	303	case notes were reviewed and extracted the data by applying a structured

												questionnaire. At each hospital, 200 women receiving CS in 2009 were retrieved from the operation theater records. The identities of the women were cross-checked with the admission and delivery registers, and their case notes with partographs collected.
Andersgaard et al.[99]	2008	Norway	1976	1995	0.850	N.R.	All direct maternal deaths	N.R.	maternal death	mixed	117,521	The maternal deaths were identified through the Cause of Death Registry, Statistics Norway, and Medical Birth Registry of Norway. Copies of the hospital case records and the maternal death autopsies were requested.
Rippmann[91]	1965	Switzerland	1940	1963	0.832	N.R.	all maternal deaths	N.R.	maternal death	N.R.	3132	N.R.
Hou et al.[65]	2017	China	2011	2011	0.711	Cross sectional study	all deliveries, all births greater than 24 weeks gestation	N.R.	inpatient maternal death, neonatal death	All hospitals were secondary or tertiary care public hospitals	59,415	Data was extracted from medical records and discharge summaries by trained medical staff on a standardized coded form.
Bloom et al.[5]	2005	United States	1999	2000	0.881	A prospective observational study	all caesarean births	emergency n=2163, elective n=34979	maternal death	multiple university-based hospitals	37,142	Detailed information were abstracted directly from maternal and infant charts by specially trained and certified research nurses.
Ojo et al.[89]	1988	Nigeria	1982	1986	0.452	retrospective analysis	all maternal deaths after caesarean section	N.R.	maternal mortality after caesarean section	Teaching hospital	1992	case records.
Gundumure[52]	2002	Zambia	1998	1998	0.419	retrospective	all caesarean sections	N.R.	maternal mortality	Teaching hospital	1,880	cases of CS were identified using the CS register kept in the theatres. The labour ward delivery register was used to identify any

												information that was not clearly entered in the theatre register. Specific data was collected from patient case files. If this was not available, the two registers provided sufficient core data. Regarding maternal mortality, this was cross-checked with the register of maternal deaths in which cases that had CS had been previously identified.
Engin-Üstün et al.[92]	2019	Turkey	2012	2015	0.778	population-based retrospective review	all pregnancy-associated maternal deaths	N.R.	maternal death	mixed	2642257	Data was collected from National Maternal Mortality Surveillance database of Ministry of Health.
Sachs et al.[101]	1988	United States	1954	1985	0.860	N.R.	all deaths directly due to caesarean section	N.R.	Caesarean section-related maternal mortality	mixed	121,217	the Maternal Mortality Committee of the Massachusetts Medical Society constructed a data base to include the listings of all known maternal deaths that occurred in the Commonwealth between 1954-198. Population statistics used in this study were obtained from the Massachusetts Department of Public Health.
Longombe et al.[119]	1990	Zaire/ Democratic Republic of the Congo	1983	1987	0.356	retrospective study	all caesarean sections	N.R.	maternal mortality, early neonatal mortality	referral	1014	N.R.
Cisse et al.[75]	1998	Senegal	1996	1996	0.379	Prospective longitudinal study	All women undergoing caesarean sections	N.R.	maternal death	N.R.	2436	For each case, an individual file with 30 variables was completed.
Evrard et al.[64]	1977	United States	1965	1975	0.860	N.R.	all deliveries	N.R.	post-caesarean-section	mixed	12,941	The Rhode Island State Health Department was able to supply the total

									deaths			number of deliveries by occurrence from 1965 through 1975 and the total number of caesarean sections for 1968 through 1975. The number of caesarean sections for 1965, 1966, and 1967 was calculated as follows: A letter was sent to each hospital in which babies were delivered during those years, requesting the number of deliveries and the number of caesarean sections. Protocols for the maternal deaths during the study period were obtained from the Maternal Mortality Committee of the State Medal Society of Rhode Island.
de la Fuente et al.[61]	1977	Spain	1965	1974	0.754	N.R.	all the caesarean operations	N.R.	Post-caesarean maternal deaths	N.R.	7,562	Hospital records.
Maswime et al.[38]	2016	South Africa	2013	2014	0.685	A retrospective study	all maternal deaths due to bleeding during and after caesarean	N.R.	maternal death due to bleeding during and after caesarean	Three of the study hospitals are university teaching hospitals in Johannesburg with tertiary referral functions, and four are regional (secondary level) hospitals as part of the local referral system.	43137	maternal deaths due to bleeding during and after caesarean that occurred at seven hospitals in Johannesburg, South Africa, between January 1, 2013, and December 31, 2014, were audited as a case series. Hospitals in South Africa are required to keep all clinical notes in cases of maternal death.
Kilsztajn et al.[1]	2007	Brazil	2001	2003	0.698	N.R.	All caesarean sections	N.R.	maternal death	Public health hospital	371981	Birth certificates data that is responsible for the compilation and diffusion of Sao Paulo

												State vital statistics; public health hospital data for 2001–2003 recorded and publicized by the Brazilian Health Ministry for Sao Paulo State residents and hospitals.
Amirikia et al.[112]	1981	United States	1965	1979	0.860	N.R.	All caesarean sections	N.R.	maternal mortality	referral center	9,718	N.R.
Bolaji et al.[10]	1993	Ireland	1973	1987	0.764	15-year survey	All deliveries	N.R.	Post caesarean section deaths	Teaching hospital	3572	The clinical research unit in the department of Obstetrics and Gynaecology routinely abstracts and codes information from all birth records for a computer file.
Fenton et al.[127]	2003	Malawi	1998	2000	0.368	prospective observational study	All caesarean sections	emergency n= 7622, elective n= 448	maternal mortality	Two hospitals were central hospitals, generally serving the urban populations, and 25 were district hospitals, serving the rural population	8070	trained each participating anaesthetist to record operative and postoperative events and then checked the data sheets against hospital theatre records during routine district visits.
Ikeako et al.[63]	2009	Nigeria	2005	2009	0.479	retrospective review	all caesarean deliveries, exclusion criteria were women with ruptured uterus	emergency n= 184, elective n= 97	maternal death related to caesarean section, early neonatal death	secondary healthcare facility, referral centre	291	The labour ward and theatre registers provided information on the total number of deliveries and caesarean sections. The case notes of all those who had caesarean section were examined in detail. The medical records were reviewed by trained staff using pre-established and piloted data extracted forms.
Tadesse et al.[31]	1996	Ethiopia	1991	1992	0.283	prospective hospital-based study	All women who delivered	n= 57 elective caesarean section, n=	maternal death, Early neonatal deaths	Teaching hospital	318	The antenatal chart and delivery records were reviewed and abstracted according to pre-

								261 emergency caesarean section				prepared protocol.
Okonta et al.[43]	2003	Nigeria	1996	2000	0.452	audit	All caesarean sections	n= 712 emergency n= 181 elective.	maternal deaths associated with caesarean sections, early neonatal death	Teaching Hospital	1031	The hospital records. The labour ward and theatre registers provided information on the total number of deliveries and caesarean sections (CS). Further detailed information was obtained from patients' case notes and the detailed case summaries of every delivery kept in the department.
Mekbib et al.[6]	1994	Ethiopia	1987	1992	0.283	retrospective study	all patients who underwent CS	emergency n= 586, elective n=59	CS-related maternal mortality, neonatal death	Teaching Hospital	645	Hospital records.
Ezechi et al.[85]	2002	Nigeria	2000	2002	0.452	descriptive study	All mothers that were delivered by caesarean section	N.R.	mortality associated with caesarean section	private hospital	391	N.R.
Daniel et al.[74]	2016	Nigeria	2009	2011	0.484	descriptive longitudinal cross-sectional study	All caesarean sections except those who had a caesarean section hysterectomy following uterine rupture	emergency n=288, elective CS n=216	maternal deaths associated with CS	Tertiary hospital	504	Maternal outcomes were extracted from the case notes and operation files and documented in a proforma.
Bukar et al.[44]	2009	Nigeria	2001	2003	0.452	retrospective study	All caesarean sections	n=181 emergency, n= 69 elective.	maternal death, neonatal death	Tertiary institution	250	The records were obtained from the Medical records department, postnatal and labour ward registers and the theatre.
Njokanma et al.[79]	2002	Nigeria	1983	1997	0.452	descriptive study	All caesarean sections	n=686 emergency CS, n=454 elective	maternal death, early neonatal deaths	Private hospital	1140	Hospital records, neonatal chart and in the delivery register.
Etuk et al.[94]	2001	Nigeria	1993	1997	0.452	N.R.	All caesarean section deaths,	N.R.	maternal mortality	Teaching hospital	1540	The case notes of all maternal deaths

							excluding those following uterine rupture		following caesarean section			following caesarean section were reviewed. The theatre register within the same period was also reviewed to find the total number of caesarean sections performed and the cadre of surgeons who carried out the operation.
Ibekwe et al.[36]	2006	Nigeria	2000	2002	0.452	Retrospective review	all caesarean sections	84% (n=196) of sections were emergency and 16% were elective (n=37)	maternal death	teaching hospital	233	case records of patients were reviewed
Ali[24]	1995	Ethiopia	1991	1992	0.283	prospective study	all Caesarean deliveries	n=92 emergency, n=8 elective	maternal death, neonatal death	Teaching hospital	100	A data collection format was prepared to collect data for all Caesarean deliveries in Jimma Hospital from 23 June 1991 to 23 September 1992. The form was filled by interns working in the department after careful orientation and close follow-up.
Imarengiaye et al.[96]	2001	Benin	1986	1995	0.354	N.R.	Admitted to ICU following caesarean section	emergency n=2102, elective n=584	maternal death	Tertiary/teaching hospital	2686	Hospital records of patients were studied.
Greenhill[57]	1930	United States	1915	1929	0.860	N.R.	All caesarean sections	N.R.	maternal death	N.R.	874	N.R.
Onoh et al.[41]	2015	Nigeria	2002	2011	0.479	case series	all the caesarean deliveries	emergency n=1,576 elective n=521	maternal death	Teaching hospital	2,097	The delivery register was used to select all women who had caesarean delivery, and their folders were retrieved from the record department. The patients' folders, antenatal ward, labor ward, theater, postnatal ward, and newborn special intensive care

												unit registers were utilized for the data collection.
Ugwu et al.[95]	2011	Nigeria	2005	2009	0.479	retrospective analysis	all the caesarean sections	n=918 emergency caesarean, n=62 elective CS	maternal death	Teaching hospital	980	Case notes, labour ward and theatre records.
Aisien et al.[113]	2002	Nigeria	1994	1998	0.452	retrospective analysis	cases of caesarean section	n=1875 emergency procedure, n= 208 elective CS	Maternal Mortality Associated with Caesarean Section, early neonatal mortality	Teaching Hospital	2083	Information on those who delivered by caesarean section was documented in the theatre operation book, labour ward record and case notes of patients, and these were analysed. Records of caesarean section babies in the special baby care unit were also analysed for their perinatal outcome.
Oyewumi[49]	2018	South Africa	2014	2014	0.685	descriptive retrospective audit	all women who underwent caesarean section	Emergency n= 815, while elective n=65	maternal deaths	public district hospital	880	The ward register at the hospital was used to manually retrieve each patient folder and, using a data- collection sheet agreed on with the clinical staff of the department and data was manually collected through careful scrutiny of each folder for agreed variables.
Okezie et al.[103]	2007	Nigeria	2001	2004	0.452	N.R.	all patients who had lower segment caesarean section	emergency n=460, elective n=280	maternal death	Teaching Hospital	740	Hospital records.
Raphael et al.[33]	2015	Nigeria	2008	2011	0.484	retrospective descriptive study	patients who had caesarean section	n=1300 emergency caesarean, n= 666 elective caesarean section	maternal mortality post-caesarean section	Teaching Hospital	1,966	Patient files.
Ijaiya et al.[46]	2001	Nigeria	1990	1999	0.452	retrospective study	all caesarean deliveries	n= 2,529 emergency,	maternal deaths	Teaching Hospital	2,764	The records of caesarean sections were obtained

								n= 235 elective	following caesarean section			from patients' case notes, labour ward and theatre records and mortality register.
Krause et al.[58]	1979	Germany	1956	1976	0.801	retrospective study	all deliveries	N.R.	maternal death	university hospital	1468	N.R.
Alegre Villariz et al.[72]	1977	Spain	1972	1975	0.754	retrospective study	cases of caesarean section	N.R.	maternal death	N.R.	1499	N.R.
Kinenkinda et al.[21]	2017	Democratic Republic of Congo	2009	2013	0.419	multicenter study, retrospective descriptive and analytical study	all caesarean deliveries	urgent n=1309, non-urgent n=2016	maternal mortality	N.R.	3643	Birth records, partograms, operating reports, and neonatal cards were the source of information.
Muziarelli et al.[68]	1989	Italy	1974	1987	0.769	Retrospective study	all caesarean sections	N.R.	maternal mortality	N.R.	747	clinical files
González et al.[66]	1975	Mexico	1972	1972	0.650	N.R.	patients undergoing caesarean section	N.R.	Post-caesarean maternal mortality	N.R.	700	The files of 700 patients were reviewed in whom caesarean section was performed in the period included in the procedure.
Pekhlivanov[53]	1975	Bulgaria	1949	1973	0.694	N.R.	all caesarean sections	N.R.	maternal mortality	N.R.	1112	material of the obstetric-gynecological ward at the first municipal hospital in the town of Plovdiv.
Poradovsky et al.[126]	1968	Czechoslovak Republic/ Czech Republic	1962	1966	0.730	N.R.	all obstetric interventions	N.R.	maternal death	mixed	21981	N.R.
Imbert et al.[42]	2003	Senegal	1997	1997	0.380	Prospective study	All emergency caesarean sections	n=370 emergency, n=32 elective	maternal mortality	Referral/Teaching Hospital	370	On a standardized sheet we noted: age, medical and obstetric history, admission method, direct or by evacuation. The indications of CS, clinical status and preoperative assessment of mothers on admission, modalities of anesthesia as well as the outcome of CS at the end of the hospital and at three months for mother and newborns

												born on discharge from the hospital between D8 and one month.
Picaud et al.[106]	1990	Gabon	two 4-year periods (1981-1984 and 1985-1988)		0.620	comparative study	All caesarean sections	N.R.	maternal mortality	Referral/Teaching Hospital	1213	N.R.
Szczepanski et al.[116]	1975	Poland	1960	1973	0.712	N.R.	All caesarean sections	N.R.	maternal mortality	N.R.	3116	N.R.
Carazzone et al.[34]	1978	Italy	1972	1976	0.769	N.R.	all deliveries	N.R.	maternal death	specialized provincial hospital body	2,940	we have collected data of the whole hospital and not of each division.
Georgiades et al.[67]	1972	Austria	1959	1970	0.795	N.R.	all caesarean deliveries	N.R.	maternal mortality	university hospital	575	Put together the patient inventory of the clinic.
Chavez Azuela et al.[81]	1967	Mexico	1962	1966	0.650	retrospective study	all maternal deaths	N.R.	maternal death	N.R.	6,495	Clinical records.
Kartushina[8]	1972	Ukraine	1958	1969	0.705	N.R.	maternal deaths from caesarean section	N.R.	postoperative mortality	N.R.	1653	N.R.
Buttmann et al.[7]	1973	Germany	1957	1972	0.801	N.R.	all caesarean deliveries	N.R.	maternal mortality	N.R.	530	N.R.
Zhu et al.[15]	2000	China	1978	1997	0.502	A retrospective study	maternal deaths of caesarean section	N.R.	Maternal mortality	mixed	623534	Sources 1978-1997 Shanghai Maternal and Child Health Report, Maternal Death Cases and Municipal Expert Evaluation Data on Maternal Deaths. Second, collecting data through the city's three-level maternal and child health network, through Shanghai.
Strobel[28]	1967	Germany	1950	1966	0.801	N.R.	all obstetric interventions	N.R.	maternal death	university hospital	896	N.R.
Warm et al.[45]	1966	Germany	1939	1963	0.801	N.R.	maternal deaths of caesarean section	N.R.	Maternal mortality	university hospital	2800	N.R.
Kambo et al.[172]	2002	India	1993–1994 and 1998–1999		0.471	N.R.	7017 consecutive caesareans	emergency n=5767, elective n=1250	maternal mortality	teaching hospital	7017	N.R.
Fesseha et al.[139]	2011	Ethiopia	2008	2009	0.402	retrospective record review	All caesarean sections	emergency n=174, elective	maternal mortality and early	Mixed	267	The data source was the national baseline assessment of

								n=48	neonatal death			emergency obstetric and newborn care—a cross-sectional, facility-based survey of 797 facilities. Two instruments were used to collect the data for the present paper: a retrospective record review of 267 caesarean deliveries; and a 12-month summary of each facility's statistics on vaginal and abdominal deliveries
Ojiyi et al.[140]	2012	Nigeria	2004	2008	0.474	descriptive retrospective study	All patients who underwent Caesarean section	emergency n=192, elective n=166	maternal mortality	Teaching Hospital	358	case records were retrieved from the medical records department.
Landry et al.[191]	2014	9 facilities in Bangladesh (rural), Guinea (urban), Mali (urban), Niger (urban), Uganda (rural).	2009	2010	0.227	retrospective record review	All caesarean sections	N.R.	maternal death	Referral, private, public, faith based	2941	Data for the study were collected using a patient record abstraction form and key informant interview guides. The physician was responsible for extracting clinical information from the clinical files. When individual patient files could not be located, hospital registers (e.g., from the delivery room, operating theater, referral, and maternity ward) were used to locate data of interest. No partographs were found in patient files at both Guinea sites, and fewer than 2% of patient records at the Bangladesh site had partographs. The majority of patient files from the Niger sites included a partograph; however, at two of these sites, fewer than 3%

												were completed correctly.
Garba et al.[141]	2011	Nigeria	2006	2007	0.479	descriptive study	All patients that were delivered by caesarean section	emergency n= 812, elective n= 126	maternal death	Teaching Hospital	938	case notes were retrieved.
Sørbye et al.[142]	2011	Tanzania	2000	2007	0.431	cohort study	All deliveries	Emergency n= 5412, elective n= 1353	maternal death and neonatal death	tertiary hospital	6765	Data from the medical birth registry at the zonal referral hospital KCMC. Trained midwives conducted interviews and collected case record information in the days after birth.
Adekanle et al.[189]	2013	Nigeria	2005	2010	0.485	retrospective study	All caesarean sections	Emergency n= 556, elective n= 132	maternal death	Teaching Hospital	688	Labour ward logbook and case records were looked into, and all information extracted.
Dillen et al.[188]	2007	Northern Namibia	2001	2002	0.540	retrospective observational study	All caesarean sections	N.R.	maternal death	District hospital	576	Information from the 'caesarean section record book' was used. The doctor who determined the indication for caesarean, was responsible for filling the record book.
Madoue et al.[144]	2015	Chad	2015	2015	0.407	transversal and descriptive survey	All patients who had undergone caesarean section	Caesareans section performed in emergency had represented 56.5%. The remaining 43.5% were a prophylactic caesarean section	maternal death	Tertiary hospital	170	All patients who had undergone caesarean section during the study period (from May 08th, 2015 to August 09th, 2015) were studied. Consent from the patient was obtained after explaining to them the need for this survey.
Akasheh et al.[39]	2000	Jordan	1991	1997	0.669	N.R.	All caesarean sections	N.R.	maternal death	Military hospital	1339	The hospital records of all patients undergoing abdominal delivery at QAMH, Amman, Jordan.
Boogaard et al.[190]	2016	Burundi	data from patients discharged between		0.408	prospective household survey	all women who underwent a C-section	N.R.	caesarean-related deaths	district hospital	228	using a semi-structured questionnaire. Data were extracted from a dedicated EmONC centre

			July and September 2012. The study was conducted between July and October 2014.									electronic database. Each unique patient identity number in the database was cross-checked with clinical files for data validation. Two nurses who were knowledgeable in emergency obstetric were selected and trained as interviewers.
Okogbenin et al.[147]	2004	Nigeria	1991	2000	0.452	retrospective study	all caesarean sections	N.R.	maternal death	Teaching Hospital	2218	Labor ward, theatre and intensive care unit records.
Wu et al.[154]	2000	China	1990	1997	0.537	Retrospective analysis	All caesarean sections	N.R.	maternal death, Early neonatal deaths	Teaching hospital	1922	Detailed medical records of all women, they were written by the department's obstetricians.
Kandasamy et al.[157]	2009	Afghanistan	2006	2006	0.419	retrospective review	All caesarean deliveries	Emergency n=237, Elective n=151	maternal death	Public maternity hospital	392	operating room logbooks which contain clinical information on all caesarean deliveries that occur in the hospital.
K. Chu et al.[156]	2012	Democratic Republic of Congo, Burundi, and Sierra Leon	2010	2011	0.021	Prospective study	Women undergoing Caesarean section	emergency n=1229, elective n=47	maternal and early neonatal death	District hospital	1276	Data was prospectively collected by trained data collectors using a standardized paper form and then entered into an electronic database. Outcome data on maternal and early neonatal death were documented
Kor-Anantakul et al.[170]	2008	Thailand	2001	2003	0.665	prospective cohort study	All deliveries of women who resided within 5km radius of the hospital	Elective n= 112, Unscheduled n= 75	maternal mortality and early neonatal death	Tertiary hospital	187	The nursing staff interviewed and examined the patients, emphasis on clinical details of postpartum complications on day 2 and between days 5 and 7. If the patient was discharged before day 5, they made a home visit.
Diallo et al.[149]	1998	Guinea	1994	1995	0.302	descriptive type prospective	All elective caesarean sections	N.R.	maternal death	University hospital	434	A survey sheet was the essential material support of this work,

						study						sometimes the data have been supplemented by those of hospital documents.
Yaïch et al.[158]	2012	Côte d'Ivoire: Ivory Coast	2010	2010	0.442	descriptive retrospective study	All emergency caesarean sections	emergency n=513	maternal mortality, neonatal mortality	University hospital / teaching hospital	513	anesthetic and obstetric records of all parturient who underwent caesarean Emergency Hospital of Cocody in Abidjan.
Cebekulu et al.[151]	2006	South Africa	2004 and 2005		0.620	cohort study	Term singleton live pregnancies with cephalic presentation and no previous scar.	N.R.	maternal death, neonatal death	Referral hospital	5765	Each day, the delivery register was examined for second stage caesarean sections done in the preceding 24 h. An attempt was made to contact all subjects telephonically 2 weeks after delivery, to identify clinical problems that may have arisen after discharge.
Ngowa et al.[168]	2015	Cameroon	2012	2012	0.526	descriptive analysis	All caesarean sections	urgent n=269, prophylactic n=191	maternal death	2 University hospitals	460	Data has been collected with participants, in their medical records and in the operating room register.
Diawara et al.[150]	2014	Mali	2007	2008	0.390	descriptive cross-sectional study	All caesarean sections	N.R.	post-operative maternal death	mixed	143	To collect the data, they used a survey form filled out from the supports used in the context of the reference-evacuation (reference / evacuation notebooks, registers of birth, operating protocol, death and partograms).
Rahlenbeck et al.[153]	2002	Rwanda	1997	2000	0.322	N.R.	All delivery	N.R.	maternal mortality after or during caesarean section	District hospital	896	Data from hospital delivery records.
Teguete et al.[166]	2012	Mali	1985	2003	0.256	Retrospective study	All deliveries	elective n= 858, emergency n=243	maternal mortality and neonatal mortality	Tertiary referral centre	4517	A complete database of all obstetric admissions focusing on characteristics of delivered

												women, mode of delivery, caesarean indications, and maternal, fetal and immediate neonatal outcome was built to include all deliveries recorded at Point G National Hospital between January 1, 1985 and December 31, 2003. Data were collected from these complete obstetric files, as well as hospital birth registries, registries of on-call midwives, surgical reports, admissions records for the intensive care service, records from the internal medicine and urology services, and hospital death records.
Eshiet et al.[169]	2003	Nigeria	1995	2000	0.452	Retrospective study	All emergency caesarean sections	920 emergency CS	Anaesthetic related death	Teaching hospital	920	Information was obtained from anaesthetic record charts, theatre and ward records.
Soren et al.[145]	2016	India	over a period of one year, <2016		0.618	Prospective study	All caesarean sections	emergency n=1436, elective n=624	maternal mortality, neonatal mortality	Teaching hospital	2060	N.R.
Nana et al.[143]	2011	Cameroon	2007	2007	0.481	cross-sectional and analytic study	All caesarean sections	Emergency caesarean section predominated in the two groups (90.2% and 86.7% for the RHM and the faith-based hospital, resp.).	maternal mortality	referral centers	91	Data collection was done using a pre-tested questionnaire. Patients were interviewed before and after surgery. The surgical term and nurses in each of the hospital was taught to file the questionnaire.
Diarra et al.[146]	2006	Mali	2005	2005	0.363	Cross-sectional	All caesarean sections	elective n=37,	maternal death after	mixed	200	Sources of data: survey sheet, birth records, CPN

						study		emergency n=163	CS, early neonatal death			registers and notebooks, reading, interview.
Goswami et al.[167]	2013	India	2005	2010	0.565	prospective study	all women who died during pregnancy or within 42 days of being pregnant	N.R.	maternal death	tertiary care hospital	8471	Summaries of all maternal deaths in obstetrics wards were available in the department and their case records were retrieved. Case records of the women dying in the non-obstetrics wards were screened every 3 months in the hospital record section to identify maternal deaths.
Abebe et al.[160]	2016	Ethiopia	2012	2013	0.439	retrospective analysis	pregnant women who had undergone either caesarean or vaginal delivery. All caesarean sections except those who had a uterine rupture	n=653 emergency CS, n=70 elective CS	maternal death, immediate newborn death	Referral hospital	723	Pre-tested questioner was used to collect mothers' information and analysis of eligible patient records.
Rasoarimah andry et al.[186]	2001	Madagascar	1998	1998	0.456	retrospective study	All caesarean sections. Excluded from our study the cases of suturing conservative after uterine rupture	N.R.	maternal death, neonatal death	Central university hospital	529	all the documented caesarean operations (treatment sheet load) performed during this period. The sheet has several variables.
Nahar et al.[165]	2009	Bangladesh	1996	1996	0.436	prospective descriptive study	Caesarean section sample randomly selected	Emergency n= 63, Elective n= 37	maternal death, early neonatal death	Medical college hospital	100	detailed history was taken from all the cases, general and abdominal examination was done from date of admission up to the day of discharge. Labour patient was monitored by doing partogram. Puerperal period up to the day of discharge was observed.
Waalewijn	2017	Sierra	2011	2016	0.430	prospective	The first 50	Elective C-	maternal	Training	1178	data from associate

et al.[187]		Leone				study	caesarean sections performed by each trainee who has performed a minimum of 50 caesarean sections. - C-sections with unknown operation time were excluded, as well as operations lasting longer than four hours	sections n= 155, emergency n=1023	mortality	hospitals		clinician's surgical logbooks obtained in a surgical task-sharing training programme. After every C-section, trainees collected and entered operation-related data in a paper-based format. Supervisors signed the logbooks after every correctly inputted procedure.
Akar et al.[185]	2004	Turkey	1982	2001	0.589	retrospective study	All maternal deaths	N.R.	maternal death	Research hospital / teaching hospital	126779	Data on maternal deaths were obtained from hospital records, death registration lists, and patient files.
Okafor et al.[155]	2008	Nigeria	1998	2006	0.452	observational retrospective study	Caesarean sections deaths	N.R.	anaesthetic related maternal deaths during caesarean section	Teaching hospital	1579	The obstetric theater records were reviewed for deaths during anaesthesia for caesarean section and their hospital records examined for demographics, obstetric/anesthetic records and cause of death.
Ghazi et al.[162]	2012	Pakistan	2006	2007	0.511	cross-sectional comparative study	All caesarean sections. Patients having previous myomectomy, hysterotomy or classical C/S were excluded from the study.	emergency n=50, elective n=50	maternal death	Tertiary care hospital	100	All expecting mothers admitted through OPD or emergency, of any age or parity undergoing C/S were recruited in the study. Postoperative complications were recorded from recovery room till patient was discharged from the ward.
Nelissen et al.[164]	2013	Tanzania	2009	2011	0.487	prospective cross-sectional study	All maternal near misses and maternal deaths	N.R.	maternal death	Referral hospital	74	Data were obtained from the patient record. The facility medical staff was questioned in case

												of doubt or missing information.
K.M. Chu et al.[161]	2010	Central African Republic (CAR), South Sudan, Ivory coast, DRC, Haiti, Somalia, Chad, Niger, Burundi, Sierra Leone, Mali, Indonesia, Pakistan	2001	2008	0.350	retrospective cohort study	patients undergoing surgical procedures.	N.R.	maternal death	Mixed	3233	Data were prospectively collected using a standardized database. Baseline characteristics and operative mortality were recorded in databases at the time of the procedure.
Sekirime et al.[178]	2009	Uganda	N.R. , <2009	N.R.	0.457	descriptive observational concurrent prospective study.	emergency caesarean section	n= 478 emergency	maternal death	Tertiary referral	478	All those recruited were from the Mulago Hospital labor ward and were operated in the same theatre by doctors of or above the rank of a senior housing officer. The patients were followed up postoperatively for primary outcomes.
Davies et al.[183]	2016	Eastern Democratic Republic of Congo, Central African Republic, and South Sudan.	2011	2013	0.201	Prospective cohort study	A surgical inpatient was anyone who underwent an operation (including obstetric) or who was managed by the surgical team.	Emergency n=4,613, elective n= 33	perioperative mortality	District	4646	A standardized surgical data collection tool in Excel was used to collect individual patient data on surgical inpatients admitted to MSF facilities. The attending surgeon recorded data postoperatively or after exit (discharge, death, default) of the patient.
Chilopora et al.[179]	2007	Malawi	2005	2005	0.373	Prospective study	All women undergoing caesarean section	N.R.	maternal death, early neonatal death	District hospital	2131	All women undergoing caesarean section were followed up from the time the decision to do a caesarean section was made until discharge

												from hospital. Women were asked to come back for review seven days after discharge. A structured data collection sheet was used to retrieve information on admission diagnosis, indication for surgery, preoperative condition, designation of surgeon and type of surgery.
Gonzales et al.[180]	2013	Peru	2000	2010	0.700	secondary analysis	All caesarean sections	elective n=82,621, emergency n= 69,489	Maternal mortality	43 public health facilities (40 hospitals and 3 health centres	152,110	secondary analysis from a dataset of the Perinatal Information System (Sistema Informático Perinatal).
Adisso et al.[182]	2006	Benin	2002	2002	0.419	retrospective, descriptive, exhaustive and analytical study	all women who have undergone a caesarean.	N.R.	maternal death	University	1745	patient files were retained.
Richard et al.[175]	2008	Burkina Faso	2003	2006	0.324	Before after study	all women with emergency or elective caesarean delivery in the district hospital	emergency n=1206, elective n=165	post-caesarean maternal deaths	District hospital	1371	• Routine data from the district hospital (admissions, deliveries, complications, referrals) (2003–2006). • Caesarean delivery forms designed to record all major obstetric interventions performed for life-saving indications. Nonroutine data were collected from the main city hospitals, including the university hospital (2003–2005). • Individual prescription cards for women having a caesarean delivery. This card shows all surgical procedures and treatment prescribed

												during each woman's hospital stay and the cost (2005). • Referral and feedback forms (2004–2006). • Criteria of quality grids for intrapartum and postpartum care (2003–2005)
Meda et al.[174]	2016	Burkina Faso	2009	2010	0.375	cross-sectional study	women who were delivered by caesarean in any health center in Burkina	Emergency n= 568, elective n=100	maternal death	any health center in Burkina	668	For every selected case of caesarean delivery, a questionnaire was filled in using the medical record, the partogram, the register of the operating room, and the register of delivery.
Asıcıoglu et al.[163]	2014	Turkey	2008	2011	0.743	observational study,	Caesarean sections for singleton term pregnancies without major fetal abnormalities or significant maternal disease or complications	N.R.	maternal death, neonatal death	Tertiary/teaching hospital	8072	N.R.
Basak et al.[181]	2011	India	2005	2006	0.548	prospective comparative cohort study.	Caesarean section for obstructed labour	N.R.	maternal mortality, neonatal mortality	Teaching hospital	50	N.R.
Gessessew et al.[176]	2011	Ethiopia	2006	2008	0.377	retrospective study	All deliveries	N.R.	maternal death	11 hospitals and 2 health centers with CEmOC status in Tigray.	2835	Data were collected using questionnaires, one concerning the facility and the other concerning the patient. Data were extracted from registries, operating theater books, and other relevant charts.
McCord et al.[173]	2009	Tanzania	2006	2006	0.452	prospective review	major emergency obstetrical surgery/ All emergency caesarean	n= 1087 emergency	maternal death	district hospitals	1087	Operating room and maternity records. In each of fourteen hospitals a nurse/midwife and an assistant medical officer

							sections					worked together to create a detailed record for each patient.
Souza et al.[159]	2010	Angola, DRC, Kenya, Uganda, Nigeria, Niger, Cuba, Brazil, Mexico, Peru Argentina, Ecuador, Paraguay, Nepal, Nicaragua, India, Cambodia, Vietnam Philippines, Thailand, Sri-Lanka, Algeria	Data collection took place during 2004 and 2005 in Africa and the Americas and during 2007 and 2008 in Asia.		0.511	a multi-country, facility-based survey	All women giving birth at the facility during the study period were included	N.R.	maternal mortality, Early neonatal deaths up to hospital discharge	Mixed	73,718	Data were obtained from women's medical records. Trained staff reviewed medical records of all women and their babies before discharge from the hospital, and abstracted data daily to their forms for individual data collection. The hospital coordinator supervised data collection, resolving or clarifying unclear medical notes before forms were sent for data entry. Attending staff updated incomplete records before discharge.
Pereira et al.[138]	1996	Mozambique	1992	1992	0.215	nonrandomised analysis, Prospective study	All caesarean sections	elective n=145, emergency n=1926	maternal death, early neonatal death	Central/university hospital	2071	N.R.
Khawaja et al.[184]	2004	Pakistan	2000	2001	0.456	descriptive study,	All caesarean sections	34 sections were elective (11%) and 266 were emergency caesarean deliveries (89%).	maternal death	tertiary care hospital	300	A senior house officer charted details of the subjects on a specifically designed proforma. A partogram was maintained during every labour by the registrar.
Ouédraogo et al.[152]	2015	Burkina Faso	2005	2008	0.344	retrospective study	All caesarean sections	Caesarean section was performed in an emergency in 87% of cases, was programmed in 13% of	maternal death, early neonatal death	District	3381	Data were collected from the computer database of records of caesareans at the hospital. The computer database of caesarean maternity files from Sector 30 CMA was the source of the

								cases.				information. They also consulted the registers of the operating room, the delivery room and monthly activity reports.
Rabiu et al.[148]	2011	Nigeria	2008	2009	0.491	retrospective audit	All singleton emergency caesarean sections without significant maternal or foetal disease.	Elective Emergency n=879 (28.7%) n=2182(71.3%) (of overall CS not just cases)	maternal death, neonatal death	Teaching	347	The case notes of all the patients who had intrapartum C/S were retrieved and studied.
Begum et al.[171]	2014	Bangladesh	2012	2013	0.572	case series	All multiparous women with previous one lower segment caesarean section who presented at term (37 completed weeks to 42 weeks) were included in the study. All women with history of previous classical caesarean section were excluded.	Emergency n=46, elective n=69	maternal mortality	Tertiary hospital	115	The data were recorded through proforma.
Seal et al.[177]	2010	India	2005	2006	0.548	hospital-based cohort study	caesarean sections for the following criteria: Inclusion criteria were singleton live pregnancies at term (37 to 41 completed weeks) in nulliparous women with vertex presentation.	N.R.	maternal mortality, neonatal death	Teaching hospital	1826	N.R.

							Pregnancies with major fetal abnormalities, malpresentations, or significant maternal disease or pregnancy complications (such as gestational hypertension, diabetes, intrauterine growth restriction, and prelabour rupture of membranes) were excluded					
Chau-In et al.[111]	2010	Thailand	2003	2004	0.683	multi-center study, prospective survey	All women receiving anaesthesia during caesarean section	Emergency n=5,760, elective n= 10936	maternal death related to anaesthesia	Mixed	16,697	Details of pre-anesthetic conditions, anesthetic management, intra-operative events and peri-operative complications among consecutive patients within 24 hours of post-operative were recorded on standardized forms. The responsible anesthetist/nurse anesthetist asked four key questions, what is/ are adverse events, who, when, and how the event occurred? Each case was reviewed by the preliminary quality assurance (QA) committee, comprising three anesthetists from different university hospitals, to assess whether the inclusion criteria were met. Contact was made with the anesthetist involved

												or the admitting hospital's anesthetic records reviewed.
Júnior et al.[55]	2014	Brazil	2003	2004	0.697	retrospective cohort study	liveborn normally formed fetuses from single term pregnancies.	elective n=334, emergency n=251	maternal death, neonatal death	public teaching hospital	585	Data were collected from medical records following a questionnaire.
MATERNAL AND PERINATAL MORTALITY COMMITTEE[51]	1969	Australia	1966	1967	0.866	prospective study	all caesarean sections	elective n=1,264 emergency n=2236	maternal mortality, neonatal death	Mixed	3,500	Every hospital with obstetric beds was provided with a questionnaire to be completed by the surgeon before the patient was discharged from hospital. 'The Section of Maternal and Infant Care of the Department of Public Health checked the returns and ensured that all maternal and perinatal deaths relevant to the survey were included.
Moldin et al.[20]	1984	Sweden	1973	1979	0.816	N.R.	all caesarean sections	N.R.	maternal mortality	mixed	63075	From the medical birth registration. Death certificates for maternal deaths associated with parturition or puerperium during the study period were obtained from the National Central Bureau of Statistics. The type of birth in each case of maternal death was determined by means of the medical birth register of the National Board of Health and Welfare. Autopsy was performed in all cases included in this study.
Rubin et al.[16]	1981	US	1975	1976	0.860	N.R.	Georgia residents aged 10 to 44 years	N.R.	maternal mortality	mixed	15,188	Obtained computer file data on live births and deaths occurring in

							had died up to 14 months after delivery of a live-born infant regardless of the cause of death entered on the death certificate.					Georgia from the Office of Health Planning and Evaluation of the Georgia Department of Human Resources. This office processes and tabulates data from the birth and death certificates collected by the Vital Records Unit of the same department. Obtained additional information from medical examiners' reports, physician and hospital records, police reports and the family of the deceased
Bruce et al.[50]	1966	Chile	1961	1965	0.703	N.R.	all caesarean operations	N.R.	maternal mortality, neonatal mortality	N.R.	771	Clinical records corresponding to all caesarean operations.
Abbassi et al.[18]	2001	Morocco	1994	1997	0.499	retrospective review	All caesarean sections	N.R.	maternal death	Teaching hospital	3,231	Reviewed all the files of the caesarean sections performed at the Lalla Meryem maternity hospital of the Ibn University Hospital.
Pinsker et al.[87]	1982	Mexico	[in the span of seven years], <1982		0.652	N.R.	all maternal deaths	N.R.	maternal death, neonatal death	N.R.	22495	The observations captured in the Maternal Mortality Committee of the hospital, regarding the early mothers who eventually practiced Caesarean operation, in order to study some factors involved in its death.
Beck et al.[13]	1984	Austria	1975	1982	0.795	Individual case analysis	all maternal deaths	N.R.	maternal death	mixed	43061	All obstetric-gynecological departments are contacted every year and asked to provide documents on maternal deaths. All pathological-anatomical institutes and forensic medicine institutes were also be

												contacted in order to ensure that the maternal deaths are recorded without gaps. They informed them of cases in which signs of an existing or up to 6 weeks past pregnancy could be ascertained on the basis of an autopsy. The information on the section frequency was taken from a national survey by Baumgarten and Schrock.
Saving Mothers 2017[133]	N.R.	South Africa	2018	2018	0.705	Annual Report on Confidential inquiries into maternal death	all maternal deaths	N.R.	maternal mortality	mixed	248381	Data was obtained from the District Health Information System (DHIS) for live births and maternal deaths per district for 2017 on 23rd July 2018. The NCCEMD data was obtained from the Maternal Morbidity and Mortality Audit System (MaMMAS) database in 7th September 2018, once all provinces had submitted their data. The DHIS data is almost exclusively from public hospitals (although some private hospitals do submit data to the DHIS).
Slaytor et al.[130]	2004	Australia	1997	1999	0.892	maternal death report	all maternal deaths	N.R.	maternal mortality	mixed	159201	maternal mortality data was collected from the State and Territory Maternal Mortality Committees. The composition of these Committees usually comprises some or all of the following experts—obstetricians, obstetric physicians, midwives, pathologists, general

												practitioners, epidemiologists, and Aboriginal and Torres Strait Islander and consumer representatives. Each State and Territory Committee has developed different ways to maximise the maternal death notifications; this may include notifications from health departments, hospitals, attending practitioners, coroner's office, Registrar of Births, Deaths and Marriages and review of the perinatal and hospital morbidity collections. The sources of information reviewed include any hospital admissions, autopsy, toxicology, police and coroners' reports, and other ancillary information.
NCCEMD[131]	N.R.	South Africa	data entered before 2017		0.704	Seventh triennial report on confidential enquiries into maternal deaths	all maternal deaths	N.R.	maternal mortality	mixed	708024	Data used in this report consist of the maternal deaths that occurred and were reported to the NCCEMD secretariat and were entered on the MaMMAS database before 15 May 2017.
NCCEMD[132]	N.R.	South Africa	2002	2004	0.617	Report on Confidential Enquiries into Maternal Deaths	all maternal deaths	N.R.	maternal mortality	mixed	477210	the facility completes a Maternal Death Notification Form (MDNF) which is sent to the provincial office within 7 days of the maternal death. The provincial MCWH coordinator informs the secretariat of the

												NCCEMD that a death has occurred. The NCCEMD issues a unique file number for the case. The Province forwards all documentation to a Provincial Assessor. The Provincial Assessor team comprising of a doctor and midwife is responsible for completion of the assessor's form. The assessor must complete and return all documentation to the Province within 30 days. All documentation is then forwarded to the NCCEMD for collations and analysis. The NCCEMD uses this data to compile reports on maternal deaths in South Africa.
Munjanja[134]	N.R.	Zimbabwe	2006	2006	0.429	retrospective, descriptive study	all maternal deaths (A study subject was a woman aged 12-49 years resident in the sampled districts. She must have been alive at the start of the study period, and during that period she might have died, delivered one or more living or dead babies, or survived)	N.R.	maternal death	mixed	1942	All notification forms sent to the MoHCW head office of women who had died between 1st January and 31st December 2006 were collected for analysis. To identify non-institutional maternal deaths in the community, all deaths of women of reproductive age were identified from the village, ward and district death registers. If the registers or the facilities did not have records with the cause of death, then the family were visited and were asked to produce any medical records on the illness of their deceased relative. If there were no

												records, a maternal verbal autopsy was conducted.
Maswime et al.[23]	2016	South Africa	2013	2014	0.691	prospective cross-sectional study	all deliveries	N.R.	Maternal deaths from BDACS	public hospitals	70095	Interviews with the clinical head of obstetrics in each hospital, using a structured questionnaire.
Högberg et al.[120]	1989	Sweden	1951	1980	0.816	N.R.	all maternal deaths related to caesarean section	N.R.	maternal death	mixed	82,901	All certificates of death related to pregnancy, childbirth and the puerperium for the years 1951-80 were retrieved from the Swedish Central Bureau of Statistics, together with hospital records and autopsy reports from the various departments of obstetrics and Gynaecology. The numbers of abdominal and vaginal deliveries were obtained from the annual reports of the obstetrical departments for the years 1951-72, and from the Swedish Medical Birth Registry for the years 1973-80 (10).
Wong, et al.[76]	2006	Canada	1987	2004	0.863	N.R.	all maternal deaths	N.R.	maternal death	mixed	179541	The BC Vital Statistics Agency provided data.
Wiebenga[78]	1992	Malawi	1989 and 1990		0.303	N.R.	all maternal deaths	N.R.	maternal death	tertiary and teaching hospital	1856	Records of all maternal deaths at the Chatinkha Maternity Wing of QECH in 1989 and 1990 were reviewed. In 1989 several records were missing, and the information was then obtained from death books and nursing records kept on each ward. Death files of the female medical and surgical wards were

												scanned for patients with a pregnancy reported at the time of death or during the preceding 42 days. In 1990 files were completed immediately after the patient's death and missing laboratory and other test reports collected.
Ounsa et al.[35]	2011	Sudan	2004	2010	0.452	retrospective descriptive, hospital-based study	all maternal deaths	4901 elective - 12252 emergency	maternal death	teaching hospital	17153	Maternal mortality records were reviewed.
Pagnoni et al.[110]	1990	Italy	1977	1989	0.769	retrospective study	patients with general anesthesia carried out for both elective and emergency CS	elective 40.5%, emergency 59.53%	anesthesia-related maternal mortality	teaching hospital	13217	Used case studies relating to the period of time.
Osegi et al.[136]	2020	Nigeria	2013	2017	0.527	retrospective descriptive study	All patients that delivered by caesarean section between 1st January 2013 and 31st December, 2017 in the records of the Federal Medical Centre, Yenagoa	Emergency and urgent caesarean sections constituted 81.3% of caesarean sections and 18.7% were elective caesarean sections	maternal death	tertiary hospital	1,654	Labour ward, theatre, and postnatal ward records were used to retrieve data.
Subedi et al.[135]	2019	Nepal	2018	2018	0.579	prospective comparative study	all the patients undergoing caesarean section either elective or emergency caesarean sections	399 (86.5%) were emergency and 62 (13.5%) were elective CS.	maternal death	Teaching Hospital	461	The cases were enrolled, detailed history noted in a predesigned proforma. In cases of maternal mortality, further details were taken from the records of the deceased patients.
Chama et al.[137]	2000	Nigeria	1995	1996	0.452	N.R.	patients who had either an elective or emergency caesarean	There were 174 (87´9%) emergencies with 18 (9%)	maternal death	Teaching Hospital	198	The case notes of patients who had either an elective or emergency caesarean section at the University of Maiduguri

							section	unbooked cases. All the 24 (12´1%) elective caesarean sections were booked patients.				Teaching Hospital (UMTH) Maiduguri, from January 1995 to December 1996 inclusively were retrieved and analysed
van Ham et al.[192]	1997	The Netherlands	1983	1992	0.830	retrospective study	all caesarean sections	primary elective n=718, primary acute n=859, Primary CS n=1577, Secondary CS n=1070, Emergency CS n=1929	maternal death	Teaching hospital	2647	N.R.
Benaron et al.[193]	1971	United States	1959	1963	0.860	survey	all deliveries	N.R.	maternal death	N.R.	412	Well documented records. Autopsies were performed in all cases of direct maternal death. All perinatal records and autopsy protocols were studied and abstracted.
Tomta et al.[194]	2003	Togo	2002	2002	0.428	prospective and descriptive study	All caesarean sections	In 89.6% of the cases (n = 285), it was an emergency.	early perioperative mortality	Teaching hospital	306	Data collection was carried out using a survey form, immediately after death, a detailed description of the perioperative complications and causes of death is recorded.
Drazancic[195]	2005	Croatia	1991	2003	0.720	N.R.	all deliveries	N.R.	maternal death	N.R.	62,392	death records presented to the conference or perinatal mortality in Croatia.
Semeshi et al.[196]	1970	Hungary	1964	1968	0.704	N.R.	1000 caesarean sections	N.R.	maternal mortality, neonatal mortality	Teaching hospital	1000	N.R.

Abbreviations:
N.R.=Not reported, CS= Caesarean section

Table 5: Quality assessment for 196 included studies

Author	1) Is the definition of maternal death reported? (Y/N/Unclear)	2) Are causes of death during or after caesarean section reported in at least 95% of cases? (Y/N/ Unclear)	3) Has the study included all women or a random selection of women who have undergone caesarean section? (Y/N/ Unclear)	4) Is the source of information for outcome assessment adequate? (Y/N/ Unclear)	Overall Score
Okafor et al.[122]	N	Y	Y	Y	High quality
Lilford et al.[26]	N	Y	Y	Y	High quality
Holmer et al.[128]	N	Y	Y	Y	High quality
Crichton et al.[30]	N	N	Y	Unclear	Low quality
Shorunmu et al.[62]	N	N	N	Y	Low quality
Anger et al.[73]	N	N	Y	Y	Low quality
Kim et al.[129]	N	N	Y	Y	Low quality
Harfouche et al.[32]	N	Y	Y	Y	High quality
Nolens et al.[107]	Y	Y	N	Y	High quality
Huda et al.[82]	N	Y	Y	Y	High quality
Fawole et al.[70]	N	N	Y	Y	Low quality
Ekanem et al. [56]	N	Y	N	Y	Low quality
Idoko et al.[102]	N	N	Y	Y	Low quality
McKenzie[118]	Y	N	Y	Y	High quality
Kuzma[11]	Y	Y	Y	Y	High quality
Sultan et al.[97]	N	N	N	Y	Low quality
Rutgers et al. [83]	Y	Y	Y	Y	High quality
Remy et al.[22]	Y	Y	Y	Y	High quality
Kalisa et al.[121]	N	N	N	Y	Low quality
Loh et al.[47]	Y	N	Y	Y	High quality
Andrade et al.[84]	N	Y	Y	Y	High quality
Chattopadhyay et al.[98]	N	Y	Y	Unclear	Low quality
Krone et al.[4]	N	Y	Y	Unclear	Low quality
Zahran et al.[17]	Y	N	Y	Y	High quality
Aboyeji et al.[90]	Y	N	Y	Y	High quality
Rasul et al.[71]	Y	Y	Y	Unclear	High quality
Muylder[125]	N	Y	Y	Y	High quality
Rojas et al.[27]	N	Y	Y	Y	High quality
Campbell[9]	Y	Y	Y	Y	High quality
Kamilya et al.[114]	N	Y	Y	Y	High quality

Schuitemaker et al.[109]	N	Y	Y	Y	High quality
Kallianidis et al.[3]	N	Y	Y	Y	High quality
Anaya-Prado et al.[12]	N	N	Y	Y	Low quality
Oladapo et al.[115]	N	Y	N	Y	Low quality
Armon[86]	Y	Y	Y	N	High quality
Ozumba et al.[117]	N	Y	Y	Unclear	Low quality
Clark et al.[124]	N	N	Y	Y	Low quality
Gebhardt et al.[80]	N	Y	Y	Y	High quality
Gessessew[59]	N	N	Y	Y	Low quality
Briand et al.[105]	Y	Y	N	Y	High quality
Wirakusumah[54]	Y	Y	Y	Y	High quality
Bishop et al.[48]	N	N	Y	Y	Low quality
Chi et al.[19]	Y	Y	Y	Y	High quality
Petitti et al.[40]	N	N	Y	Y	Low quality
Buowari et al.[25]	N	N	Y	Y	Low quality
Utuk et al.[14]	N	N	Y	Y	Low quality
Nyamtema et al.[37]	N	Y	Y	Y	High quality
Mukherji et al.[69]	N	Y	Y	Y	High quality
Igberase et al.[77]	N	Y	Y	Y	High quality
Tsen et al.[123]	N	Y	Y	Y	High quality
Palanisamy et al.[88]	N	Y	N	Y	Low quality
Enohumah et al.[2]	Y	Y	Y	Y	High quality
Nwobodo et al.[108]	N	N	Y	Y	Low quality
Swende et al.[104]	N	Y	Y	Y	High quality
Zongo et al.[100]	N	Y	Y	Y	High quality
Talebi Doluee et al.[93]	N	N	Y	Y	Low quality
Löfgren et al.[60]	Y	Y	Y	Y	High quality
Maaløe et al.[29]	N	Y	N	Y	Low quality
Andersgaard et al.[99]	Y	Y	Y	Y	High quality
Rippmann[91]	N	Y	Y	Unclear	Low quality
Hou et al.[65]	N	N	Y	Y	Low quality
Bloom et al.[5]	N	N	Y	Y	Low quality
Ojo et al.[89]	N	N	Y	Y	Low quality

Gundumure[52]	N	Y	Y	Y	High quality
Engin-Üstün et al.[92]	N	N	Y	Y	Low quality
Sachs et al.[101]	N	Y	Y	Y	High quality
Longombe et al.[119]	N	N	Y	Unclear	Low quality
Cisse et al.[75]	N	N	Y	Y	Low quality
Evrard et al.[64]	N	Y	Y	Y	High quality
de la Fuente et al.[61]	N	N	Y	Unclear	Low quality
Maswime et al.[38]	Y	Y	Y	Y	High quality
Kilsztajn et al.[1]	N	N	Y	Y	Low quality
Amirikia et al.[112]	N	Y	Y	Y	High quality
Bolaji et al.[10]	N	Y	Y	Y	High quality
Fenton et al.[127]	Y	N	Y	Y	High quality
Ikeako et al.[63]	N	Y	N	Y	Low quality
Tadesse et al.[31]	N	Y	Y	Y	High quality
Okonta et al.[43]	N	Y	Y	Y	High quality
Mekbib et al.[6]	N	Y	Y	Y	High quality
Ezechi et al.[85]	N	Y	Y	Y	High quality
Daniel et al.[74]	N	Y	N	Y	Low quality
Bukar et al.[44]	N	Y	Y	Y	High quality
Njokanma et al.[79]	N	Y	N	Y	Low quality
Etuk et al.[94]	N	Y	N	Y	Low quality
Ibekwe et al.[36]	N	N	Y	Y	Low quality
Ali[24]	N	N	Y	Y	Low quality
Imarengiaye et al.[96]	N	N	N	Y	Low quality
Greenhill[57]	N	Y	Y	Unclear	Low quality
Onoh et al.[41]	Y	Y	Y	Y	High quality
Ugwu et al.[95]	N	Y	Y	Y	High quality
Aisien et al.[113]	N	N	Y	Y	Low quality
Oyewumi[49]	N	Y	Y	Y	High quality
Okezie et al.[103]	N	Y	Y	Y	High quality
Raphael et al.[33]	N	Y	Y	Y	High quality
Ijaiya et al.[46]	N	Y	Y	Y	High quality
Krause et al.[58]	N	Y	Y	Unclear	Low quality
Alegre Villariz et al.[72]	N	Y	Y	Unclear	Low quality

Kinenkinda et al.[21]	N	N	Y	Y	Low quality
Muziarelli et al.[68]	N	Y	Y	Y	High quality
González et al.[66]	N	Y	Y	Y	High quality
Pekhlivanov[53]	N	Y	Y	Y	High quality
Poradovsky et al.[126]	N	N	Y	Unclear	Low quality
Imbert et al.[42]	N	Y	N	Y	Low quality
Picaud et al.[106]	N	Y	Y	Y	High quality
Szczepanski et al.[116]	N	Y	Y	Unclear	Low quality
Carazzone et al.[34]	N	Y	Y	Y	High quality
Georgiades et al.[67]	N	Y	Y	Y	High quality
Chavez Azuela et al.[81]	N	Y	Y	Y	High quality
Kartushina[8]	N	Y	Y	Unclear	Low quality
Buttmann et al.[7]	N	Y	Y	Unclear	Low quality
Zhu et al.[15]	N	Y	Y	Y	High quality
Strobel[28]	N	N	Y	Unclear	Low quality
Warm et al.[45]	N	N	Y	Unclear	Low quality
Kambo et al.[172]	N	Y	Y	Y	High quality
Fesseha et al.[139]	N	N	Y	Y	Low quality
Ojiyi et al.[140]	N	N	Y	Y	Low quality
Landry et al.[191]	N	N	Y	Y	Low quality
Garba et al.[141]	N	Y	Y	Y	High quality
Sørbye et al.[142]	N	N	Y	Y	Low quality
Adekanle et al.[189]	N	N	Y	Y	Low quality
Dillen et al.[188]	N	Y	Y	Y	High quality
Madoue et al.[144]	N	N	Y	Y	Low quality
Akasheh et al.[39]	N	Y	Y	Y	High quality
Boogaard et al.[190]	N	Y	Y	Y	High quality
Okogbenin et al.[147]	N	N	Y	Y	Low quality
Wu et al.[154]	N	Y	Y	Y	High quality
Kandasamy et al.[157]	Y	Y	Y	Y	High quality
K. Chu et al.[156]	Y	N	Y	Y	High quality
Kor-Anantakul et	N	Y	Y	Y	High quality

al.[170]					
Diallo et al.[149]	N	N	N	Y	Low quality
Yaïch et al.[158]	N	Y	N	Y	Low quality
Cebekulu et al.[151]	N	Y	N	Y	Low quality
Ngowa et al.[168]	Y	Y	Y	Y	High quality
Diawara et al.[150]	N	N	Y	Y	Low quality
Rahlenbeck et al.[153]	N	N	Y	Y	Low quality
Teguete et al.[166]	N	Y	Y	Y	High quality
Eshiet et al.[169]	Y	Y	N	Y	High quality
Soren et al.[145]	N	N	Y	Y	Low quality
Nana et al.[143]	N	N	Y	Y	Low quality
Diarra et al.[146]	N	N	Y	Y	Low quality
Goswami et al.[167]	Y	N	N	Y	Low quality
Abebe et al.[160]	N	Y	N	Y	Low quality
Rasoarimahandry et al.[186]	N	Y	Y	Y	High quality
Nahar et al.[165]	N	Y	Y	Y	High quality
Waalewijn et al.[187]	N	N	N	Y	Low quality
Akar et al.[185]	Y	N	Y	Y	High quality
Okafor et al.[155]	Y	Y	Y	Y	High quality
Ghazi et al.[162]	N	N	Y	Y	Low quality
Nelissen et al.[164]	Y	N	Y	Y	High quality
K.M. Chu et al.[161]	N	N	Y	Y	Low quality
Sekirime et al.[178]	N	Y	N	Y	Low quality
Davies et al.[183]	Y	N	Y	Y	High quality
Chilopora et al.[179]	N	N	Y	Y	Low quality
Gonzales et al.[180]	Y	N	Y	Y	High quality
Adisso et al.[182]	N	Y	Y	Y	High quality
Richard et al.[175]	N	N	Y	Y	Low quality
Meda et al.[174]	N	N	Y	Y	Low quality
Asıcıoglu et al.[163]	N	Y	N	Y	Low quality
Basak et al.[181]	N	N	N	Y	Low quality
Gessessew et al.[176]	N	N	Y	Y	Low quality
McCord et al.[173]	N	N	N	Y	Low quality
Souza et al.[159]	N	N	Y	Y	Low quality
Pereira et al.[138]	N	Y	Y	Y	High quality

Khawaja et al.[184]	N	Y	Y	Y	High quality
Ouédraogo et al.[152]	N	Y	Y	Y	High quality
Rabiu et al.[148]	N	Y	N	Y	Low quality
Begum et al.[171]	N	Y	N	Y	Low quality
Seal et al.[177]	N	N	N	Y	Low quality
Chau-In et al.[111]	N	Y	Y	Y	High quality
Júnior et al.[55]	N	Y	N	Y	Low quality
MATERNAL AND PERINATAL MORTALITY COMMITTEE[51]	N	Y	Y	Y	High quality
Moldin et al.[20]	Y	Y	Y	Y	High quality
Rubin et al.[16]	Y	Y	Y	Y	High quality
Bruce et al.[50]	N	Y	Y	Y	High quality
Abbassi et al.[18]	Y	Y	Y	Y	High quality
Pinsker et al.[87]	N	Y	Y	Y	High quality
Beck et al.[13]	N	N	Y	Y	Low quality
Saving Mothers 2017[133]	N	N	Y	Y	Low quality
Slaytor et al.[130]	Y	Y	N	Y	High quality
NCCEMD[131]	N	Y	Y	Y	High quality
NCCEMD[132]	Y	N	Y	Y	High quality
Munjanja[134]	Y	N	Y	Y	High quality
Maswime et al.[23]	N	Y	Y	Y	High quality
Högberg et al.[120]	N	N	Y	Y	Low quality
Wong, et al.[76]	Y	Y	Y	Y	High quality
Wiebenga[78]	Y	Y	Y	Y	High quality
Ounsa et al.[35]	N	Y	Y	Y	High quality
Pagnoni et al.[110]	N	Y	N	Y	Low quality
Osegi et al.[136]	N	N	Y	Y	Low quality
Subedi et al.[135]	N	Y	Y	Y	High quality
Chama et al.[137]	N	Y	Y	Y	High quality
van Ham et al.[192]	N	Y	Y	Y	High quality
Benaron et al.[193]	N	Y	Y	Y	High quality
Tomta et al.[194]	Y	Y	Y	Y	High quality
Drazancic[195]	N	Y	Y	Y	High quality
Semeshi et al.[196]	N	Y	Y	Unclear	Low quality

Abbreviations:
Y=Yes, N=No

Bibliography of Included Studies

1.Kilsztajn, S., Carmo, M. S. N. do, Machado, L. C. J., Lopes, E. S., & Lima, L. Z. (2007). Caesarean sections and maternal mortality in Sao Paulo. *European Journal of Obstetrics, Gynecology, and Reproductive Biology*, *132*(1), 64–69. https://doi-org.proxy1.lib.uwo.ca/10.1016/j.ejogrb.2006.06.005

2.Enohumah, K. O., Imarengiaye, C. O., K.O., E., Enohumah, K. O., & Imarengiaye, C. O. (2006). Factors associated with anaesthesia-related maternal mortality in a tertiary hospital in Nigeria. *Acta Anaesthesiologica Scandinavica*, *50*(2), 206–210. https://doi-org.proxy1.lib.uwo.ca/10.1111/j.1399-6576.2006.00945.x

3.Kallianidis, A. F., Schutte, J. M., van Roosmalen, J., van den Akker, T., & Maternal Mortality and Severe Morbidity Audit Committee of the Netherlands Society of Obstetrics and Gynecology (2018). Maternal mortality after cesarean section in the Netherlands. European journal of obstetrics, gynecology, and reproductive biology, 229, 148–152. https://doi.org/10.1016/j.ejogrb.2018.08.586

4.Krone, H. A., & Mattheus, J. (1975). Die mütterliche Mortalität beim Kaiserschnitt im Vergleich zur vaninalen Entbindung [Maternal mortality in cesarean section as compared to vaginal delivery]. *Fortschritte der Medizin*, *93*(27), 1266–1268. . Retrieved from https://www.scopus.com/inward/record.uri?eid=2-s2.0-18144447299&partnerID=40&md5=9b76667f2dbe3624e80cbde23b3c3952

5.Bloom, S. L., Spong, C. Y., Weiner, S. J., Landon, M. B., Rouse, D. J., Varner, M. W., Moawad, A. H., Caritis, S. N., Harper, M., Wapner, R. J., Sorokin, Y., Miodovnik, M., O'Sullivan, M. J., Sibai, B., Langer, O., Gabbe, S. G., & National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network (2005). Complications of anesthesia for cesarean delivery. *Obstetrics and gynecology*, *106*(2), 281–287. http://dx.doi.org/10.1097/01.AOG.0000171105.39219.55

6.Mekbib, T. A., & Teferi, B. (1994). Caesarean section and foetal outcome at Yekatit 12 Hospital, Addis Abeba, Ethiopia, 1987-1992. *Ethiopian Medical Journal*, *32*(3), 173–179. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med3&NEWS=N&AN=7957129

7.Buttmann, W., & Neumann-Redlin, E. (1973). [Caesarean section and perinatal mortality in small city hospital (author's transl)]. *Geburtshilfe Frauenheilkd.*, *33*(11), 882–885. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med1&NEWS=N&AN=4203465

8.Kartushina, L. M. (1972). [Causes of maternal mortality associated with Cesarean section]. *Pediatr Akus Ginekol.*, *5*, 45–47. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med1&NEWS=N&AN=4658820

9.Campbell, G. R. (1974). Maternal mortality at Goroka Base Hospital. *Papua and New Guinea Medical Journal*, *17*(4), 335–341.Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed2&NEWS=N&AN=6511060

10.Bolaji, I. I., & Meehan, F. P. (1993). Caesarean section survey in Galway--1973 through 1987. *European Journal of Obstetrics, Gynecology, and Reproductive Biology*, *48*(1), 1–8. https://doi-org.proxy1.lib.uwo.ca/10.1016/0028-2243(93)90045-e
11.Kuzma, T. (2017). Caesarean Sections in a National Referral Hospital in Addis Ababa, Ethiopia: Trends, Predictors and Outcomes. *Journal of Obstetrics and Gynaecology Canada*, *39*(5), 394.
12.Anaya-Prado, R., Madrigal-Flores, S., Reveles-Vázquez, J. A., Ramírez-Barba, E. J., Frías-Terrones, G., Godínez-Rubí, J. M. (2008). Maternal morbidity associated with cesarean section. *Cirugia y Cirujanos*, *76*(6), 467–472. . Retrieved from https://www.scopus.com/inward/record.uri?eid=2-s2.0-77956293951&partnerID=40&md5=70c19f5dc227496680851c09d3c9dd37
13.Beck, A., & Vutuc, C. (1984). Die Mortalität und Letalität der Sectio caesarea [Mortality and fatality in cesarean section]. *Geburtshilfe und Frauenheilkunde*, *44*(7), 421–424. https://doi-org.proxy1.lib.uwo.ca/10.1055/s-2008-1036689
14.NN Utuk, AM Abasiattal, AJ Umolyoho, E. U. (2010). Indications and Trends of Caesarean Section at a Tertiary Hospital in South-south Nigeria. *Nigerian Hospital Practice*, *5*(5), 64-67.
15.Zhu, L., Zhou, B., & Qin, M. (2000). [Analysis on maternal deaths of cesarean section in Shanghai]. *Zhonghua fu chan ke za zhi*, *35*(3), 153–156. https://doi.org/10.1017/CBO9781107415324.004
16.Rubin, G. L., Peterson, H. B., Rochat, R. W., McCarthy, B. J., & Terry, J. S. (1981). Maternal death after cesarean section in Georgia. *American journal of obstetrics and gynecology*, *139*(6), 681–685. https://doi-org.proxy1.lib.uwo.ca/10.1016/0002-9378(81)90485-3
17.Zahran, K. M., Fadel, K. A., Ahmed, S. M., & El-Gazzar, A. F. (2017). Maternal mortality in an academic institution in Upper Egypt. *Journal of obstetrics and gynaecology : the journal of the Institute of Obstetrics and Gynaecology*, *37*(3), 315–319. https://dx.doi.org/10.1080/01443615.2016.1242559
18.Abbassi, H., Aboulfalah, A., Morsad, F., Matar, N., Himmi, A., & Mansouri, A. E. (2000). Complications maternelles des césariennes: analyse rétrospective de 3,231 interventions à la maternité universitaire de Casablanca, Maroc [Maternal complications of cesarean section: retrospective analysis of 3,231 interventions at the Casablanca University Hospital, Morocco]. *Sante (Montrouge, France)*, *10*(6), 419–423. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med4&NEWS=N&AN=11226939
19.Chi, I. C., Whatley, A., Wilkens, L., & Potts, M. (1986). In-hospital maternal mortality risk by cesarean and vaginal deliveries in two less developed countries--a descriptive study. *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics*, *24*(2), 121–131. http://dx.doi.org/10.1016/0020-7292%2886%2990006-8

20.Moldin, P., Hokegard, K. H., Nielsen, T. F.(1984). Cesarean section and maternal mortality in Sweden 1973-1979. *Acta Obstetricia et Gynecologica Scandinavica*, *63*(1), 7–11. https://doi-org.proxy1.lib.uwo.ca/10.3109/00016348409156266
21.Kinenkinda, X., Mukuku, O., Chenge, F., Kakudji, P., Banzulu, P., Kakoma, J. B., & Kizonde, J. (2017). Césarienne à Lubumbashi, République Démocratique du Congo II: facteurs de risque de mortalité maternelle et périnatale [Risk factors for maternal and perinatal mortality among women undergoing cesarean section in Lubumbashi, Democratic Republic of Congo II]. *The Pan African medical journal*, *26*, 208. https://dx.doi.org/10.11604/pamj.2017.26.208.12148
22.Remy, N., Jaluvka, V., & Weitzel, H. K. (1993). Mortalität und Letalität nach Schnittentbindung in West-Berlin 1975 bis 1989 [Mortality and fatalities after cesarean section in West Berlin 1975 to 1989]. *Zentralblatt fur Gynakologie*, *115*(1), 7–12. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med3&NEWS=N&AN=8438632
23.Maswime, T.S., & Buchmann, E.J. (2016). Inequities in resources and preparedness for surgical complications of caesarean section in southern gauteng hospitals. *South African Journal of Obstetrics and Gynaecology*, *22*(1), 21–24. https://doi.org/10.7196/SAJOG.2016.v22i1.1039
24.Ali Y. (1995). Analysis of caesarean delivery in Jimma Hospital, south-western Ethiopia. *East African medical journal*, *72*(1), 60–63. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed5&NEWS=N&AN=125079507
25.Buowari, Y. D. (2012). Indications for Caesarean Section at a Nigerian District Hospital. *Nigerian Health Journal, 12*(2), 43-46.
26.Lilford, R. J., van Coeverden de Groot, H. A., Moore, P. J., & Bingham, P. (1990). The relative risks of caesarean section (intrapartum and elective) and vaginal delivery: a detailed analysis to exclude the effects of medical disorders and other acute pre-existing physiological disturbances. *British Journal of Obstetrics and Gynaecology*, *97*(10), 883–892. https://doi-org.proxy1.lib.uwo.ca/10.1111/j.1471-0528.1990.tb02442.x
27.Rojas, L., Ramirez, R., & Cantillo, J. (1974). Mortalidad materna en el instituto materno infantil de Bogota, Colombia [Maternal mortality at the Mother and Child Institute, Bogota, Colombia]. *Revista Colombiana de Obstetricia y Ginecologia*, *25*(2), 127–149. Retrieved from https://www.scopus.com/inward/record.uri?eid=2-s2.0-0016346194&partnerID=40&md5=e1db4df92479b4ce65c4b11c1ca6da61
28.Strobel E. (1967). Abdominale Schnittentbindung und Geburtshilfliche Ergebnisse [Abdominal surgical delivery and obstetrical results]. *Geburtshilfe und Frauenheilkunde*, *27*(9), 859–868. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med1&NEWS=N&AN=5590982

29.Maaløe, N., Bygbjerg, I. C., Onesmo, R., Secher, N. J., & Sorensen, B. L. (2012). Disclosing doubtful indications for emergency cesarean sections in rural hospitals in Tanzania: a retrospective criterion-based audit. *Acta obstetricia et gynecologica Scandinavica*, *91*(9), 1069–1076. https://doi.org/10.1111/j.1600-0412.2012.01474.x
30.Crichton, D., & Knobel, J. (1973). The principles of prevention of avoidable maternal death. A study of 538 consecutive maternal deaths in the obstetric unit, King Edward 8th Hospital, Durban, 1953-1971. *South African medical journal = Suid-Afrikaanse tydskrif vir geneeskunde*, *47*(42), 2005–2010. . Retrieved from https://www.scopus.com/inward/record.uri?eid=2-s2.0-0015692939&partnerID=40&md5=01abd0aade342350d1af86edf68c7fa0
31.Tadesse, E., Adane, M., & Abiyou, M. (1996). Caesarean section deliveries at Tikur Anbessa Teaching Hospital, Ethiopia. *East African medical journal*, *73*(9), 619–622.
32.Harfouche, M., Hosseinipour, M., Kaliti, S., & Wilkinson, J. (2015). Quality Indicators and Outcomes of Emergency Caesarean Deliveries at a District-level Maternity Hospital. *African journal of reproductive health*, *19*(3), 61–67. Retrieved from https://www.scopus.com/inward/record.uri?eid=2-s2.0-0015692939&partnerID=40&md5=01abd0aade342350d1af86edf68c7fa0
33.Raphael, A. A., Muhammad, Z., & Iman, H. (2015). An audit of caesarean section in a tertiary hospital northwest Nigeria. *Tropical Journal of Obstetrics and Gynaecology*, *32*(2), 6-12.
34.Carazzone, P., Torretta, G. M., Leone, G., & Massano, A. (1978). Il taglio cesareo oggi [Cesarean section today]. *Minerva ginecologica*, *30*(5), 438–442. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med1&NEWS=N&AN=673241
35.Ounsa, M.A.A.E., & Mohamed, E. Y. (2011). Maternal Mortality in Ribat University Hospital, Khartoum, Sudan: Seven years of experience. *Sudan Journal of Medical Sciences*, *6*(4), 277-280.
36.Ibekwe, P. C., & Obuna, J. A. (2006). Appraisal of indications for Ceasarean section in Abakaliki, Nigeria. *Tropical Journal of Obstetrics and Gynaecology*, *23*(2), 150–152.
37.Nyamtema, A., Mwakatundu, N., Dominico, S., Mohamed, H., Shayo, A., Rumanyika, R., Kairuki, C., Nzabuhakwa, C., Issa, O., Lyimo, C., Kasiga, I., & van Roosmalen, J. (2016). Increasing the availability and quality of caesarean section in Tanzania. *BJOG : an international journal of obstetrics and gynaecology*, *123*(10), 1676–1682. https://doi.org/10.1111/1471-0528.14223
38.Maswime, S., & Buchmann, E. (2016). Causes and avoidable factors in maternal death due to cesarean-related hemorrhage in South Africa. *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics*, *134*(3), 320–323. https://doi.org/10.1016/j.ijgo.2016.03.013

39. Akasheh, H. F., & Amarin, V. (2000). Caesarean sections at Queen Alia Military Hospital, Jordan: a six-year review. *Eastern Mediterranean health journal = La revue de sante de la Mediterranee orientale = al-Majallah al-sihhiyah li-sharq al-mutawassit*, *6*(1), 41–45.
40. Petitti, D. B., Cefalo, R. C., Shapiro, S., & Whalley, P. (1982). In-hospital maternalmortality in the United States: time trends and relation to method of delivery. *Obstetrics and Gynecology*, *59*(1), 6–12. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med2&NEWS=N&AN=7078850
41. Onoh, R. C., Eze, J. N., Ezeonu, P. O., Lawani, L. O., Iyoke, C. A., & Nkwo, P. O. (2015). A 10-year appraisal of cesarean delivery and the associated fetal and maternal outcomes at a teaching hospital in southeast Nigeria. *International journal of women's health*, *7*, 531–538. https://doi.org/10.2147/IJWH.S81338
42. Imbert, P., Berger, F., Diallo, N. S., Cellier, C., Goumbala, M., Ka, A. S., & Petrognani, R. (2003). Pronostic maternel et pédiatrique des césariennes en urgence: etude prospective à l'Hôpital Principal de Dakar, Sénégal [Maternal and infant prognosis of emergency cesarean section: prospective study of the Principal Hospital in Dakar, Senegal]. *Medecine tropicale : revue du Corps de sante colonial*, *63*(4-5), 351–357. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med4&NEWS=N&AN=14763288
43. Okonta, P. I., Otoide, V. O., & Okogbenin, S. A. (2003). Caesarean Section at the University of Benin Teaching Hospital Revisited. *Tropical Journal of Obstetrics and Gynaecology*, *20*(1), 63-66. https://doi.org/10.4314/tjog.v20i1.14404
44. Bukar, M., Audu, B. M., & Massa, A. A. (2009). Caesarean delivery at the Federal Medical Centre Gombe: a 3-year experience. *Nigerian journal of medicine : journal of the National Association of Resident Doctors of Nigeria*, *18*(2), 179–183. https://doi-org.proxy1.lib.uwo.ca/10.4314/njm.v18i2.45060
45. Warm, R., & Felker, A. (1966). 25 Jahre Kaiserschnitt (1939 bis 1963). Versuch einer Bilanz an Hand von 2800 Fällen. 2. Untersuchungen über Mortalität und Morbidität [25 years of cesarean section (1939 to 1963). Attempted assessment based on 2,800 cases. 2. A study of mortality and morbidity]. *Zentralblatt fur Gynakologie*, *88*(29), 963–970. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med1&NEWS=N&AN=5998487
46. Ijaiya, M. A., & Aboyeji, P. A. (2001). Caesarean Delivery: The Trend Over a Ten-Year Period at Ilorin, Nigeria. *Nigerian Journal of Surgical Research, 3*(1), 11-18.
47. Loh, F. H., Arulkumaran, S., Montan, S., & Ratnam, S. S. (1994). Maternal mortality: evolving trends. *Asia-Oceania Journal of Obstetrics and Gynaecology*, *20*(3), 301–304. https://doi-org.proxy1.lib.uwo.ca/10.1111/j.1447-0756.1994.tb00474.x
48. Bishop, D., Dyer, R. A., Maswime, S., Rodseth, R. N., van Dyk, D., Kluyts, H. L., Tumukunde, J. T., Madzimbamuto, F. D., Elkhogia, A. M., Ndonga, A., Ngumi, Z., Omigbodun, A. O., Amanor-Boadu, S. D., Zoumenou, E., Basenero, A., Munlemvo, D. M., Youssouf, C., Ndayisaba, G., Antwi-Kusi, A., Gobin, V., … ASOS investigators (2019).

Maternal and neonatal outcomes after caesarean delivery in the African Surgical Outcomes Study: a 7-day prospective observational cohort study. *The Lancet. Global health*, *7*(4), e513–e522. https://doi.org/10.1016/S2214-109X(19)30036-1

49. Oyewumi, A. (2018). A clinical audit of caesarean section delivery at Helderberg District Hospital, Somerset West, South Africa.
50. Bruce, J., & Mayorga, L. (1966). Estudio crítico de las actuales indicaciones de operación CES'AREA EN Valdivia [Critical study of current indications for cesarean section in Valdivia]. *Revista chilena de obstetricia y ginecologia*, *31*(2), 72–80. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med1&NEWS=N&AN=5997537
51. Maternal and perinatal mortality committee. (1969). Caesarean section in New South Wales, 1966-1967: a mortality and morbidity study. *The Medical journal of Australia*, *1*(7), 319–323. https://doi.org/10.5694/j.1326-5377.1969.tb116960.x
52. Gundumure, G. (2002). Characteristics and determinants of caesarean section and cord prolapse at the University Teaching Hospital, Lusaka.
53. Pekhlivanov K. (1975). Maĭchinata smurtnost pri sectio caesarea [Maternal mortality in sectio caesarea]. *Akusherstvo i ginekologiia*, *14*(3), 182–185. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med2&NEWS=N&AN=7377520
54. Wirakusumah, F. F. (1995). Maternal and perinatal mortality/morbidity associated with cesarean section in Indonesia. *Journal of Obstetrics and Gynaecology (Tokyo, Japan)*, *21*(5), 475–481. https://doi-org.proxy1.lib.uwo.ca/10.1111/j.1447-0756.1995.tb01040.x
55. Machado Júnior, L. C., Sevrin, C. E., Oliveira, E., Araújo, J. C., Barbosa Carvalho, H., Washington Zamboni, J., Marcolin, M., Munhoz, W., Caruso, P., Ferreira Awada, P., Zanetti Giunta, R., Sancovski, M., & Peixoto, S. (2014). Association between mode of delivery and neonatal deaths and complications in term pregnancy: a cohort study in Brazil. *Minerva pediatrica*, *66*(2), 111–122. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med10&NEWS=N&AN=24835444
56. Ekanem, A. D., Udoma, E. J., Etuk, S. J., & Eshiet, A. I. (2008). Outcome of emergency caesarean sections in Calabar, Nigeria: Impact of the seniority of the medical team. *Journal of Obstetrics and Gynaecology : The Journal of the Institute of Obstetrics and Gynaecology*, *28*(2), 198–201. https://dx.doi.org/10.1080/01443610801912329
57. Greenhill, J. P. (1930). An analysis of 874 cervical cesarean sections performed at the Chicago lying-in hospital. *American Journal of Obstetrics and Gynecology*, *19*(5), 613–632. https://doi.org/10.1016/S0002-9378(30)90502-9
58. Krause, W., Möbius, W., Günther, M., Eichhorn, K. H., Creutzburg, P., Mönch, A., Knappe, M., & Kunath, H. (1979). Die mütterliche und kindliche Mortalität und Morbidität nach Sectio im Zeitraum von 1956--1976 an der Universitäts-

Frauenklinik Jena [The maternal and perinatal mortality and morbitity in attendance to Caesarean section in the period from 1956--1976 at the UFK-Jena (author's transl)]. *Zeitschrift fur Geburtshilfe und Perinatologie*, *183*(2), 136–147. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med1&NEWS=N&AN=442730

59. Gessessew A. (2007). Maternal complications--in a zonal hospital. *Ethiopian medical journal*, *45*(1), 47–54. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed10&NEWS=N&AN=47188454
60. Löfgren, J., Kadobera, D., Forsberg, B. C., Mulowooza, J., Wladis, A., & Nordin, P. (2015). District-level surgery in Uganda: Indications, interventions and perioperative mortality. *Surgery*, *158*(1), 7–16. https://doi.org/10.1016/j.surg.2015.03.022
61. de la Fuente, P., Hernandez-Garcia, J. M., Escalante, J. M., & Usandizaga, J. A. (1977). Cesarean operation: indications and maternal and fetal mortality. *Contributions to gynecology and obstetrics*, *3*, 135–141. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med1&NEWS=N&AN=852293
62. Shorunmu, T.O., Nathaniel, G.V., Oloyede, O.A., Adefuye, P.O., Ayodeji, A.B., & Ukweduan, I.M. & Olusegun, O.O. (2015). The impact of decision – delivery interval on maternal and fetal outcome: a three- year experience in a tertiary hospital. *Tropical Journal of Obstetrics and Gynaecology*, *32*(1), 46-54.
63. Ikeako, L. C., Nwajiaku, L., & Ezegwui, H. U. (2009). Caesarean section in a Secondary Health Hospital in Awka, Nigeria. *Nigerian Medical Journal*, *50*(3), 64.
64. Evrard, J. R., & Gold, E. M. (1977). Cesarean section and maternal mortality in Rhode Island. Incidence and risk factors, 1965-1975. *Obstetrics and gynecology*, *50*(5), 594–597. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed2&NEWS=N&AN=8223576
65. Hou, L., Hellerstein, S., Vitonis, A., Zou, L., Ruan, Y., Wang, X., & Zhang, W. (2017). Cross sectional study of mode of delivery and maternal and perinatal outcomes in mainland China. *PloS one*, *12*(2), e0171779. https://doi-org.proxy1.lib.uwo.ca/10.1371/journal.pone.0171779
66. González, H. P., de la Garza Quintanilla, G., Garnica, S. V., & Bautista Ancira, M. J. (1975). Morbilidad materna post-cesárea (análisis de 700 casos) [Post-cesarean maternal mortality (analysis of 700 cases)]. *Ginecologia y obstetricia de Mexico*, *37*(220), 93–102. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med1&NEWS=N&AN=1123162
67. Georgiades, E., & Reinold, E. (1972). Sectio caesarea an der I. Universitäts-Frauenklinik Wien. Bericht über die Jahre 1959 bis 1970 [Cesarean section in the 1. University Women's Hospital of Vienna. Report on the years 1959-1970]. *Zentralblatt fur Gynakologie*, *94*(23), 737–742. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med1&NEWS=N&AN=5078311

68.Muziarelli, A., Trentadue, R., & Di Masi, M. (1989). Studio retrospettivo sul taglio cesareo negli anni 1974-87 [Retrospective study of cesarean section in the years 1974-87]. *Minerva ginecologica*, *41*(7), 353–358. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med3&NEWS=N&AN=2608205
69.Mukherji, J., & Samaddar, J. C. (1995). How safe is caesarean section. *Journal of obstetrics and gynaecology (Tokyo, Japan)*, *21*(1), 17–21. https://doi-org.proxy1.lib.uwo.ca/10.1111/j.1447-0756.1995.tb00892.x
70.Fawole, A. O., Shah, A., Fabanwo, A. O., Adegbola, O., Adewunmi, A. A., Eniayewun, A. B., Dara, K., El-Ladan, A. M., Umezulike, A. C., Alu, F. E., Adebayo, A. A., Obaitan, F. O., Onala, O. E., Usman, Y., Sullayman, A. O., Kailani, S., & Sa'id, M. (2012). Predictors of maternal mortality in institutional deliveries in Nigeria. *African health sciences*, *12*(1), 32–40. Retrieved from http://ajol.info/index.php/ahs/article/view/75616/66153
71.Rasul, N., Rashid, M., Yousaf, F., & Sohail, R. (2016). Maternal mortality audit one year study in gynae unit 2 of services hospital Lahore. *Pakistan Journal of Medical and Health Sciences*, *10*(4), 1370–1373. Retrieved from https://www.scopus.com/inward/record.uri?eid=2-s2.0-85013158210&partnerID=40&md5=9c436482fbd1ee72e1361e84c5cc380c
72.Alegre Villariz, A., Garitano Caballero, C., Gándara Ibarra, A., & Aranguren Duo, G. (1977). Aspectos clínicos y estadísticos de la cesárea (revisión de 1.499 casos) [Statistical and clinical studies on cesarean section (review of 1,499 cases)]. *Acta obstetrica y ginecologica hispano-lusitana*, *25*(8), 459–478. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med1&NEWS=N&AN=607743
73.Anger, H., Frye, L., Burkhardt, G., Ononge, S., Durocher, J., Dabash, R., & Kayaga, J.(2018). Stillbirth, comorbidities and multicausality in maternal deaths with obstetric hemorrhage in uganda. *International Journal of Gynecology and Obstetrics*, *143*(Supplement 3), 286. /http://dx.doi.org/10.1002/ijgo.12582
74.Daniel, C. N., & Singh, S. (2016). Caesarean delivery: An experience from a tertiary institution in north western Nigeria. *Nigerian Journal of Clinical Practice*, *19*(1), 18–24. https://dx.doi.org/10.4103/1119-3077.164350
75.Cisse, C. T., Faye, E. O., de Bernis, L., Dujardin, B., & Diadhiou, F. (1998). Césariennes au Sénégal: couverture des besoins et qualité des services [Cesarean sections in Senegal: coverage of needs and quality of services]. *Sante (Montrouge, France)*, *8*(5), 369–377. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed6&NEWS=N&AN=29472558
76.Wong, A. B., & Etches, D. J. (2006). Maternal mortality in British Columbia, 1987-2004. *British Columbia Medical Journal*, *48*(2), 76–80. Retrieved from https://www.scopus.com/inward/record.uri?eid=2-s2.0-33646702339&partnerID=40&md5=db4ffc996ed7e3d0fa0cf9404981dcab
77.Igberase, G. O., Ebeigbe, P. N., & Andrew, B. O. (2009). High caesarean section rate: a ten year experience in a tertiary hospital in the Niger Delta, Nigeria. *Nigerian Journal of Clinical Practice*, *12*(3), 294–297. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med6&NEWS=N&AN=19803029

78.Wiebenga, J. E. (1992). Maternal mortality at Queen Elizabeth Central Hospital, 1989 to 1990. *Malawi Medical Journal : The Journal of Medical Association of Malawi*, *8*(1), 19–23. Retrieved from https://www.scopus.com/inward/record.uri?eid=2-s2.0-0026854756&partnerID=40&md5=dfa22b7c5045d1d12e7f5f13c9b6034d
79.Njokanma, F. O., Egri-Okwaji, M. T. C., Nwokoro, C. A., Orebamjo, T., & Okeke, G. C. E. (2002). Birth Asphyxia, Perinatal and Maternal Mortality Associated With Caesarean Section. *Tropical Journal of Obstetrics and Gynaecology*, *19*(1), 25-29. https://doi.org/10.4314/tjog.v19i1.14364
80.Gebhardt, G. S., Fawcus, S., Moodley, J., & Farina, Z. (2015). Maternal death and caesarean section in South Africa: Results from the 2011-2013 Saving Mothers Report of the National Committee for Confidential Enquiries into Maternal Deaths. *South African Medical Journal = Suid-Afrikaanse Tydskrif Vir Geneeskunde*, *105*(4), 287–291. /http://dx.doi.org/10.7196/SAMJ.9351
81.Chavez Azuela, J., Soberon Acevedo, J., & Castelazo Ayala, L. (1967). Operación cesárea y mortalidad materna. Factores predisponentes [Cesarean section and maternal mortality. Predisposing factors]. *Ginecologia y obstetricia de Mexico*, *22*(127), 163–172. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed1&NEWS=N&AN=89035909
82.Huda, F. A., Ahmed, A., Dasgupta, S. K., Jahan, M., Ferdous, J., Koblinsky, M., … Chowdhury, M. E. (2012). Profile of maternal and foetal complications during labour and delivery among women giving birth in hospitals in Matlab and Chandpur, Bangladesh. *Journal of Health, Population and Nutrition*, *30*(2), 131–142. https://doi.org/10.3329/jhpn.v30i2.11295
83.Rutgers, R., Van Eygen, L. (2008). Mortality related to caesarean section in rural Matebeleland North Province, Zimbabwe. *The Central African Journal of Medicine*, *54*(5/8), 24–28. https://doi-org.proxy1.lib.uwo.ca/10.4314/cajm.v54i5-8.62623
84.Andrade, A. T. L., Guerra, M. D. O., De Andrade, G. N., Araujo, D. A. D. C. A., & De Souza, J. P. (2006). Maternal mortality: 75 years of observations in a teaching maternity hospital. *Revista Brasileira de Ginecologia e Obstetricia*, *28*(7), 380–387. https://doi.org/10.1590/S0100-72032006000700002
85.Ezechi, C.O., Nwokoro, A. C., Kalu, K. E. B., Njokanma, O. F., & Okeke, C. E. G. (2002). Caesarean Morbidity and Mortality in a Private Hospital in Lagos, Nigeria. *Tropical Journal of Obstetrics and Gynaecology*, *19*(2), 97-100.
86.Armon, P. J. (1979). Maternal deaths in the Kilimanjaro region of Tanzania. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, *73*(3), 284–288. https://doi.org/10.1016/0035-9203(79)90083-X
87.Shor Pinsker, V., Chávez Azuela, J., Castelazo, E., Rivero, E., & Karchmer, S. (1982). Mortalidad materna asociada a la operación cesárea [Maternal mortality associated with cesarean operations]. *Ginecologia y obstetricia de*

Mexico, *50*(303), 189–195. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med2&NEWS=N&AN=7182234

88. Palanisamy, A., Mitani, A. A., & Tsen, L. C. (2011). General anesthesia for cesarean delivery at a tertiary care hospital from 2000 to 2005: a retrospective analysis and 10-year update. *International Journal of Obstetric Anesthesia*, *20*(1), 10–16. https://doi.org/10.1016/j.ijoa.2010.07.002
89. Ojo, V. A., Adetoro, O. O., & Okwerekwu, F. E. O. (1988). Characteristics of maternal deaths following cesarean section in a developing country. *International Journal of Gynecology and Obstetrics*, *27*(2), 171–176. https://doi.org/10.1016/0020-7292(88)90003-3
90. Aboyeji, A. P., Ijaiya, M. A., & Fawole, A. A. (2007). Maternal mortality in a Nigerian teaching hospital - A continuing tragedy. *Tropical Doctor*, *37*(2), 83–85. https://doi.org/10.1258/004947507780609167
91. Rippmann E. T. (1965). Die mütterliche Mortalität der Jahre 1940-1963 im Frauenspital Basel [Maternal mortality of the years 1940-1963 in Frauenspital Basel]. *Gynaecologia. International monthly review of obstetrics and gynecology. Revue internationale mensuelle d'obstetrique et de gynecologie. Monatsschrift fur Geburtshilfe und Gynakologie*, *160*(2), 117–128. https://doi.org/10.1159/000303368
92. Engin-Üstün, Y., Sanisoğlu, S., Keskin, H. L., Karaahmetoğlu, S., Özcan, A., Çelen, Ş., Üstün, Y., Alkan, A., Ongun, V., & Şencan, İ. (2019). Changing trends in the Turkish maternal deaths, with a focus on direct and indirect causes. *European Journal of Obstetrics and Gynecology and Reproductive Biology*, *234*, 21–25. https://doi.org/10.1016/j.ejogrb.2018.12.031
93. Talebi Doluee, M., Zabihi, H., Rezvani, B., Zarmehri, B., Najaf Najafi, M. (2018). Downward Trend in Maternal Mortality Ratio in Khorasan Razavi Province, Iran. *Journal of Midwifery & Reproductive Health*, *6*(1), 1179–1185. https://doi.org/10.22038/jmrh.2017.9967
94. Etuk, S. J., Udoma, E. J., & Ekott, M. I. (2001). Avoidable factors in maternal mortality following caesarean section (excluding ruptured uterus) in Calabar, Nigeria. *Tropical Doctor*, *31*(2), 108–109. https://doi.org/10.1177/004947550103100221
95. Ugwu, E. O., Obioha, K. C., Okezie, O. A., & Ugwu, A. O. (2011). A five-year survey of caesarean delivery at a Nigerian tertiary hospital. *Annals of medical and health sciences research*, *1*(1), 77–84. https://doi.org/10.4103/tjog.tjog_59_17
96. Imarengiaye, C. O., Otoide, V. O., Ande, A. B., & Obiaya, M. O. (2001). Anaesthesia related complications following caesarean delivery necessitating intensive care unit admissions in a tertiary centre. *African Journal of Medicine and Medical Sciences*, *30*(3), 229–232. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed7&NEWS=N&AN=37333444

97.Sultan, E. A., Shehata, S. I., Shaarawy, S. S., & Ashry, M. H. H. (2017). Near-miss cases admitted to a maternal intensive care unit, Alexandria, Egypt. *Eastern Mediterranean Health Journal*, *23*(10), 694–702. http://dx.doi.org/10.26719/2017.23.10.694
98.Chattopadhyay, S. K., Sengupta, B. S., Chattopadhyay, C., Zaidi, Z., & Showail, H. (1983). Maternal mortality in Riyadh, Saudi Arabia. *British journal of obstetrics and gynaecology*, *90*(9), 809–814. https://doi.org/10.1111/j.1471-0528.1983.tb09320.x
99.Andersgaard, A. B., Langhoff-Roos, J., & Øian, P. (2008). Direct maternal deaths in Norway 1976-1995. *Acta obstetricia et gynecologica Scandinavica*, *87*(8), 856–861. https://doi.org/10.1080/00016340802237067
100.Zongo, A., Dumont, A., Fournier, P., Traore, M., Kouanda, S., & Sondo, B. (2015). Effect of maternal death reviews and training on maternal mortality among cesarean delivery: post-hoc analysis of a cluster-randomized controlled trial. *European journal of obstetrics, gynecology, and reproductive biology*, *185*, 174–180. https://doi.org/10.1016/j.ejogrb.2014.12.023
101.Sachs, B. P., Yeh, J., Acker, D., Driscoll, S., Brown, D. A., & Jewett, J. F. (1988). Cesarean section-related maternal mortality in Massachusetts, 1954-1985. *Obstetrics and Gynecology*, *71*(3 Pt 1), 385–388. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med3&NEWS=N&AN=3347424
102.Idoko, P., & Anyanwu, M. (2018). Outcome of caesarean section at the Edward Francis Small Teaching Hospital, Banjul The Gambia. *African Health Sciences*, *18*(1), 157–165. https://doi.org/10.4314/ahs.v18i1.20
103.Okezie, A. O., Oyefara, B., & Chigbu, C. O. (2007). A 4-year analysis of caesarean delivery in a Nigerian teaching hospital: one-quarter of babies born surgically. *Journal of Obstetrics and Gynaecology*, *27*(5), 470–474. https://doi.org/10.1080/01443610701405945
104.Swende, T. Z., Agida, E. T., & Jogo, A. A. (2007). Elective caesarean section at the Federal Medical Centre Makurdi, north central Nigeria. *Nigerian Journal of Medicine: Journal of the National Association of Resident Doctors of Nigeria*, *16*(4), 372–374. https://doi.org/10.4314/njm.v16i4.37341
105.Briand, V., Dumont, A., Abrahamowicz, M., Sow, A., Traore, M., Rozenberg, P., Watier, L., & Fournier, P. (2012). Maternal and perinatal outcomes by mode of delivery in senegal and mali: a cross-sectional epidemiological survey. *PloS one*, *7*(10), e47352. https://doi.org/10.1371/journal.pone.0047352
106.Picaud, A., Nlome-Nze, A. R., Kouvahe, V., Faye, A., & Ondo-Mve, R. (1990). Les indications de césarienne et leur évolution au Centre Hospitalier de Libreville [Indications for cesarean section and their outcome at the Hospital Center in Libreville]. *Revue francaise de gynecologie et d'obstetrique*, *85*(6), 393–398. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med3&NEWS=N&AN=2202041
107.Nolens, B., Namiiro, F., Lule, J., van den Akker, T., van Roosmalen, J., & Byamugisha, J. (2018). Prospective cohort study comparing outcomes between vacuum extraction and second-stage cesarean delivery at a Ugandan tertiary

referral hospital. *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics*, *142*(1), 28–36. https://doi.org/10.1002/ijgo.1250

108. Nwobodo, E. I., Isah, A. Y., & Panti, A. (2011). Elective caesarean section in a tertiary hospital in Sokoto, north western Nigeria. *Nigerian medical journal : journal of the Nigeria Medical Association*, *52*(4), 263–265. https://doi.org/10.4103/0300-1652.93801

109. Schuitemaker, N., van Roosmalen, J., Dekker, G., van Dongen, P., van Geijn, H., & Gravenhorst, J. B. (1997). Maternal mortality after cesarean section in The Netherlands. *Acta obstetricia et gynecologica Scandinavica*, *76*(4), 332–334. http://dx.doi.org/10.1111/j.1600-0412.1997.tb07987.x

110. Pagnoni, B., Piva, L., La Rosa, M., Rossi, R., Dindelli, M., Greco, E., & Tiengo, M. (1990). Mortalità materna nel taglio cesareo: cause anestetiche [Maternal mortality in cesarean section: anesthetic causes]. *Minerva anestesiologica*, *56*(10), 1079–1084. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed4&NEWS=N&AN=21747192

111. Chau-in, W., Hintong, T., Rodanant, O., Lekprasert, V., Punjasawadwong, Y., Charuluxananan, S., & Tanudsintum, S. (2010). Anesthesia-related complications of caesarean delivery in Thailand: 16,697 cases from the Thai Anaesthesia Incidents Study. *Journal of the Medical Association of Thailand = Chotmaihet thangphaet*, *93*(11), 1274–1283. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med7&NEWS=N&AN=21114206

112. Amirikia, H., Zarewych, B., & Evans, T. N. (1981). Caesarean section: a 15-year review of changing incidence, indications, and risks. *American Journal of Obstetrics and Gynecology*, *140*(1), 81–90. https://dx.doi.org/10.1016/0002-9378(81)90261-1

113. Aisien, A. O., Lawson, J. O., & Adebayo, A. A. (2002). A five year appraisal of caesarean section in a northern Nigeria university teaching hospital. *The Nigerian postgraduate medical journal*, *9*(3), 146–150. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed7&NEWS=N&AN=35553596

114. Kamilya, G., Seal, S. L., Mukherji, J., Bhattacharyya, S. K., & Hazra, A. (2010). Maternal mortality and cesarean delivery: an analytical observational study. *The Journal of Obstetrics and Gynaecology Research*, *36*(2), 248–253. https://dx.doi.org/10.1111/j.1447-0756.2009.01125.x

115. Oladapo, O. T., Lamina, M. A., & Sule-Odu, A. O. (2007). Maternal morbidity and mortality associated with elective Caesarean delivery at a university hospital in Nigeria. *The Australian & New Zealand journal of obstetrics & gynaecology*, *47*(2), 110–114. https://dx.doi.org/10.1111/j.1479-828X.2007.00695.x

116. Szczepanski, J., Krywko, A., Arustowicz, Z., Mierzejewski, W., & Wszelaki-Lass, E. (1975). Ciaze o wysokim ryzyku w materiale cieć cesarskich w okresie 14 lat [High-risk pregnancies in the archives of cesarean section during a 14-year period]. *Wiadomosci lekarskie (Warsaw, Poland : 1960)*, *28*(11), 929–932. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med1&NEWS=N&AN=1136456

117. Ozumba, B. C., & Anya, S. E. (2002). Maternal deaths associated with cesarean section in Enugu, Nigeria. *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics*, *76*(3), 307–309. https://doi.org/http://dx.doi.org/10.1016/S0020-7292%2801%2900501-x
118. McKenzie A. G. (1998). Operative obstetric mortality at Harare Central Hospital 1992-1994: an anaesthetic view. *International journal of obstetric anesthesia*, *7*(4), 237–241. http://dx.doi.org/10.1016/S0959-289X%2898%2980045-9
119. Longombe, A. O., Wood, P. B., & Dix, R. (1990). Cesarean section--indications and risks in rural Zaire. *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics*, *33*(3), 199–202. https://dx.doi.org/10.1016/0020-7292(90)90001-2
120. Högberg U. (1989). Maternal deaths related to cesarean section in Sweden, 1951-1980. *Acta obstetricia et gynecologica Scandinavica*, *68*(4), 351–357. http://dx.doi.org/10.3109/00016348909028671
121. Kalisa, R., Rulisa, S., van den Akker, T., & van Roosmalen, J. (2016). Maternal Near Miss and quality of care in a rural Rwandan hospital. *BMC pregnancy and childbirth*, *16*(1), 324. http://dx.doi.org/10.1186/s12884-016-1119-1
122. Okafor, U. V., Ezegwui, H. U., & Ekwazi, K. (2009). Trends of different forms of anaesthesia for caesarean section in South-eastern Nigeria. *Journal of Obstetrics and Gynaecology*, *29*(5), 392–395. http://dx.doi.org/10.1080/01443610902932390
123. Tsen, L. C., Pitner, R., & Camann, W. R. (1998). General anesthesia for cesarean section at a tertiary care hospital 1990-1995: Indications and implications. *International Journal of Obstetric Anesthesia*, *7*(3), 147–152. https://doi.org/10.1016/S0959-289X(98)80001-0
124. Clark, S. L., Belfort, M. A., Dildy, G. A., Herbst, M. A., Meyers, J. A., & Hankins, G. D. (2008). Maternal death in the 21st century: causes, prevention, and relationship to cesarean delivery. *American journal of obstetrics and gynecology*, *199*(1), 36.e1–e11. http://dx.doi.org/10.1016/j.ajog.2008.03.007
125. De Muylder X. (1990). Maternal mortality audit in a Zimbabwean province. *Archives of Gynecology and Obstetrics*, *247*(3), 131–138. http://dx.doi.org/10.1007/BF02390861
126. Poradovský, K., & Sedová, A. (1968). Materská umrtnost v súvislosti s pôrodníckymi opráciami [Maternal mortality in connection with obstetrical surgery]. *Ceskoslovenska gynekologie*, *33*(8), 602–605. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med1&NEWS=N&AN=5702985
127. Fenton, P. M., Whitty, C. J., & Reynolds, F. (2003). Caesarean section in Malawi: prospective study of early maternal and perinatal mortality. *BMJ (Clinical research ed.)*, *327*(7415), 587. https://doi.org/10.1136/bmj.327.7415.587
128. Holmer, H., Kamara, M. M., Bolkan, H. A., van Duinen, A., Conteh, S., Forna, F., Hailu, B., Hansson, S. R., Koroma, A. P., Koroma, M. M., Liljestrand, J., Lonnee, H., Sesay, S., & Hagander, L. (2019). The rate and perioperative

mortality of caesarean section in Sierra Leone. *BMJ global health*, *4*(5), e001605.https://doi.org/10.1136/bmjgh-2019-001605
129. Kim, Y. M., Tappis, H., Zainullah, P., Ansari, N., Evans, C., Bartlett, L., Zaka, N., & Zeck, W. (2012). Quality of caesarean delivery services and documentation in first-line referral facilities in Afghanistan: a chart review. *BMC pregnancy and childbirth*, *12*, 14. https://dx.doi.org/10.1186/1471-2393-12-14
130. Slaytor, E. K., King, J. F., & Sullivan, E. A. (2004). Maternal deaths in Australia, 1997-1999. *AIHW Cat. No. PER 24. Sydney: AIHW National Perinatal Statistics Unit. (Maternal Deaths Series No.1)*
131. NCCEMD. (2014). Saving Mothers 2011-2013: Sixth report on confidential enquiries into maternal deaths in South Africa, Short report. *Pretoria: Department of Health*, *35*(6), 1–365. https://doi.org/10.2337/dc14-S014
132. NCCEMD. (2012). Saving mothers 2008–2010: fifth report on the confidential enquiries into maternal deaths in South Africa. *Department of Health Republic of South Africa*, 1–365. https://doi.org/10.2337/dc14-S014
133. National committee on confidential enquiries into maternal deaths. (2017). Saving Mothers 2017: Annual Report on Confidential inquiries into maternal death in South Africa. *Department of Health RSA*, 1–97. Retrieved from http://www.health.gov.za/index.php/shortcodes/2015-03-29-10-42-47/2015-04-30-08-18-10/2015-04-30-08-24-27/category/559-saving-mothers#
134. Munjanja. (n.d.). Maternal and perinatal mortality study 2007. *Ministry of Health and Child Welfare Zimbabwe*. https://doi.org/10.1017/CBO9781107415324.004
135. Subedi, A., Shrestha, J., Adhikari, K. M., Shrestha, A., & Gurung, S. (2019). Comparison of Maternal and Perinatal Outcome in Elective and Emergency Cesarean Section in a Tertiary Care Centre. *Birat Journal of Health Sciences*, *4*(1), 616–620. https://doi.org/10.3126/bjhs.v4i1.23933
136. Osegi, N., & Makinde, O. I. (2019). Towards optimizing caesarean section: a five-year review of caesarean sections at a Southern Nigeria hospital. *International Journal of Reproduction, Contraception, Obstetrics and Gynecology*, *9*(1), 205. https://doi.org/10.18203/2320-1770.ijrcog20196021
137. Chama, C. M., El-Nafaty, A. U., & Idrisa, A. (2000). Caesarean morbidity and mortality at Maiduguri, Nigeria. *Journal of Obstetrics and Gynaecology*, *20*(1), 45–48. https://doi.org/10.1080/01443610063453
138. Pereira, C., Bugalho, A., Bergström, S., Vaz, F., & Cotiro, M. (1996). A comparative study of caesarean deliveries by assistant medical officers and obstetricians in Mozambique. *BJOG: An International Journal of Obstetrics and Gynaecology*, *103*(6), 508–512. https://doi.org/10.1111/j.1471-0528.1996.tb09797.x
139. Fesseha, N., Getachew, A., Hiluf, M., Gebrehiwot, Y., & Bailey, P. (2011). A national review of cesarean delivery in Ethiopia. *International Journal of Gynecology and Obstetrics*, *115*(1), 106–111. https://doi.org/10.1016/j.ijgo.2011.07.011

140. Ojiyi, E.E., Dike, E., Anolue, F., & Chukwulebe, A.E. (2012). Appraisal Of Caesarean Section At The Imo State University Teaching Hospital, Orlu, Southeastern Nigeria. *The Internet Journal of Gynecology and Obstetrics*, *16*(2).
141. Garba, N. A.., & Muhammed, Z. (2011). Caesarean Morbidity and Mortality at Aminu Kano Teaching Hospital, Kano-a Two-Year Review. *Borno Medical Journal*, *8*(1), 10-14.
142. Sørbye, I. K., Vangen, S., Oneko, O., Sundby, J., & Bergsjø, P. (2011). Caesarean section among referred and self-referred birthing women: A cohort study from a tertiary hospital, northeastern Tanzania. *BMC Pregnancy and Childbirth*, *11*. 55. https://doi.org/10.1186/1471-2393-11-55
143. Nana, P. N., Fomulu, J. N., Djenabou, A., Mbu, R. E., Tonye, R., Wandji, J. C., & Leke, R. J. I. (2011). Epidemio-Clinical Factors Associated with Caesarean Section in Two Referral Hospitals (Public/Faith-Based), Far-North Region, Cameroon. *Clinics in Mother and Child Health*, *8*, 1–5. https://doi.org/10.4303/cmch/c100602
144. Madoue, G.B., Madoue, K.B., Mahamat, H.A., Abbo, M.D., Hassan, M., & Sakine, M. (2015). Caesarean Section in the Context of Exemption Fees for Emergency Care. *Sudan Medical Journal*, 51(3), 18-23. https://doi.org/10.12816/0027114
145. Soren, R., Maitra, N., Patel, P. K., & Sheth, T. (2016 Elective Versus Emergency Caesarean Section: Maternal Complications and Neonatal Outcomes. *IOSR Journal of Nursing and Health Science*, *5*(5), 1-4. https://doi.org/10.9790/1959-0505080104
146. Diarra, M.G. (2006). Etude de la césarienne à la maternité de l'hôpital Nianankoro FOMBA de Ségou du 1er Janvier au 31 Décembre 2005. *Facultie de medicine: UNIVERSITE DE BAMAKO.*
147. Okogbenin, S. A., & Otoide, V. O. (2004). Cardiac arrest complicating cesarean delivery in a Nigerian center. *International Journal of Gynecology and Obstetrics*, *86*(1), 50–51. https://doi.org/10.1016/j.ijgo.2004.04.005
148. Rabiu, K. A., Adewunmi, A. A., Akinola, O. I., Eti, A. E., & Tayo, A. O. (2011). Comparison of maternal and neonatal outcomes following caesarean section in second versus first stage of labour in a Tertiary Hospital in Nigeria. *The Nigerian Postgraduate Medical Journal*, *18*(3), 165–171.
149. Diallo, F. B., Diallo, M. S., Bangoura, S., Diallo, A. B., & Camara, Y. (1998). Cesarienne= Facteur De Reduction De Morbidite Et De Mortalite Foetao-Maternelle. *Médecine d'Afrique Noire*, *45*(6). Retrieved from http://www.santetropicale.com/Resume/64501.pdf
150. Diawara, A., Sangho, H., Tangara, I., Cisse, M.O., Traore, M.N., & Konate, S. (2014). Complications post cesarienne et gratuite de la cesarienne au Mali = cas d'un centre de sante de district. *Mali Medical*, *29*(1), 40-43.
151. Cebekulu, L., & Buchmann, E. J. (2006). Complications associated with cesarean section in the second stage of labor. *International Journal of Gynecology and Obstetrics*, *95*(2), 110–114. https://doi.org/10.1016/j.ijgo.2006.06.026

152. Ouédraogo, C. M., Ouédraogo, A., Ouattara, A., & Lankoandé, J. (2015). La pratique de la césarienne dans un hôpital de district à Ouagadougou Aspects épidémiologiques, cliniques et pronostiques à propos de 3 381 cas. *Medecine et Sante Tropicales*, *25*(2), 194–199. https://doi.org/10.1684/mst.2015.0443
153. Rahlenbeck, S., & Hakizimana, C. (2002). Deliveries at a district hospital in Rwanda, 1997-2000. *International Journal of Gynecology and Obstetrics*, *76*(3), 325–328. https://doi.org/10.1016/S0020-7292(01)00564-1
154. Wu, W. L. (2000). Cesarean delivery in Shantou, China: A retrospective analysis of 1922 women. *Birth*, *27*(2), 86–90. https://doi.org/10.1046/j.1523-536x.2000.00086.x
155. Okafor, U., Ezegwui, H. (2008). Maternal Deaths During Caesarean Delivery In A Developing Country-Perspective From Nigeria. *The Internet Journal of Third World Medicine*, *8*(1)
156. Chu, K., Cortier, H., Maldonado, F., Mashant, T., Ford, N., & Trelles, M. (2012). Cesarean Section Rates and Indications in Sub-Saharan Africa: A Multi-Country Study from Medecins sans Frontieres. *PLoS ONE*, *7*(9), e44484. https://doi.org/10.1371/journal.pone.0044484
157. Kandasamy, T., Merialdi, M., Guidotti, R. J., Betrán, A. P., Harris-Requejo, J., Hakimi, F., Van Look, P. F., & Kakar, F. (2009). Cesarean delivery surveillance system at a maternity hospital in Kabul, Afghanistan. *International Journal of Gynecology and Obstetrics*, *104*(1), 14–17. https://doi.org/10.1016/j.ijgo.2008.08.024
158. Yaïch, P., Ouattara, A., Koffi, N., Chiaké, A., Sanou, J., Itéké, F., & Kane, M. (2012). Césariennes en urgence : pronostic materno-foetal au CHU de Cocody D'Abidjan. *Revue Africaine d'Anesthésiologie et de Médecine d'Urgence*, *17*(1).
159. Souza, J. P., Gülmezoglu, A. M., Vogel, J., Carroli, G., Lumbiganon, P., Qureshi, Z., … Say, L. (2013). Moving beyond essential interventions for reduction of maternal mortality (the WHO Multicountry Survey on Maternal and Newborn Health): A cross-sectional study. *The Lancet*, *381*(9879), 1747–1755. https://doi.org/10.1016/S0140-6736(13)60686-8
160. Abebe, F. E., Gebeyehu, A. W., Kidane, A. N., & Eyassu, G. A. (2016). Factors leading to cesarean section delivery at Felegehiwot referral hospital, Northwest Ethiopia: A retrospective record review. *Reproductive Health*, *13*(1), 6. https://doi.org/10.1186/s12978-015-0114-8
161. Chu, K. M. (2010). Operative Mortality in Resource-Limited Settings. *Archives of Surgery*, *145*(8), 721-725. https://doi.org/10.1001/archsurg.2010.137
162. Ghazi, A., Karim, F., Hussain, A. M., Ali, T., & Jabbar, S. (2012). Maternal morbidity in emergency versus elective caesarean section at a tertiary care hospital. *Journal of Ayub Medical College, Abbottabad : JAMC*, *24*(1), 10–13.
163. Asicioglu, O., Güngördük, K., Yildirim, G., Asicioglu, B. B., Güngördük, C. O., Ark, C., Günay, T., & Yenigül, N. (2014). Second-stage vs first-stage caesarean delivery: Comparison of maternal and perinatal outcomes. *Journal of Obstetrics and Gynaecology*, *34*(7), 598–604. https://doi.org/10.3109/01443615.2014.920790

164.Nelissen, E. J., Mduma, E., Ersdal, H. L., Evjen-Olsen, B., van Roosmalen, J. J. M., & Stekelenburg, J. (2013). Maternal near miss and mortality in a rural referral hospital in northern Tanzania: A cross-sectional study. *BMC Pregnancy and Childbirth*, *13*, 141. https://doi.org/10.1186/1471-2393-13-141
165.Nahar, K. (2009). Indications of Caesarean Section - Study of 100 cases in Mymensingh Medical College Hospital. *Journal of Shaheed Suhrawardy Medical College*, *1*(1), 6–10. https://doi.org/10.3329/jssmc.v1i1.12167
166.Teguete, I., Traore, Y., Sissoko, A., Djire, M.Y., Thera, A., Dolo, T., Mounkoro, N., Traore, M., & Dolo, A. (2012). Determining Factors of Cesarean Delivery Trends in Developing Countries: Lessons from Point G National Hospital (Bamako - Mali). *Cesarean Delivery, Raed Salim, IntechOpen*, 161-200. https://doi.org/10.5772/47914
167.Goswami, D., Rathore, A. M., Batra, S., Dubey, C., Tyagi, S., & Wadhwa, L. (2013). Facility-based review of 296 maternal deaths at a tertiary centre in India: Could they be prevented? *Journal of Obstetrics and Gynaecology Research*, *39*(12), 1569–1579. https://doi.org/10.1111/jog.12099
168.Ngowa, J. D., Ngassam, A., Fouogue, J. T., Metogo, J., Medou, A., & Kasia, J. M. (2015). Complications maternelles précoces de la césarienne: à propos de 460 cas dans deux hôpitaux universitaires de Yaoundé, Cameroun [Early maternal complications of cesarean section: about 460 cases in two university hospitals in Yaounde, Cameroon]. *The Pan African medical journal*, *21*, 265. https://doi.org/10.11604/pamj.2015.21.265.6967
169.Eshiet, A. I., Udoma, E. J., Ekanem, A. D., & Dada, A. (2003). Effect Of Anaesthesia On Morbidity And Mortality In Emergency Caesarean Section Patients In Calabar, Nigeria. *Nigerian Journal of Physiological Sciences*, *18*(1-2), 77-81. https://doi.org/10.4314/njps.v18i1.32624
170.Kor-Anantakul, O., Suwanrath, C., Lim, A., & Chongsuviwatwong, V. (2008). Comparing complications in intended vaginal and caesarean deliveries. *Journal of obstetrics and gynaecology : the journal of the Institute of Obstetrics and Gynaecology*, *28*(1), 64–68. https://doi.org/10.1080/01443610701812207
171.Begum, K. S., Khan, N. U., & Akter, F. (2014). Factors Affecting the Pregnancy Outcome in Patients with Previous One Caesarean Section. *Medicine Today*, *26*(1), 01–03. https://doi.org/10.3329/medtoday.v26i1.21300
172.Kambo, I., Bedi, N., Dhillon, B. S., & Saxena, N. C. (2002). A critical appraisal of cesarean section rates at teaching hospitals in India. *International Journal of Gynecology and Obstetrics*, *79*(2), 151–158. https://doi.org/10.1016/S0020-7292(02)00226-6
173.McCord, C., Mbaruku, G., Pereira, C., Nzabuhakwa, C., & Bergstrom, S. (2009). The quality of emergency obstetrical surgery by assistant medical officers in Tanzanian district hospitals. *Health Affairs*, *28*(5), w876–w885. https://doi.org/10.1377/hlthaff.28.5.w876
174.Meda, I. B., Millogo, T., Baguiya, A., Ouédraogo/Nikiema, L., Coulibaly, A., & Kouanda, S. (2016). Rate of and factors associated with indications for cesarean deliveries: Results of a national review in Burkina Faso. *International Journal of Gynecology and Obstetrics*, *135*, S51–S57. https://doi.org/10.1016/j.ijgo.2016.08.010

175.Richard, F., Ouédraogo, C., & De Brouwere, V. (2008). Quality cesarean delivery in Ouagadougou, Burkina Faso: A comprehensive approach. *International Journal of Gynecology and Obstetrics*, *103*(3), 283–290. https://doi.org/10.1016/j.ijgo.2008.08.008
176.Gessessew, A., Barnabas, G. A., Prata, N., & Weidert, K. (2011). Task shifting and sharing in Tigray, Ethiopia, to achieve comprehensive emergency obstetric care. *International Journal of Gynecology and Obstetrics*, *113*(1), 28–31. https://doi.org/10.1016/j.ijgo.2010.10.023
177.Seal, S. L., Kamilya, G., Mukherji, J., Bhattacharyya, S. K., De, A., & Hazra, A. (2010). Outcome in second- versus first-stage cesarean delivery in a teaching institution in Eastern India. *American Journal of Perinatology*, *27*(6), 507–512. https://doi.org/10.1055/s-0030-1248936
178.Sekirime, W. K., & Lule, J. C. (2009). Outcome of cesarean section in asymptomatic HIV-1 infection in Kampala, Uganda. *Journal of Obstetrics and Gynaecology Research*, *35*(4), 679–688. https://doi.org/10.1111/j.1447-0756.2008.01002.x
179.Chilopora, G., Pereira, C., Kamwendo, F., Chimbiri, A., Malunga, E., & Bergström, S. (2016). Postoperative outcome of caesarean sections and other major emergency obstetric surgery by clinical officers and medical officers in Malawi. *Malawi Medical Journal*, *28*(3), 94–98. https://doi.org/10.1186/1478-4491-5-17
180.Gonzales, G. F., Tapia, V. L., Fort, A. L., & Betran, A. P. (2013). Pregnancy outcomes associated with Cesarean deliveries in Peruvian public health facilities. *International Journal of Women's Health*, *5*(1), 637–645. https://doi.org/10.2147/IJWH.S46392
181.Basak, S., Kanungo, S., & Majhi, C. (2011). Symphysiotomy: Is it obsolete? *Journal of Obstetrics and Gynaecology Research*, *37*(7), 770–774. https://doi.org/10.1111/j.1447-0756.2010.01431.x
182.Adisso, S., Takpara, I., Teguete, I., Gbegnide, H., Chobli, M., & Alihonou, E. (2006). Pronostic maternel selon le type d'anesthésie pour la césarienne en milieu urbain au Bénin. *Fondation Genevoise pour la Formation et la Recherche Médicales.*
183.Davies, J. F., Lenglet, A., Van Wijhe, M., & Ariti, C. (2016). Perioperative mortality: Analysis of 3 years of operative data across 7 general surgical projects of Médecins Sans Frontières in Democratic Republic of Congo, Central African Republic, and South Sudan. *Surgery (United States)*, *159*(5), 1269–1278. https://doi.org/10.1016/j.surg.2015.12.022
184.Khawaja, N. P., Yousaf, T., & Tayyeb, R. (2004). Analysis of caesarean delivery at a tertiary care hospital in Pakistan. *Journal of obstetrics and gynaecology : the journal of the Institute of Obstetrics and Gynaecology*, *24*(2), 139–141. https://doi-org.proxy1.lib.uwo.ca/10.1080/01443610410001645415
185.Akar, M. E., Eyi, E. G. Y., Yilmaz, E. S., Yuksel, B., & Yilmaz, Z. (2004). Maternal deaths and their causes in Ankara, Turkey, 1982-2001. *Journal of Health, Population and Nutrition*, *22*(4), 420–428. https://doi.org/10.3329/jhpn.v22i4.292

186. Andriamady Rasoarimahandry, C. L., Andrianarivony, M. O., & Ranjalahy, R. J. (2001). Indications et pronostic de l'opération césarienne là maternitée de Befelatanana - CHU d'Antananarivo (à propos de 529 cas, durant l'année 1998). *Gynecologie Obstetrique et Fertilite*, *29*(12), 900–904. https://doi.org/10.1016/S1297-9589(01)00240-5
187. Waalewijn, B. P., van Duinen, A., Koroma, A. P., Rijken, M. J., Elhassein, M., & Bolkan, H. A. (2017). Learning Curve Characteristics for Caesarean Section Among Associate Clinicians: A Prospective Study from Sierra Leone. *World Journal of Surgery*, *41*(12), 2998–3005. https://doi.org/10.1007/s00268-017-4202-5
188. van Dillen, J., Meguid, T., Petrova, V., & van Roosmalen, J. (2007). Caesarean section in a semi-rural hospital in Northern Namibia. *BMC Pregnancy and Childbirth*, *7*, 2. https://doi.org/10.1186/1471-2393-7-2
189. Adekanle, D. A., Adeyemi, A. S., & Fasanu, A. O. (2013). Caesarean section at a tertiary institution in Southwestern Nigeria—A 6-year audit. *Open Journal of Obstetrics and Gynecology*, *3*(3), 357–361. https://doi.org/10.4236/ojog.2013.33066
190. Van Den Boogaard, W., Manzi, M., De Plecker, E., Caluwaerts, S., Nanan-N'zeth, K., Duchenne, B., Etienne, W., Juma, N., Ndelema, B., & Zachariah, R. (2016). Caesarean sections in rural Burundi: How well are mothers doing two years on? *Public Health Action*, *6*(2), 72–76. https://doi.org/10.5588/pha.15.0075
191. Landry, E., Pett, C., Fiorentino, R., Ruminjo, J., & Mattison, C. (2014). Assessing the quality of record keeping for cesarean deliveries: Results from a multicenter retrospective record review in five low-income countries. *BMC Pregnancy and Childbirth*, *14*(1), 139. https://doi.org/10.1186/1471-2393-14-139
192. van Ham, M. A., van Dongen, P. W., & Mulder, J. (1997). Maternal consequences of caesarean section. A retrospective study of intra-operative and postoperative maternal complications of caesarean section during a 10-year period. *European journal of obstetrics, gynecology, and reproductive biology*, *74*(1), 1–6. https://doi.org/10.1016/s0301-2115(97)02725-5
193. Benaron, H. W., & Tucker, B. E. (1971). The effect of obstetric management and factors beyond clinical control on maternal mortality rates at the Chicago Maternity Center from 1959 to 1963. *American journal of obstetrics and gynecology*, *110*(8), 1113–1118. https://doi.org/10.1016/0002-9378(71)90310-3
194. Tomta, K., Maman, F. O., Agbétra, N., Baeta, S., Ahouangbévi, S., & Chobli, M. (2003). Mortalité maternelle: implication anesthésique au CHU de Lomée (Togo) [Maternal deaths and anesthetics in the Lomé (Togo) University Hospital]. *Sante (Montrouge, France)*, *13*(2), 77–80.
195. Drazancic, A. (2005). Maternal mortality. *Gynaecologia et Perinatologia*, *14*(1), 7–17. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed9&NEWS=N&AN=40593029
196. Semeshi, I., Chepli, I., Khed'i, R., Fupnik, P., Shikloshi, D., Sani, L., & Sekeĭ, L. (1970). Analiz 1000 operatsiĭ kesareva secheniia [Analysis of 1000 cesarean sections]. *Akusherstvo i ginekologiia*, *46*(1), 55–57.

APPENDIX F: ELEMENTS OF DATA ANALYSIS FOR PERIOPERATIVE MATERNAL AND NEONATL MORTALITY, RESULTS OF SENSITIVITY ANALYSES FOR POMMR AND PONMR

	Number of studies	POMMR per 100,000 (95% CI)	p value for heterogeneity between sub-groups	
			By HDI	By decade
Pre-1970s	24	540.34 (370.46-739.87)		
High HDI	11	540.66 (294.59-854.23)	0.978	
Low HDI	13	545.23 (314.96-833.95)		
1970s-1980s	30	188.28 (138.83-244.41)		
High HDI	9	54.97 (37.79-75.12)	<0·00001	
Low HDI	21	388.57(238.49-571.84)		
1990s-2000s	103	627.82 (531.80-730.85)		<0·00001
High HDI	7	16.22 (7.85-27.31)	<0·00001	
Low HDI	96	774.08 (648.83-909.15)		
2010s-2020s	39	354.75 (263.00-457.88)		
High HDI	NR	NR	N/A	
Low HDI	39	354.75 (263.00-457.88)		
Type of hospital			By hospital type	
Teaching/tertiary	93	653.44 (500.69-824.02)		
Mixed	40	167.91 (123.54-218.15)		
Private	3	365.35 (163.50-634.61)		
Public	5	8.52 (0.13-25.99)	<0·00001	
District	16	992.17 (570.97-1518.27)		
Referral	10	883.68 (279.07-1759.36)		
Military	1	0.00 (0.00-286.07)		
Overall	196	443.39 (396.74-492.30)		

HDI=human development index. NR=not reported. N/A=not available.

Table 6: Sensitivity analysis for the risk of perioperative maternal mortality during or following caesarean section in low and high HDI countries with random effects model

	Number of Studies	POMMR per 100,000 (95% CI)	p value for heterogeneity between sub-groups	
			By HDI	By decade
Pre-1970s	24	84.92 (73.73-96.74)		
High HDI	11	41.78 (31.50-53.12)	<0·00001	
Low HDI	13	197.42 (169.86-226.79)		
1970s-1980s	29	26.81 (23.56-30.22)		
High HDI	9	47.72 (42.58-53.13)	0.072	
Low HDI	20	17.64 (13.70-21.95)		<0·00001
1990s-2000s	83	15.01 (12.81-17.35)		
High HDI	5	15.80 (13.62-18.13)	<0·00001	
Low HDI	78	80.16 (74.37-86.10)		
2010s-2020s	32	6.21 (5.07-7.44)		
High HDI	NR	NR	N/A	
Low HDI	32	6.21 (5.07-7.44)		
Type of hospital			By hospital type	
Teaching/tertiary	70	76.94 (66.41-88.04)		
Mixed	39	27.37 (25.86-28.90)		
Private	3	324.53 (248.90-408.78)		
Public	5	10.70 (6.43-15.80)		<0·00001
District	15	656.34 (559.20-760.44)		
Referral	8	242.04 (153.37-345.26)		
Military	1	0.00 (0.00-286.07)		
Overall	168	14.43 (13.27-15.63)		

HDI=human development index. NR=not reported. N/A=not available.

Table 7: Sensitivity analysis for the risk of perioperative maternal mortality during or following caesarean section involving studies without a specific subgroup of patients

	Number of Studies	POMMR per 100,000 (95% CI)	p value for heterogeneity between sub-groups	
			By HDI	By decade
Pre-1970s	2	340.03 (270.16-417.69)		<0·00001
High HDI	1	200.00 (96.91-412.28)	0.102	
Low HDI	1	371.43 (297.74-463.27)		
1970s-1980s	4	297.26 (188.93-427.67)		
High HDI	NR	NR	N/A	
Low HDI	4	297.26 (188.93-427.67)		
1990s-2000s	34	189.64 (168.97-211.22)		
High HDI	1	78.08 (54.37-112.11)	<0·00001	
Low HDI	33	242.43 (217.65-268.23)		
2010s-2020s	18	10.30 (1.92-23.87)		
High HDI	NR	NR	N/A	
Low HDI	18	10.30 (1.92-23.87)		
Type of hospital			By hospital type	
Teaching/tertiary	29	65.63 (42.07-92.97)	<0·00001	
Mixed	7	255.64 (228.32-284.30)		
Private	3	324.53 (248.90-408.78)		
Public	1	37.09 (25.32-54.35)		
District	9	606.96 (502.09-720.89)		
Referral	5	495.62 (382.07-620.45)		
Military	NR	NR		
Overall	58	142.51 (127.54-158.10)		

HDI=human development index. NR=not reported. N/A=not available.

Table 8: Sensitivity analysis for the risk of perioperative maternal mortality during or following caesarean section for studies with prospective data collection

	Number of Studies	POMMR per 100,000 (95% CI)	p value for heterogeneity between sub-groups	
			By HDI	By decade
Pre-1970s	12	34.42 (25.59-44.20)		<0·00001
High HDI	5	25.27 (16.66-35.16)	0.00014	
Low HDI	7	78.80 (52.01-109.80)		
1970s-1980s	24	25.04 (21.87-28.37)		
High HDI	8	47.24 (42.10-52.65)	0.0084	
Low HDI	16	14.37 (10.74-18.39)		
1990s-2000s	69	13.67 (11.53-15.94)		
High HDI	6	13.40 (11.33-15.63)	<0·00001	
Low HDI	63	72.72 (66.96 -78.65)		
2010s-2020s	20	23.26 (21.42-25.16)		
High HDI	NR	NR	N/A	
Low HDI	20	23.26 (21.42-25.16)		
Type of hospital			By hospital type	
Teaching/tertiary	61	64.87 (55.29-75.03)	<0·00001	
Mixed	32	26.09 (24.62-27.60)		
Public	3	5.43 (2.10-10.01)		
District	7	1009.79 (785.03-1260.06)		
Referral	4	1427.65 (1087.24-1810.67)		
Military	1	0.00 (0.00-286.07)		
Overall	125	16.71 (15.49-17.96)		

HDI=human development index. NR=not reported. N/A=not available.

Table 9: Sensitivity analysis for the risk of perioperative maternal mortality during or following caesarean section for studies with retrospective data collection

	Number of Studies	POMMR per 100,000 (95% CI)	p value for heterogeneity between sub-groups	
			By HDI	By decade
Pre-1970s	20	73.48 (62.82-84.78)		<0·00001
High HDI	7	26.10 (17.45-36.01)	<0·00001	
Low HDI	13	197.42 (169.86-226.79)		
Type of hospital				By hospital type
Teaching/tertiary	91	50.24 (41.79-59.27)		
Mixed	40	27.86 (26.35-29.39)		
Private	3	324.53 (248.90-408.78)		
Public	5	10.70 (6.43-15.80)		<0·00001
District	16	694.57 (596.78-799.05)		
Referral	10	406.60 (330.33-489.10)		
Military	1	0.00 (0.00-286.07)		
Overall	192	10.28 (9.26-11.34)		

Data for the other decades and their corresponding HDI categories are the same as the main analysis. HDI=human development index.

Table 10: Sensitivity analysis for the risk of perioperative maternal mortality during or following caesarean section involving studies after the 1960s

RESULTS OF SENSITIVITY ANALYSES FOR POMMR

	Number of studies	PONMR per 100,000 (95% CI)	p value for heterogeneity between sub-groups	
			By HDI	By decade
Pre-1970s	NR	NR		0.032
High HDI	NR	NR	N/A	
Low HDI	NR	NR		
1970s-1980s	2	1204.86 (769.73-1730.68)		
High HDI	NR	NR	N/A	
Low HDI	2	1204.86 (769.73-1730.68)		
1990s-2000s	14	1610.32 (1446.01-1782.85)		
High HDI	NR	NR	N/A	
Low HDI	14	1610.32 (1446.01-1782.85)		
2010s-2020s	3	2327.67 (1581.54-3204.01)		
High HDI	NR	NR	N/A	
Low HDI	3	2327.67 (1581.54-3204.01)		
Types of hospitals			By hospital type	
Teaching/tertiary	11	1951.34 (1761.34-2150.54)	<0·00001	
Mixed	1	3466.93 (1908.42-5431.99)		
Public	1	510.20 (140.03-1840.93)		
District	1	147.89 (63.18-345.74)		
Referral	2	2333.06 (1472.00-3374.84)		
Overall	19	1605.67 (1452.40-1766.07)		

HDI=human development index. NR=not reported. N/A=not available.

Table 11: Sensitivity analysis for the risk of perioperative neonatal mortality following caesarean section for studies with retrospective data collection

	Number of studies	PONMR per 100,000 (95% CI)	p value for heterogeneity between sub-groups	
			By HDI	By decade
Pre-1970s	1	2857.14 (2354.78-3462.87)		<0·00001
High HDI	1	2857.14 (2354.78-3462.87)	N/A	
Low HDI	NR	NR		
1970s-1980s	NR	NR		
High HDI	NR	NR	N/A	
Low HDI	NR	NR		
1990s-2000s	15	699.71 (645.15-756.09)		
High HDI	NR	NR	N/A	
Low HDI	15	699.71 (645.15-756.09)		
2010s-2020s	3	4737.93 (4252.02-5248.59)		
High HDI	NR	NR	N/A	
Low HDI	3	4737.93 (4252.02-5248.59)		
Type of hospital			By hospital type	
Teaching/tertiary	8	258.29 (156.41-378.25)	<0·00001	
Mixed	4	1178.36 (1103.15-1255.89)		
Private	1	1403.51 (865.73-2267.69)		
District	2	5326.82 (4595.85-6108.14)		
Referral	2	455.41 (359.13-562.87)		
Overall	19	923.31 (865.41-982.84)		

HDI=human development index. NR=not reported. N/A=not available.

Table 12: Sensitivity analysis for the risk of perioperative neonatal mortality following caesarean section for studies with prospective data collection

	Number of studies	Events	PONMR per 100,000 (95% CI)	p value for heterogeneity between sub-groups	
				By HDI	By decade
Pre-1970s	3	157/5271	2929.21 (981.90-5846.84)		0.626
High HDI	1	100/3500	2857.14 (2354.78-3462.87)	0.738	
Low HDI	2	57/1771	2656.04 (1950.83-3463.90)		
1970s-1980s	3	58/24564	1154.34 (0.00 -4820.07)		
High HDI	NR	NR	NR	N/A	
Low HDI	3	58/24564	1154.34 (0.00 -4820.07)		
1990s-2000s	29	1521/129966	1989.36 (1434.43-2626.25)		
High HDI	NR	NR	NR	N/A	
Low HDI	29	1521/129966	1989.36 (1434.43-2626.25)		
2010s-2020s	8	529/68357	3532.85 (871.55-7817.42)		
High HDI	NR	NR	NR	N/A	
Low HDI	8	529/68357	3532.85 (871.55-7817.42)		
Type of hospital				By hospital type	
Teaching/tertiary	21	690/93480	2431.27 (1470.96-3609.40)	0.084	
Mixed	6	1071/81542	2613.09 (1198.48-4520.26)		
Private	1	16/1140	1403.51 (865.73-2267.69)		
Public	1	2/392	510.20 (140.03-1840.93)		
District	4	263/7301	4351.92 (309.58-12570.43)		
Referral	4	124/18034	1219.60 (243.89-2859.25)		
Overall	43	2265/228158	2310.37 (1729.35-2968.78)		

HDI=human development index. NR=not reported. N/A=not available.

Table 13: Sensitivity analysis for the risk of perioperative neonatal mortality during or following caesarean section in low and high HDI countries with random effects model

META-REGRESSIONS FOR POMMR

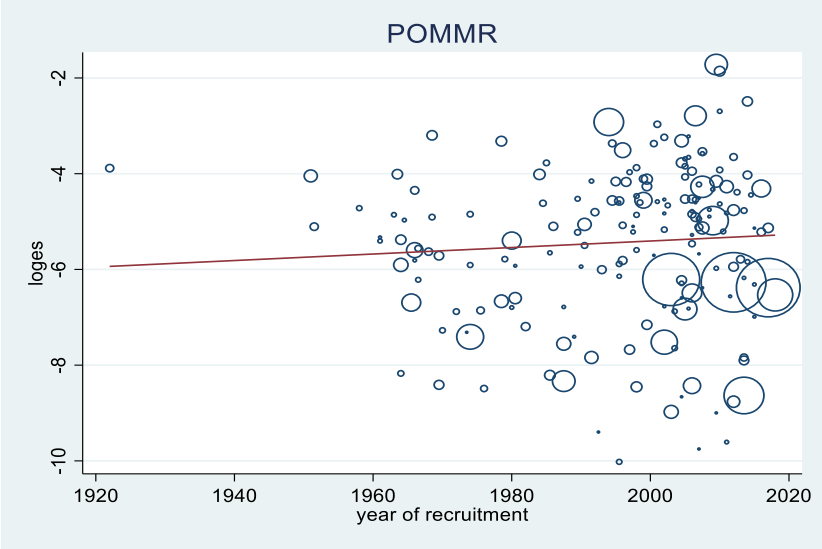


Figure 2: Meta-regression for risk of maternal mortality by year. (slope 0.0068, 95%CI -0.0075 to 0.021; p=0.351).

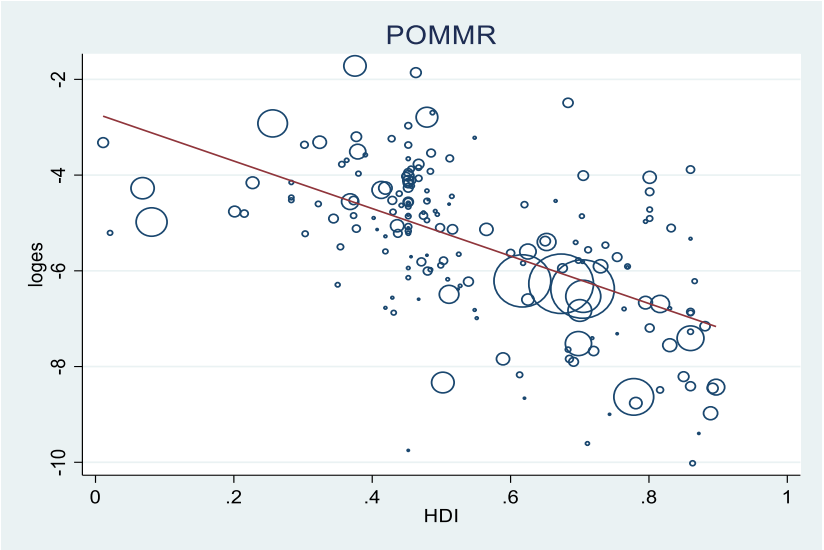


Figure 3: Meta-regression for risk of maternal mortality by HDI. (slope -4.96, 95%CI -5.99 to -3.94; p<0.00001).

META-REGRESSIONS FOR PONMR

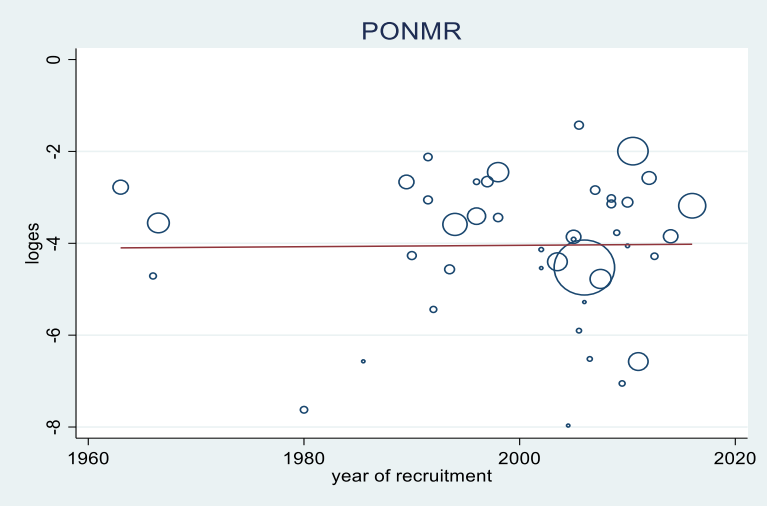


Figure 4: Meta-regression for risk of neonatal mortality by year. (slope 0.0015, 95%CI -0.036 to 0.039; p=0.937).

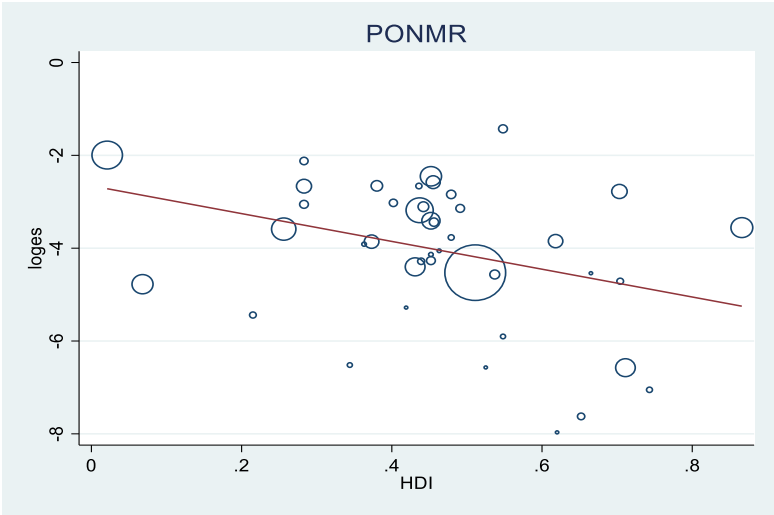
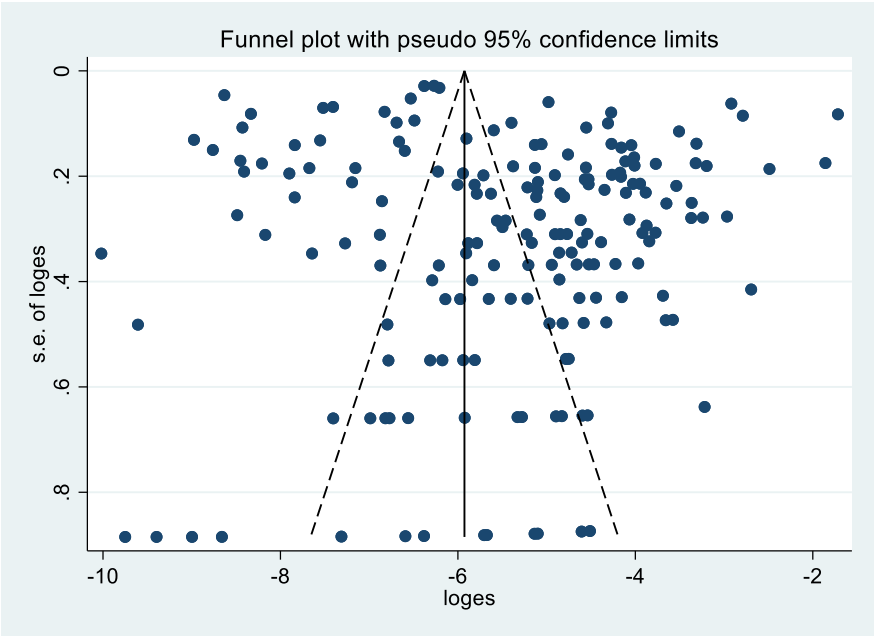


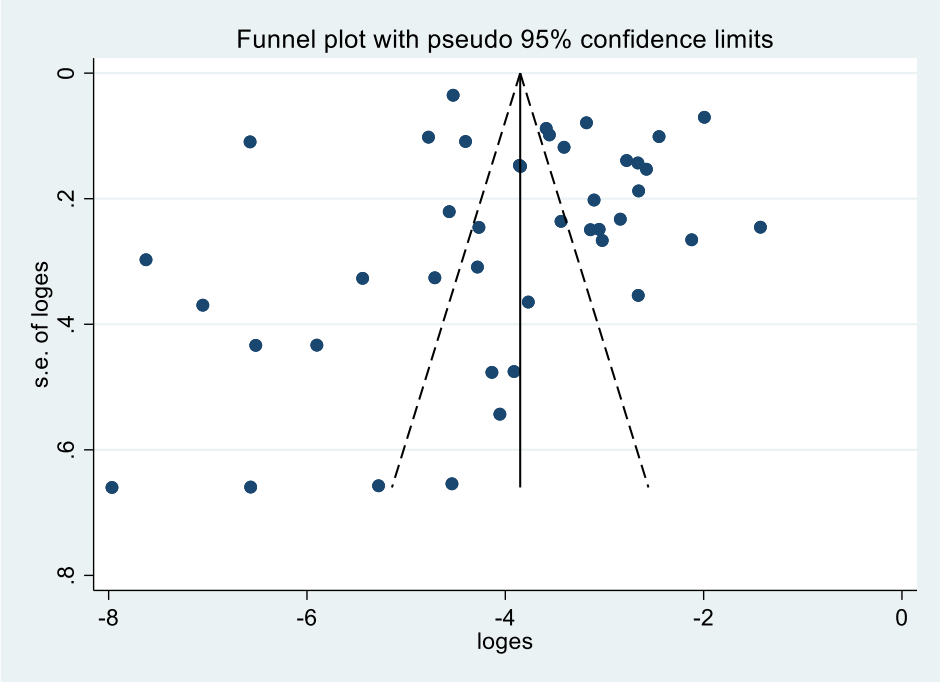
Figure 5: Meta-regression for risk of neonatal mortality by HDI. (slope -2.99, 95%CI -5.67 to 0-.317; p=0.029).

FUNNEL PLOTS AND EGGER'S TEST OUTPUTS FOR POMMR AND PONMR



```
Egger's test for small-study effects:
Regress standard normal deviate of intervention
effect estimate against its standard error
Number of studies =  180                              Root MSE      =    10.9
------------------------------------------------------------------------------
     Std_Eff |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
       slope |  -6.275655   .1598629   -39.26   0.000    -6.591125   -5.960185
        bias |   3.555182   1.142764     3.11   0.002     1.300073     5.81029
------------------------------------------------------------------------------
Test of H0: no small-study effects          P = 0.002
```

Figure 6: Publication bias for POMMR




```
Egger's test for small-study effects:
Regress standard normal deviate of intervention
effect estimate against its standard error
Number of studies =  42                                 Root MSE      =   8.574
------------------------------------------------------------------------------
     Std_Eff |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
       slope |  -3.902888   .2751817   -14.18   0.000    -4.459051   -3.346725
        bias |   .5207273   2.066654     0.25   0.802    -3.656135     4.69759
```

```
------------------------------------------------------------------------------
Test of H0: no small-study effects          P = 0.802
```

Figure 7: Publication bias for PONMR

APPENDIX G: CAUSE OF DEATH STUDY CHARACTERISTICS, QUALITY ASSESSMENT AND BIBLIOGRAPHY OF INCLUDED STUDIES

Table 14: Characteristics of 131 studies that reported on causes of caesarean-related deaths

Author	Year of publication	Country	Start year	End year	HDI	Type of study	Population	Urgency (n)	Primary outcomes	Total caesarean sections	Source of Data	Method of detection for Cause of death
Okafor et al.[90]	2009	Nigeria	2003	2006	0.467	Retrospective survey	patients that had caesarean delivery	elective n=319, emergency n=410	maternal mortality	729	The hospital records case notes, labour ward and theatre records of patients that had caesarean delivery at the University of Nigeria Teaching hospital (UNTH).	
Lilford et al.[19]	1990	South Africa	1975	1986	0.625	Retrospective review	108 deaths from each method of delivery	emergency n=23045 CS, elective n= 8524 CS	maternal mortality	31564	case-notes of women who died after delivery.	Autopsies were performed.
Holmer et al.[95]	2019	Sierra Leone	2016	2016	0.413	retrospective study	all caesarean sections and all reported in-facility maternal deaths	N.R.	In-facility maternal mortality	7357	All Sierra Leonean health facilities performing caesarean sections in 2016 were visited and numbers of caesarean sections, deliveries and maternal deaths reported in facility logbooks were recorded. The Sierra Leone MoHS provided access to the MDSR database, containing patient-level information on all maternal deaths notified through its system in 2016. Every maternal death after caesarean section was validated through on-site facility logbook review (including all available patient files, hospital	

											logbooks, operating room logbooks and blood bank logbooks).	
Crichton et al.[23]	1973	South Africa	1961	1971	0.625	N.R.	deliveries conducted in the unit over a period of 19 years. patients were Bantu and Indians from Durban, its suburb. and remote areas of Natal and Zululand. Unbooked patients admitted as emergencies with advanced sequelae of complications, produced the majority of the maternal deaths.	N.R.	maternal death	21000	N.R.	Each maternal death was discussed shortly after the event, with those responsible, and again at staff meetings within a week.
Anger et al.[50]	2018	Uganda	2016	2018	0.516	N.R.	all maternal deaths	N.R.	maternal death	4908	Data was extracted from narrative reports of all maternal deaths that occurred among women delivering at 6 rural hospitals in Uganda	
Nolens et al.[78]	2018	Uganda	207	2015	0.515	prospective observational cohort study	Women with a term singleton pregnancy in vertex presentation who delivered by vacuum extraction or SSCD (second-stage caesarean delivery)	N.R.	maternal death	425	Data were extracted from medical records and the admission, discharge, and mortality registers.	
Ekanem et al.[40]	2008	Nigeria	2000	2001	0.452	N.R.	All emergency caesarean sections	n= 349 emergency CS	maternal mortality	349	ward and obstetric theatre registers including case notes of women who had caesarean section in UCTH.	Since autopsy was not performed on any of the dead patients, the cause of death was determined largely on clinical grounds at departmental mortality review meetings.
McKenzie[87]	1998	Zimbabwe	1992	1994	0.480	A prospective review	Major obstetric procedures	N.R.	anaesthetic-associated	8502	Data were obtained from theatre registers, post-	Decisions on causes of death and avoidability were

									maternal deaths		mortem reports and (in all but four cases) the case notes.	made from mortality meetings and confidential discussions. Separate mortality meetings were convened by the Division of Anaesthetics and the Division of Obstetrics and Gynaecology, but in cases of possible anaesthetic-associated death, each Division invited the other to attend. The Division of Obstetrics and Gynaecology used prepared maternal mortality report forms; the author kept a book in which anaesthetists were requested to record details of all deaths occurring within 24 h of anaesthesia. Autopsy was performed in 16 of the 22 cases
Kuzma[9]	2016	Ethiopia	2009	2014	0.429	retrospective cohort study	all deliveries of gestational age ≥ 28 weeks	Emergency n= 574, elective n= 839	maternal death	1413	Patient medical records.	
Rutgers et al.[59]	2008	Zimbabwe	1998	2000	0.457	Retrospective cross-sectional.	all caesarean deliveries	n=168 elective CS, n= 925 emergency CS	maternal death related to a CS	1093	Delivery registers, admission books, hospital medical records, maternal mortality notification forms and monthly mortality reporting form.	
Remy et al.[17]	1993	Germany	1975	1989	0.801	retrospective	all maternal deaths	N.R.	maternal death	29257	All intra- and postpartum maternal deaths could be recorded via the Senate Department for Health and Social Affairs of West Berlin and the gynecological clinics or departments. The medical chief's consent could be obtained from the medical records.	The cause of death was confirmed in 67% of the cases by autopsy, death reports and medical records
Kalisa et al.[89]	2016	Rwanda	2013	2014	0.509	prospective cohort study	All pregnant women admitted for delivery or pregnancy related complications, and who sustained severe acute maternal	N.R.	maternal death	1442	captured relevant data for every woman who presented with severe acute maternal morbidity or died during admission, by using available medical records.	Autopsies were not performed and the underlying causes of death were only based on clinical records.

							morbidity					
Andrade et al.[60]	2006	Brazil	1927	2001	0.613	retrospective study	deaths that occurred in the hospital during the study period, considering only deaths from direct and indirect obstetric causes. Patients who were transferred to the ICU of other hospitals and died there were excluded	N.R.	maternal death	35,365	Patient records regarding their clinical history and data from death certificates.	Autopsies were not performed
Chattopadhyay et al.[71]	1983	Saudi Arabia	1978	1980	0.698	N.R.	All maternal deaths	N.R.	maternal death	2924	N.R.	Total absence of autopsy information
Krone et al. [3]	1975	Germany	1963	1974	0.801	N.R.	all deliveries	N.R.	maternal mortality	1350	Examined the obstetrics of the clinic.	
Zahran et al.[13]	2017	Egypt	2012	2012	0.675	retrospective cohort	All maternal deaths	N.R.	maternal death	9,908	Medical records of cases that fulfilled the WHO definition of maternal mortality. The registers of the hospital admissions and Intensive care unit were also reviewed to collect the data required to calculate the indices in our study.	
De Muylder[93]	1990	Zimbabwe	1985	1987	0.498	N.R.	All the delivery deaths occurring in all the health facilities, Exclusions: deaths due to abortion, ectopic pregnancy or choriocarcinoma	N.R.	maternal death	3,602	the Maternal Child Health (MCH) National Committee strongly recommended a post-mortem examination for every maternal death. All these cases were regularly discussed with the consultant, the physicians and the nursing staff involved: the clinical data, medical chart and autopsy findings were reviewed.	All these cases were regularly discussed with the consultant, the physicians and the nursing staff involved: the clinical data, medical chart and autopsy findings were reviewed.
Rojas et al.[20]	1974	Colombia	1966	1970	0.600	clinical study	deaths in patients who were pregnant, shuffled or were in the postpartum period.	N.R.	maternal death	5,003	statistical and pathological anatomy files were reviewed. autopsy study and anatomopathological study (biopsy or surgical specimen) were conducted.	autopsy study and anatomopathological study (biopsy or surgical specimen) were conducted.

Campbell[7]	1974	Papua New Guinea	1964	1973	0.377	N.R.	all maternal deaths due to pregnancy and childbirth	N.R.	maternal death	709	Death certificates for the 10-year period, were reviewed. The case notes of all females dying in the child-bearing age were studied.	Death certificates and case notes.
Kamilya et al.[83]	2010	India	2003	2006	0.539	retrospective cohort study	All deliveries without significant maternal disease or complications	N.R.	maternal death	13627	hospital records, admission and treatment records	Maternal deaths and their causes were assessed, based on detailed information on the circumstances of death collected from admission and treatment records.
Schuitemaker et al.[80]	1997	Netherlands	1983	1992	0.830	A nationwide confidential enquiry (retrospective cross-check)	all cases of maternal death.	N.R.	maternal death following caesarean section	108,587	information on maternal deaths is collected by MMC, the National Bureau of Statistics (CBS) and the Dutch Perinatal Database (DPD). All obstetric departments in The Netherlands were asked for additional cases.	Nationwide Confidential Enquiry into the Causes of Maternal Deaths, instituted by the Maternal Mortality Committee (MMC) of the Dutch Association of Obstetrics and Gynaecology (DAOG).
Kallianidis et al.[2]	2018	Netherlands	1999	2013	0.897	nationwide retrospective cohort study	all maternal deaths reported to the Dutch Maternal Mortality and Severe Morbidity Audit Committee (MMSMAC).	N.R.	maternal death following caesarean section	393,443	All available medical records of cases reported to the Dutch Maternal Mortality and Severe Morbidity Audit Committee were assessed by two researchers, and one or two additional experts in case of contradicting opinions, based on a set of pre-identified clinical criteria.	After a case is reported, all medical records are requested to be sent to the MMSMAC. These include antenatal charts, microbiology and laboratory results, theatre records, autopsy reports and local maternal death reviews. The MMSMAC classifies underlying causes of death, mode of death and audits substandard care factors.
Oladapo et al.[84]	2007	Nigeria	1990	2005	0.452	Retrospective analysis	all elective Caesarean deliveries	164 elective Caesarean sections	maternal death	164	Information was obtained from a combination of theatre records, labour ward registers and case files retrieved from the Medical Record Department of the hospital.	
Armon[62]	1979	Tanzania	1971	1977	0.373	survey	All deaths occurring within the hospital during pregnancy or the first six weeks of the puerperium	N.R.	maternal death	1,271	Post-mortem examination was performed in 35 % of the cases. In the remaining cases the diagnosis was made on clinical grounds (including the findings of laparotomy).	Post-mortem examination.
Ozumba et	2002	Nigeria	1994	1999	0.452	N.R.	All maternal deaths	n= 1153 emergency	Maternal deaths	1684	N.R.	

al.[86]							associated with caesarean section	caesarean n= 531 elective	associated with caesarean section			
Clark et al.[92]	2008	United States	2000	2006	0.889	retrospective study	all maternal deaths	N.R.	maternal death	458,097	medical records and augmented when necessary by interviews with involved health care providers.	Cause of death, preventability, and causal relationship to mode of delivery were examined.
Gebhardt et al.[57]	2015	South Africa	2011	2013	0.673	N.R.	all maternal deaths	N.R.	maternal death during or after CS	655686	Data from the completed 2011 - 2013 triennial review.	The triennial data are analysed and organised into categories according to the major causes of maternal deaths; each category is reviewed by an expert in the field.
Briand et al.[76]	2012	Mali and Senegal	2007	2008	0.068	Cross-sectional survey nested in a randomised cluster trial	All singleton pregnancies, without immediate life-threatening complication.	N.R.	in-hospital maternal mortality, early neonatal mortality	11,255	Data was collected from medical records by trained midwives who were supervised by the national coordinators of the survey. To avoid under-reporting of in-hospital maternal mortality, a complementary procedure was carried out to identify the eligible maternal deaths among all the female deaths that occurred in the facility using the various registries available (admissions, hospitalizations, operating theatres and morgues).	
Wirakusumah [39]	1995	Indonesia	1981-1983 and 1988-1990		0.525	Retrospective cohort	Maternal deaths associated with caesarean section	N.R.	in-hospital maternal mortality, early neonatal death	1424	Maternity Care Monitoring Records of Hasan Sadikin Hospital Bandung. To study the maternal mortality in detail in data were collected independently from the following sources: abstracts from the delivery room registry and the medical records of the Department; daily case reports recorded by residents who contain information about the patients (characteristics as well as detailed diagnoses and procedures).	None of the women who died in-hospital were autopsied.
Chi et al.[15]	1986	2 less developed countries: The annual per capita	1977	1980	0.011	N.R.	women consecutively admitted to the five hospitals for delivery and	N.R.	In-hospital maternal deaths	857	Maternity Record	When a death occurs, the attending physician reports the details surrounding the death to FHI in a Death Report Form that includes:

		income was about US$ I 05 for Country A in 1980 and US$ 560 for Country B in 1982					for problems associated with late pregnancy, labor and/or delivery.					patient's primary and general conditions upon arrival, pertinent events surrounding labor and delivery, principal and contributing causes of death, and dates of admission, delivery and death. No autopsy was performed on any of the in-hospital maternal deaths.
Nyamtema et al.[27]	2016	Tanzania	2012	2014	0.503	Before-after intervention study design	All caesarean sections	N.R.	maternal death	5868	delivery logbooks, case files and operation records.	
Mukherji et al.[48]	1995	India	1988	1993	0.436	retrospective analysis	maternal deaths following caesarean section	N.R.	maternal death following CS	8,017	hospital records.	Since post mortems were not done the diagnosis of pulmonary embolism could not be confirmed.
Igberase et al.[54]	2009	Nigeria	1995	2004	0.452	retrospective review	all patients who had caesarean delivery	Emergency n=1124, Elective n=653	maternal death	1,777	The data from case notes, antenatal and theatre records of patients who had caesarean delivery over a ten-year period in the Baptist medical center, Ekuwere extracted and analysed.	
Tsen et al.[91]	1998	United States	1990	1995	0.872	N.R.	all parturient who underwent general anesthesia for caesarean section (includes data of patients undergoing all types of anesthesia)	N.R.	maternal mortality	12040	the hospital's database and medical records.	
Palanisamy et al.[64]	2011	United States	2000	2005	0.889	retrospective analysis	all caesarean deliveries under general anesthesia	N.R.	anesthesia-related maternal mortality	15468	the obstetric database at the institution and medical records.	
Enohumah et al.[1]	2006	Nigeria	1991	2000	0.452	retrospective study	patients who had undergone surgical procedures in pregnancy or puerperium	N.R.	anesthesia-related maternal mortality	2323	Information was assessed from available records: the master register in the Labour and Delivery Operating Room, Labour and Delivery records, Intensive Care Unit records and patient charts and maternal mortality database.	The reports of post-mortem examinations were reviewed where available. Departmental mortality review meetings were also evaluated.

Nwobodo et al.[79]	2011	Nigeria	2002	2010	0.474	retrospective analysis	all the patients that had caesarean section	emergency n=1784, elective n= 498	maternal deaths	2284	The records from the labor room and operating theater were retrieved and checked for caesarean deliveries. The delivery records of patients that had elective caesarean sections were obtained and relevant variables extracted.	
Zongo et al.[73]	2015	Senegal and Mali	2007	2011	0.081	cluster-randomized controlled trial	All deliveries	N.R.	hospital-based maternal death	40,975	hospital-based maternal death, was measured as the vital status of the mother (dead or alive) at hospital discharge	
Talebi Doluee et al.[67]	2018	Iran	2010	2014	0.781	retrospective cross-sectional study	all maternal deaths	N.R.	maternal mortality	280957	Data was collected from the reports of Maternal Mortality Committee of Mashhad University of Medical Sciences, Mashhad, Iran. The Committee was consisted of trained professionals in this field including a gynecologist, an anesthesiologist, a hospital director, a representative of the Deputy Minister of Health, a midwife, a nurse, and a forensics expert. The number of live births per year was obtained from the Statistics Center of Mashhad University of Medical Sciences, Mashhad, Iran.	The cause of death was determined based on the existing evidence, documented prenatal care, hospitalization records, verbal reports, and autopsy results.
Löfgren et al.[43]	2015	Uganda	2011	2011	0.494	A prospective, questionnaire-based study	all major and minor operative procedures	N.R.	perioperative mortality	496	using 2 pretested questionnaires, one for data collection in the operating room and one for data collection on the ward. Forms filled in the operation room were cross- checked with the operating room registers and the forms filled in on the ward. If required, clinical notes from the wards and registers at the time of admission were checked to correct any inconsistency.	
Maaløe et al.[22]	2012	Tanzania	2009	2010	0.479	retrospective criterion-based audit.	All emergency caesarean sections	emergency n=303, elective n=35	maternal death, Early neonatal deaths	303	case notes were reviewed and extracted the data by applying a structured	

											questionnaire. At each hospital, 200 women receiving CS in 2009 were retrieved from the operation theater records. The identities of the women were cross-checked with the admission and delivery registers, and their case notes with partographs collected.	
Andersgaard et al.[72]	2008	Norway	1976	1995	0.850	N.R.	All direct maternal deaths	N.R.	maternal death	117,521	The maternal deaths were identified through the Cause of Death Registry, Statistics Norway, and Medical Birth Registry of Norway. Copies of the hospital case records and the maternal death autopsies were requested.	Cause of Death Registry and the Medical Birth Registry of Norway (MBRN).
Rippmann[66]	1965	Switzerland	1940	1963	0.832	N.R.	all maternal deaths	N.R.	maternal death	3132	N.R.	
Bloom et al.[4]	2005	United States	1999	2000	0.881	A prospective observational study	all caesarean births	emergency n=2163, elective n=34979	maternal death	37,142	Detailed information were abstracted directly from maternal and infant charts by specially trained and certified research nurses.	The charts of all maternal deaths were reviewed in detail to determine whether the death was related to the anesthetic procedure. The initial review was conducted by the principal investigator at each site, followed by a central review conducted by 3 members of the protocol subcommittee.
Ojo et al.[65]	1988	Nigeria	1982	1986	0.452	retrospective analysis	all maternal deaths after caesarean section	N.R.	maternal mortality after caesarean section	1992	case records.	Post-mortem examinations were refused by the relatives of the patients because of the prevailing local customs of immediate burial of the dead.
Gundumure[37]	2002	Zambia	1998	1998	0.419	retrospective	all caesarean sections	N.R.	maternal mortality	1,880	cases of CS were identified using the CS register kept in the theatres. The labour ward delivery register was used to identify any information that was not clearly entered in the theatre register. Specific data was collected from patient case files. If this was not available, the two registers provided sufficient core data. Regarding maternal mortality, this was	

											cross-checked with the register of maternal deaths in which cases that had CS had been previously identified.	
Sachs et al.[74]	1988	United States	1954	1985	0.860	N.R.	all deaths directly due to caesarean section	N.R.	Caesarean section-related maternal mortality	121,217	the Maternal Mortality Committee of the Massachusetts Medical Society constructed a data base to include the listings of all known maternal deaths that occurred in the Commonwealth between 1954-198. Population statistics used in this study were obtained from the Massachusetts Department of Public Health.	Maternal Mortality Committee of the Massachusetts Medical Society is comprised of obstetricians from both teaching and community hospitals, pathologists, internists, anesthesiologists, and a representative from the Public Health Department. In specific cases, relevant specialists were consulted. After notification of a maternal death, the chairman assigns Committee members to study the death and to submit a report to the Committee. An autopsy examination is encouraged; if one has been performed, the Committee's pathologists review relevant slides and information. In each case, a primary cause of death is assigned. The Committee's report is then shared with the physicians who cared for the patient.
Cisse et al.[52]	1998	Senegal	1996	1996	0.379	Prospective longitudinal study	All women undergoing caesarean sections	N.R.	maternal death	2436	For each case, an individual file with 30 variables was completed.	
Evrard et al.[45]	1977	United States	1965	1975	0.860	N.R.	all deliveries	N.R.	post-caesarean-section deaths	12,941	The Rhode Island State Health Department was able to supply the total number of deliveries by occurrence from 1965 through 1975 and the total number of caesarean sections for 1968 through 1975. The number of caesarean sections for 1965, 1966, and 1967 was calculated as follows: A letter was sent to each hospital in which babies	Protocols for the maternal deaths during the study period were obtained from the Maternal Mortality Committee of the State Medal Society of Rhode island.

											were delivered during those years, requesting the number of deliveries and the number of caesarean sections. Protocols for the maternal deaths during the study period were obtained from the Maternal Mortality Committee of the State Medal Society of Rhode Island.	
Maswime et al.[18]	2016	South Africa	2013	2014	0.685	A retrospective study	all maternal deaths due to bleeding during and after caesarean	N.R.	maternal death due to bleeding during and after caesarean	43137	maternal deaths due to bleeding during and after caesarean that occurred at seven hospitals in Johannesburg, South Africa, between January 1, 2013, and December 31, 2014, were audited as a case series. Hospitals in South Africa are required to keep all clinical notes in cases of maternal death.	All maternal death records were reviewed by a certified specialist obstetrician and gynecologist to identify the causes
Amirikia et al.[82]	1981	United States	1965	1979	0.860	N.R.	All caesarean sections	N.R.	maternal mortality	9,718	N.R.	
Bolaji et al.[8]	1993	Ireland	1973	1987	0.764	15-year survey	All deliveries	N.R.	Post caesarean section deaths	3572	The clinical research unit in the department of Obstetrics and Gynaecology routinely abstracts and codes information from all birth records for a computer file.	
Ikeako et al.[44]	2009	Nigeria	2005	2009	0.479	retrospective review	all caesarean deliveries, exclusion criteria were women with ruptured uterus	emergency n= 184, elective n= 97	maternal death related to caesarean section, early neonatal death	291	The labour ward and theatre registers provided information on the total number of deliveries and caesarean sections. The case notes of all those who had caesarean section were examined in detail. The medical records were reviewed by trained staff using pre-established and piloted data extracted forms.	
Tadesse et al.[24]	1996	Ethiopia	1991	1992	0.283	prospective hospital-based study	All women who delivered	n= 57 elective caesarean section, n= 261 emergency caesarean section	maternal death, Early neonatal deaths	318	The antenatal chart and delivery records were reviewed and abstracted according to pre-prepared protocol.	

Okonta et al.[31]	2003	Nigeria	1996	2000	0.452	audit	All caesarean sections	n= 712 emergency n= 181 elective.	maternal deaths associated with caesarean sections, early neonatal death	1031	The hospital records. The labour ward and theatre registers provided information on the total number of deliveries and caesarean sections (CS). Further detailed information was obtained from patients' case notes and the detailed case summaries of every delivery kept in the department.	
Mekbib et al.[5]	1994	Ethiopia	1987	1992	0.283	retrospective study	all patients who underwent CS	emergency n= 586, elective n=59	CS-related maternal mortality, neonatal death	645	Hospital records.	
Ezechi et al.[61]	2002	Nigeria	2000	2002	0.452	descriptive study	All mothers that were delivered by caesarean section	N.R.	mortality associated with caesarean section	391	N.R.	
Daniel et al.[51]	2016	Nigeria	2009	2011	0.484	descriptive longitudinal cross-sectional study	All caesarean sections except those who had a caesarean section hysterectomy following uterine rupture	emergency n=288, elective CS n=216	maternal deaths associated with CS	504	Maternal outcomes were extracted from the case notes and operation files and documented in a proforma.	The causes of death were based on clinical findings before death as there was no postmortem examination performed on these patients.
Bukar et al.[32]	2009	Nigeria	2001	2003	0.452	retrospective study	All caesarean sections	n=181 emergency, n= 69 elective.	maternal death, neonatal death	250	The records were obtained from the Medical records department, postnatal and labour ward registers and the theatre.	Autopsy was not done and hence the causes of death were based on clinical grounds.
Njokanma et al.[56] 2002	2002	Nigeria	1983	1997	0.452	descriptive study	All caesarean sections	n=686 emergency CS, n=454 elective	maternal death, early neonatal deaths	1140	Hospital records, neonatal chart and in the delivery register.	
Etuk et al.[68]	2001	Nigeria	1993	1997	0.452	N.R.	All caesarean section deaths, excluding those following uterine rupture	N.R.	maternal mortality following caesarean section	1540	The case notes of all maternal deaths following caesarean section were reviewed. The theatre register within the same period was also reviewed to find the total number of caesarean sections performed and the cadre of surgeons who carried out the operation.	Autopsy was not carried out following any of these deaths owing to the refusal of the relatives to allow this vital examination because of the prevailing local custom of respect for the dead. Hence, the causes were based on clinical findings before death.
Imarengiaye et al.[70]	2001	Benin	1986	1995	0.354	N.R.	Admitted to ICU following caesarean	emergency n=2102, elective n=584	maternal death	2686	Hospital records of patients were studied.	

							section					
Greenhill[41]	1930	United States	1915	1929	0.860	N.R.	All caesarean sections	N.R.	maternal death	874	N.R.	
Onoh et al.[29]	2015	Nigeria	2002	2011	0.479	case series	all the caesarean deliveries	emergency n=1,576 elective n=521	maternal death	2,097	The delivery register was used to select all women who had caesarean delivery, and their folders were retrieved from the record department. The patients' folders, antenatal ward, labor ward, theater, postnatal ward, and newborn special intensive care unit registers were utilized for the data collection.	Autopsies were not done for the maternal death because of cultural belief, poverty, and illiteracy in our setting.
Ugwu et al.[69]	2011	Nigeria	2005	2009	0.479	retrospective analysis	all the caesarean sections	n=918 emergency caesarean, n=62 elective CS	maternal death	980	Case notes, labour ward and theatre records.	
Okezie et al.[75]	2007	Nigeria	2001	2004	0.452	N.R.	all patients who had lower segment caesarean section	emergency n=460, elective n=280	maternal death	740	Hospital records.	
Raphael et al.[25]	2015	Nigeria	2008	2011	0.484	retrospective descriptive study	patients who had caesarean section	n=1300 emergency caesarean, n= 666 elective caesarean section	maternal mortality post-caesarean section	1,966	Patient files.	
Ijaiya et al.[34]	2001	Nigeria	1990	1999	0.452	retrospective study	all caesarean deliveries	n= 2,529 emergency, n= 235 elective	maternal deaths following caesarean section	2,764	The records of caesarean sections were obtained from patients' case notes, labour ward and theatre records and mortality register.	Mortality register, patients relations did not usually give consent for post-mortem examination.
Krause et al.[42]	1979	Germany	1956	1976	0.801	retrospective study	all deliveries	N.R.	maternal death	1468	N.R.	
Alegre Villariz et al.[49]	1977	Spain	1972	1975	0.754	retrospective study	cases of caesarean section	N.R.	maternal death	1499	N.R.	
Muziarelli et al.[47]	1989	Italy	1974	1987	0.769	Retrospective study	all caesarean sections	N.R.	maternal mortality	747	clinical files	
Pekhlivanov[38]	1975	Bulgaria	1949	1973	0.694	N.R.	all caesarean sections	N.R.	maternal mortality	1112	material of the obstetric-gynecological ward at the first municipal hospital in the town of Plovdiv.	

Poradovsky[94]	1968	Czechoslovak Republic/ Czech Republic	1962	1966	0.730	N.R.	all obstetric interventions	N.R.	maternal death	21981	N.R.	
Imbert et al.[30]	2003	Senegal	1997	1997	0.380	Prospective study	All emergency caesarean sections	n=370 emergency, n=32 elective	maternal mortality	370	On a standardized sheet we noted: age, medical and obstetric history, admission method, direct or by evacuation. The indications of CS, clinical status and preoperative assessment of mothers on admission, modalities of anesthesia as well as the outcome of CS at the end of the hospital and at three months for mother and newborns born on discharge from the hospital between D8 and one month.	
Picaud et al.[77]	1990	Gabon	two 4-year periods (1981-1984 and 1985-1988)		0.620	comparative study	All caesarean sections	N.R.	maternal mortality	1213	N.R.	
Szczepanski et al.[85]	1975	Poland	1960	1973	0.712	N.R.	All caesarean sections	N.R.	maternal mortality	3116	N.R.	
Carazzone et al.[26]	1978	Italy	1972	1976	0.769	N.R.	all deliveries	N.R.	maternal death	2,940	we have collected data of the whole hospital and not of each division.	
Georgiades eta al.[46]	1972	Austria	1959	1970	0.795	N.R.	all caesarean deliveries	N.R.	maternal mortality	575	Put together the patient inventory of the clinic.	
Chavez Azuela et al.[58]	1967	Mexico	1962	1966	0.650	retrospective study	all maternal deaths	N.R.	maternal death	6,495	Clinical records.	
Kartushina[6]	1972	Ukraine	1958	1969	0.705	N.R.	maternal deaths from caesarean section	N.R.	postoperative mortality	1653	N.R.	
Zhu et al.[11]	2000	China	1978	1997	0.502	A retrospective study	maternal deaths of caesarean section	N.R.	Maternal mortality	623534	Sources 1978-1997 Shanghai Maternal and Child Health Report, Maternal Death Cases and Municipal Expert Evaluation Data on Maternal Deaths.	Maternal Death Cases and Municipal Expert Evaluation Data on Maternal Deaths.

											Second, collecting data through the city's three-level maternal and child health network, through Shanghai.	
Strobel[21]	1967	Germany	1950	1966	0.801	N.R.	all obstetric interventions	N.R.	maternal death	896	N.R.	
Warm et al.[33]	1966	Germany	1939	1963	0.801	N.R.	maternal deaths of caesarean section	N.R.	Maternal mortality	2800	N.R.	
Kambo et al.[120]	2002	India	1993–1994 and 1998–1999		0.471	N.R.	7017 consecutive caesareans	emergency n=5767, elective n=1250	maternal mortality	7017	N.R.	
Fesseha et al.[102]	2011	Ethiopia	2008	2009	0.402	retrospective record review	All caesarean sections	emergency n=174, elective n=48	maternal mortality and early neonatal death	17145	The data source was the national baseline assessment of emergency obstetric and newborn care—a cross-sectional, facility-based survey of 797 facilities. Two instruments were used to collect the data for the present paper: a retrospective record review of 267 cesarean deliveries; and a 12-month summary of each facility's statistics on vaginal and abdominal deliveries	
Ojiyi et al.[103]	2012	Nigeria	2004	2008	0.474	descriptive retrospective study	All patients who underwent Caesarean section	emergency n=192, elective n=166	maternal mortality	358	case records were retrieved from the medical records department.	
Garba et al.[104]	2011	Nigeria	2006	2007	0.479	descriptive study	All patients that were delivered by caesarean section	emergency n= 812, elective n= 126	maternal death	938	case notes were retrieved.	
Kandasamy et al.[110]	2009	Afghanistan	2006	2006	0.419	retrospective review	All caesarean deliveries	Emergency n=237, Elective n=151	maternal death	392	operating room logbooks which contain clinical information on all caesarean deliveries that occur in the hospital.	
Kor-Anantakul et al. [119]	2008	Thailand	2001	2003	0.665	prospective cohort study	All deliveries of women who resided within 5km radius of the hospital	Elective n= 112, Unscheduled n= 75	maternal mortality and early neonatal death	187	The nursing staff interviewed and examined the patients, emphasis on clinical details of postpartum complications on day 2 and between days 5 and 7. If the patient was discharged before day 5, they made a home visit.	

Yaïch et al.[111]	2012	Côte d'Ivoire: Ivory Coast	2010	2010	0.442	descriptive retrospective study	All emergency caesarean sections	emergency n=513	maternal mortality, neonatal mortality	513	anesthetic and obstetric records of all parturient who underwent caesarean Emergency Hospital of Cocody in Abidjan.	
Cebekulu et al.[107]	2006	South Africa	2004 and 2005		0.620	cohort study	Term singleton live pregnancies with cephalic presentation and no previous scar.	N.R.	maternal death, neonatal death	5765	Each day, the delivery register was examined for second stage caesarean sections done in the preceding 24 h. An attempt was made to contact all subjects telephonically 2 weeks after delivery, to identify clinical problems that may have arisen after discharge.	
Diawara et al.[106]	2014	Mali	2007	2008	0.390	descriptive cross-sectional study	All caesarean sections	N.R.	post-operative maternal death	143	To collect the data, they used a survey form filled out from the supports used in the context of the reference-evacuation (reference / evacuation notebooks, registers of birth, operating protocol, death and partograms).	
Teguete et al.[116]	2012	Mali	1985	2003	0.256	Retrospective study	All deliveries	elective n= 858, emergency n=243	maternal mortality and neonatal mortality	4517	A complete database of all obstetric admissions focusing on characteristics of delivered women, mode of delivery, caesarean indications, and maternal, fetal and immediate neonatal outcome was built to include all deliveries recorded at Point G National Hospital between January 1, 1985 and December 31, 2003. Data were collected from these complete obstetric files, as well as hospital birth registries, registries of on-call midwives, surgical reports, admissions records for the intensive care service, records from the internal medicine and urology services, and hospital death records.	
Eshiet et	2003	Nigeria	1995	2000	0.452	Retrospective study	All emergency caesarean	920 emergency CS	Anaesthetic related death	920	Information was obtained from anaesthetic record	Patients relatives generally did not accede to post

al.[118]							sections				charts, theatre and ward records.	mortem examination, Thus the causes of deaths were based on clinical diagnosis in all the cases.
Goswami et al.[117]	2013	India	2005	2010	0.565	prospective study	all women who died during pregnancy or within 42 days of being pregnant	N.R.	maternal death	8471	Summaries of all maternal deaths in obstetrics wards were available in the department and their case records were retrieved. Case records of the women dying in the non-obstetrics wards were screened every 3 months in the hospital record section to identify maternal deaths.	The case records were reviewed by the committee members to assess the cause of death, lacunae in care (substandard care), deficiency or non-availability of the health-service resources and possibility of its prevention at the facility. In others, families of the deceased women did not give consent for autopsy due to a cultural barrier. As a result, no autopsies were done in this series.
Abebe et al.[113]	2016	Ethiopia	2012	2013	0.439	retrospective analysis	pregnant women who had undergone either caesarean or vaginal delivery. All caesarean sections except those who had a uterine rupture	n=653 emergency CS, n=70 elective CS	maternal death, immediate newborn death	723	Pre-tested questioner was used to collect mothers' information and analysis of eligible patient records.	
Rasoarimahandry et al.[126]	2001	Madagascar	1998	1998	0.456	retrospective study	All caesarean sections. Excluded from our study the cases of suturing conservative after uterine rupture	N.R.	maternal death, neonatal death	529	all the documented caesarean operations (treatment sheet load) performed during this period. The sheet has several variables.	
Okafor et al.[109]	2008	Nigeria	1998	2006	0.452	observational retrospective study	Caesarean sections deaths	N.R.	anaesthetic related maternal deaths during caesarean section	1579	The obstetric theater records were reviewed for deaths during anaesthesia for caesarean section and their hospital records examined for demographics, obstetric/anesthetic records and cause of death.	Hospital records.
Nelissen et al.[115]	2013	Tanzania	2009	2011	0.487	prospective cross-sectional study	All maternal near misses and maternal	N.R.	maternal death	74	Data were obtained from the patient record. The facility medical staff was	Medical records; for each case, one underlying cause was identified that started

							deaths				questioned in case of doubt or missing information.	the cascade that led to maternal morbidity or mortality. All MD cases were reviewed by a selection of the authors, as well as and those cases, which were difficult to classify into an underlying cause
Sekirime et al.[123]	2009	Uganda	N.R. , <2009	N.R.	0.457	descriptive observational concurrent prospective study.	emergency caesarean section	n= 478 emergency	maternal death	478	All those recruited were from the Mulago Hospital labor ward and were operated in the same theatre by doctors of or above the rank of a senior housing officer. The patients were followed up postoperatively for primary outcomes.	
Adisso et al.[124]	2006	Benin	2002	2002	0.419	retrospective, descriptive, exhaustive and analytical study	all women who have undergone a caesarean.	N.R.	maternal death	1745	patient files were retained.	
Richard et al.[122]	2008	Burkina Faso	2003	2006	0.324	Before after study	all women with emergency or elective caesarean delivery in the district hospital	emergency n=1206, elective n=165	post-caesarean maternal deaths	1371	• Routine data from the district hospital (admissions, deliveries, complications, referrals) (2003–2006). • Caesarean delivery forms designed to record all major obstetric interventions performed for life-saving indications. Nonroutine data were collected from the main city hospitals, including the university hospital (2003–2005). • Individual prescription cards for women having a caesarean delivery. This card shows all surgical procedures and treatment prescribed during each woman's hospital stay and the cost (2005). • Referral and feedback forms (2004–2006). • Criteria of quality grids for intrapartum and postpartum care (2003–2005)	
Meda et	2016	Burkina	2009	2010	0.375	cross-sectional	women who	Emergency n=	maternal death	668	For every selected case of	Medical record.

al.[121]		Faso				study	were delivered by caesarean in any health center in Burkina	568, elective n=100			caesarean delivery, a questionnaire was filled in using the medical record, the partogram, the register of the operating room, and the register of delivery.	
Asıcıoglu et al.[114]	2014	Turkey	2008	2011	0.743	observational study,	Caesarean sections for singleton term pregnancies without major fetal abnormalities or significant maternal disease or complications	N.R.	maternal death, neonatal death	8072	N.R.	
Pereira et al.[101]	1996	Mozambiq ue	1992	1992	0.215	nonrandomised analysis, Prospective study	All caesarean sections	elective n=145, emergency n=1926	maternal death, early neonatal death	2071	N.R.	
Khawaja et al.[125]	2004	Pakistan	2000	2001	0.456	descriptive study,	All caesarean sections	34 sections were elective (11%) and 266 were emergency caesarean deliveries (89%).	maternal death	300	A senior house officer charted details of the subjects on a specifically designed proforma. A partogram was maintained during every labour by the registrar.	
Ouedraogo et al. [108]	2015	Burkina Faso	2005	2008	0.344	retrospective study	All caesarean sections	Caesarean section was performed in an emergency in 87% of cases, was programmed in 13% of cases.	maternal death, early neonatal death	3381	Data were collected from the computer database of records of caesareans at the hospital. The computer database of caesarean maternity files from Sector 30 CMA was the source of the information. They also consulted the registers of the operating room, the delivery room and monthly activity reports.	
Rabiu et al.[105]	2011	Nigeria	2008	2009	0.491	retrospective audit	All singleton emergency caesarean sections without significant maternal or foetal disease.	Elective Emergency n=879 (28.7%) n=2182(71.3%) (of overall CS not just cases)	maternal death, neonatal death	347	The case notes of all the patients who had intrapartum C/S were retrieved and studied.	
Chau-In et al.[81]	2010	Thailand	2003	2004	0.683	multi-center study, prospective	All women receiving anaesthesia	Emergency n=5,760, elective n=	maternal death related to anaesthesia	16,697	Details of pre-anesthetic conditions, anesthetic management, intra-	

						survey	during caesarean section	10936			operative events and peri-operative complications among consecutive patients within 24 hours of post-operative were recorded on standardized forms. The responsible anesthetist/nurse anesthetist asked four key questions, what is/ are adverse events, who, when, and how the event occurred? Each case was reviewed by the preliminary quality assurance (QA) committee, comprising three anesthetists from different university hospitals, to assess whether the inclusion criteria were met. Contact was made with the anesthetist involved or the admitting hospital's anesthetic records reviewed.	
MATERNAL AND PERINATAL MORTALITY COMMITTEE[36]	1969	Australia	1966	1967	0.866	prospective study	all caesarean sections	elective n=1,264 emergency n=2236	maternal mortality, neonatal death	3,500	Every hospital with obstetric beds was provided with a questionnaire to be completed by the surgeon before the patient was discharged from hospital. 'The Section of Maternal and Infant Care of the Department of Public Health checked the returns and ensured that all maternal and perinatal deaths relevant to the survey were included.	
Moldin et al.[16]	1984	Sweden	1973	1979	0.816	N.R.	all caesarean sections	N.R.	maternal mortality	63075	From the medical birth registration. Death certificates for maternal deaths associated with parturition or puerperium during the study period were obtained from the National Central Bureau of Statistics. The type of birth in each case of maternal death was determined by means of the medical birth register of the National	The records of patients delivered by CS were examined for cause of death. Autopsy was performed in all cases included in this study.

											Board of Health and Welfare. Autopsy was performed in all cases included in this study.	
Rubin et al.[12]	1981	US	1975	1976	0.860	N.R.	Georgia residents aged 10 to 44 years had died up to 14 months after delivery of a live-born infant regardless of the cause of death entered on the death certificate.	N.R.	maternal mortality	15,188	Obtained computer file data on live births and deaths occurring in Georgia from the Office of Health Planning and Evaluation of the Georgia Department of Human Resources. This office processes and tabulates data from the birth and death certificates collected by the Vital Records Unit of the same department. Obtained additional information from medical examiners' reports, physician and hospital records, police reports and the family of the deceased	A panel of obstetrician/ gynecologists reviewed each maternal death following CSD. When a consensus of the panel decided from the available clinical data that the death could reasonably be attributed to the CSD, we classified it as a caesarean-attributed death; if the death could be attributed to a cause other than the caesarean section per se, we classified it as a non¬caesarean attributed death.
Bruce et al.[35]	1966	Chile	1961	1965	0.703	N.R.	all caesarean operations	N.R.	maternal mortality, neonatal mortality	771	Clinical records corresponding to all caesarean operations.	
Abbassi et al.[14]	2001	Morocco	1994	1997	0.499	retrospective review	All caesarean sections	N.R.	maternal death	3,231	Reviewed all the files of the caesarean sections performed at the Lalla Meryem maternity hospital of the Ibn University Hospital.	
Pinsker et al.[63]	1982	Mexico	[in the span of seven years], <1982		0.652	N.R.	all maternal deaths	N.R.	maternal death, neonatal death	22495	The observations captured in the Maternal Mortality Committee of the hospital, regarding the early mothers who eventually practiced Caesarean operation, in order to study some factors involved in its death.	Maternal Mortality Committee of the hospital, Maternal Mortality Committee of the International Gynecology and Obstetrics Foundation.
Beck et al.[10]	1984	Austria	1975	1982	0.795	Individual case analysis	all maternal deaths	N.R.	maternal death	43061	All obstetric-gynecological departments are contacted every year and asked to provide documents on maternal deaths. All pathological-anatomical institutes and forensic medicine institutes were also be contacted in order to ensure that the maternal deaths are recorded without gaps. They	Hospital documents and autopsies.

											informed them of cases in which signs of an existing or up to 6 weeks past pregnancy could be ascertained on the basis of an autopsy. The information on the section frequency was taken from a national survey by Baumgarten and Schrock.	
Saving Mothers 2017[99]	N.R.	South Africa	2018	2018	0.705	Annual Report on Confidential inquiries into maternal death	all maternal deaths	N.R.	maternal mortality	248381	Data was obtained from the District Health Information System (DHIS) for live births and maternal deaths per district for 2017 on 23rd July 2018. The NCCEMD data was obtained from the Maternal Morbidity and Mortality Audit System (MaMMAS) database in 7th September 2018, once all provinces had submitted their data. The DHIS data is almost exclusively from public hospitals (although some private hospitals do submit data to the DHIS).	DHIS, National Committee for the Confidential Enquiries into Maternal Deaths (NCCEMD) and MaMMAS.
Slaytor et al.[96]	2004	Australia	1997	1999	0.892	maternal death report	all maternal deaths	N.R.	maternal mortality	159201	maternal mortality data was collected from the State and Territory Maternal Mortality Committees. The composition of these Committees usually comprises some or all of the following experts—obstetricians, obstetric physicians, midwives, pathologists, general practitioners, epidemiologists, and Aboriginal and Torres Strait Islander and consumer representatives. Each State and Territory Committee has developed different ways to maximise the maternal death notifications; this may include notifications from health departments, hospitals, attending	State and Territory Maternal Mortality Committee who obtain data from health departments, hospitals, attending practitioners, coroner's office, Registrar of Births, Deaths and Marriages and review of the perinatal and hospital morbidity collections. Each death is then comprehensively reviewed. The sources of information reviewed include any hospital admissions, autopsy, toxicology, police and coroners' reports, and other ancillary information.

											practitioners, coroner's office, Registrar of Births, Deaths and Marriages and review of the perinatal and hospital morbidity collections. The sources of information reviewed include any hospital admissions, autopsy, toxicology, police and coroners' reports, and other ancillary information.	
NCCEMD[97]	N.R.	South Africa	data entered before 2017		0.704	Seventh triennial report on confidential enquiries into maternal deaths	all maternal deaths	N.R.	maternal mortality	708024	Data used in this report consist of the maternal deaths that occurred and were reported to the NCCEMD secretariat and were entered on the MaMMAS database before 15 May 2017.	
NCCEMD[98]	N.R.	South Africa	2002	2004	0.617	Report on Confidential Enquiries into Maternal Deaths	all maternal deaths	N.R.	maternal mortality	477210	the facility completes a Maternal Death Notification Form (MDNF) which is sent to the provincial office within 7 days of the maternal death. The provincial MCWH coordinator informs the secretariat of the NCCEMD that a death has occurred. The NCCEMD issues a unique file number for the case. The Province forwards all documentation to a Provincial Assessor. The Provincial Assessor team comprising of a doctor and midwife is responsible for completion of the assessor's form. The assessor must complete and return all documentation to the Province within 30 days. All documentation is then forwarded to the NCCEMD for collations and analysis. The NCCEMD uses this data to compile reports on maternal deaths in South Africa.	The Provincial Assessor team comprising of a doctor and midwife is responsible for completion of the assessor's form. The assessor's must provide information on the primary, final and contributory causes of death.
Maswime et	2016	South Africa	2013	2014	0.691	prospective cross-sectional	all deliveries	N.R.	Maternal deaths from	70095	Interviews with the clinical head of obstetrics in each	

al.[18]						study			BDACS		hospital, using a structured questionnaire.	
Hogberg et al.[88]	1989	Sweden	1951	1980	0.816	N.R.	all maternal deaths related to caesarean section	N.R.	maternal death	82,901	All certificates of death related to pregnancy, childbirth and the puerperium for the years 1951-80 were retrieved from the Swedish Central Bureau of Statistics, together with hospital records and autopsy reports from the various departments of obstetrics and Gynaecology. The numbers of abdominal and vaginal deliveries were obtained from the annual reports of the obstetrical departments for the years 1951-72, and from the Swedish Medical Birth Registry for the years 1973-80 (10).	certificates of death related to pregnancy, child-birth and the puerperium, hospital records and autopsy reports.
Wong, et al. [53]	2006	Canada	1987	2004	0.863	N.R.	all maternal deaths	N.R.	maternal death	179541	The BC Vital Statistics Agency provided data.	The specific causes of maternal deaths for 1987–2004 were also provided by the BCVital Statistics Agency.
Wiebenga[55]	1992	Malawi	1989 and 1990		0.303	N.R.	all maternal deaths	N.R.	maternal death	1856	Records of all maternal deaths at the Chatinkha Maternity Wing of QECH in 1989 and 1990 were reviewed. In 1989 several records were missing, and the information was then obtained from death books and nursing records kept on each ward. Death files of the female medical and surgical wards were scanned for patients with a pregnancy reported at the time of death or during the preceding 42 days. In 1990 files were completed immediately after the patient's death and missing laboratory and other test reports collected.	Death files.
Ounsa et al.[112]	2011	Sudan	2004	2010	0.452	retrospective descriptive, hospital- based	All maternal deaths	n= 4901 elective, n= 12252	maternal death	17153	Hospital records.	Hospital records of maternal deaths.

						study		emergency				
Chama et al.[100]	2000	Nigeria	1995	1996	0.452	N.R.	patients who had either an elective or emergency caesarean section	There were 174 (87´9%) emergencies with 18 (9%) unbooked cases. All the 24 (12´1%) elective caesarean sections were booked patients.	maternal death	198	The case notes of patients who had either an elective or emergency caesarean section at the University of Maiduguri Teaching Hospital (UMTH) Maiduguri, from January 1995 to December 1996 inclusively were retrieved and analysed	Case notes
van Ham et al.[127]	1997	The Netherlands	1983	1992	0.830	retrospective study	all caesarean sections	primary elective n=718, primary acute n=859, Primary CS n=1577, Secondary CS n=1070, Emergency CS n=1929	maternal death	2647	N.R.	
Benaron et al.[128]	1971	United States	1959	1963	0.860	survey	all deliveries	N.R.	maternal death	412	Well documented records. Autopsies were performed in all cases of direct maternal death. All perinatal records and autopsy protocols were studied and abstracted.	Autopsies were performed in all cases of direct maternal death.
Tomta et al.[129]	2003	Togo	2002	2002	0.428	prospective and descriptive study	All caesarean sections	In 89.6% of the cases (n = 285), it was an emergency.	early perioperative mortality	306	Data collection was carried out using a survey form, immediately after death, a detailed description of the perioperative complications and causes of death is recorded.	Immediately after death, a detailed description of the perioperative complications and causes of death is recorded.
Drazancic[130]	2005	Croatia	1991	2003	0.720	N.R.	all deliveries	N.R.	maternal death	62,392	Death records presented to the conference or perinatal mortality in Croatia.	Death records.
Semeshi et al.[131]	1970	Hungary	1964	1968	0.704	N.R.	1000 caesarean sections	N.R.	maternal mortality, neonatal mortality	1000	N.R.	

Abbreviations:
N.R.=Not reported, CS= Caesarean section

Table 15: Specific causes of death along with their respective categories based on ICD-MM

Study	Specific cause	Cause of death category	Cause-specific deaths	Total deaths
Okafor et al.[90]	Failure to intubate and pulmonary aspiration	Unanticipated complications of management	1	1
Lilford et al.[19]	Myocardial infarction	Non-obstetric complications	2	43
	Placenta previa; haemorrhage	obstetric haemorrhage	1	43
	Infected broad ligament haematoma	Other obstetric complications	1	43
	Failed intubation	Unanticipated complications of management	2	43
	Pre-eclampsia	Hypertensive disorders	2	43
	Amniotic fluid embolism	Obstetric embolism	1	43
	Sepsis	Pregnancy-related infection	7	43
	Pulmonary embolism	Obstetric embolism	3	43
	Carcinoma of the oesophagus	Non-obstetric complications	2	43
	Eclampsia	Hypertensive disorders	3	43
	Trauma	Coincidental causes	1	43
	Tuberculosis meningitis	Non-obstetric complications	1	43
	Primary hepatoma	Non-obstetric complications	1	43
	Inhalation	Unanticipated complications of management	1	43
	Cerebral haemorrhage (direct)	Non-obstetric complications	5	43
	Myocarditis (indirect)	Non-obstetric complications	1	43
	Hearth failure (indirect)	Non-obstetric complications	1	43
	Not determined	Unknown/undetermined	1	43
	Known pulmonary hypertension	hypertension disorder	1	43
	Status asthmaticus	Non-obstetric complications	1	43
	Septicaemia	Pregnancy-related infection	1	43
	Hepatic failure	Non-obstetric complications	1	43
	Serum hepatitis	Non-obstetric complications	1	43
	Disseminated intravascular coagulation	Obstetric Haemorrhage	1	43
	Inhalation	Unanticipated complications of management	1	43
	Kyphoscoliosis and respiratory arrest (indirect)	Non-obstetric complications	1	43
	Pulmonary (direct)	Other obstetric complications	1	43
Holmer et al.[95]	Haemorrhage	obstetric haemorrhage	64	99
	Hypertensive disorders	Hypertensive disorders	20	99
	Sepsis	Pregnancy-related infection	12	99
	Embolism	Obstetric embolism	1	99
	Indirect causes	Non-obstetric complications	11	99
	Unknown	Unknown/undetermined	11	99

Crichton et al.[23]	Septicaemia	Pregnancy-related infection	37	78
Anger et al.[50]	Obstetric hemorrhage	obstetric haemorrhage	18	29
Nolens et al.[78]	Complete spinal block with cardiac arrest	Unanticipated complications of management	4	5
	Complete spinal block with hypoxic brain damage	Unanticipated complications of management	1	5
Ekanem et al.[40]	Sepsis	Pregnancy-related infection	3	12
	Haemorrhage	obstetric haemorrhage	3	12
	Sepsis	Pregnancy-related infection	3	12
	Haemorrhage	obstetric haemorrhage	3	12
	Anaesthetic accident	Unanticipated complications of management	2	12
	Anaesthetic complication	Unanticipated complications of management	1	12
McKenzie[87]	Anaesthetic associated	Unanticipated complications of management	21	21
Kuzma[9]	Intracranial hemorrhage/ Eclampsia	hypertensive disorders	1	2
	Multi-organ failure	Pregnancy-related infection	1	2
Rutgers et al.[59]	Haemorrhage	obstetric haemorrhage	10	18
	Anaesthetic accidents	Unanticipated complications of management	3	18
	Sepsis	Pregnancy-related infection	3	18
	Not clear	Unknown/undetermined	2	18
Remy et al.[17]	Postoperative infection	Pregnancy-related infection	6	22
	Consumption coagulopathy	obstetric haemorrhage	4	22
	Pulmonary embolism	Obstetric embolism	3	22
	Cardiovascular failure	Non-obstetric complications	3	22
	Liver disease (acute fatty liver dystrophy, acute pregnancy fatty liver)	Non-obstetric complications	2	22
	Cardiomyopathy	Non-obstetric complications	2	22
	Brain edema - eclampsia	Hypertensive disorders	1	22
	Polytrauma	Coincidental causes	1	22
Kalisa et al.[89]	Sepsis/peritonitis following caesarean section	Pregnancy-related infection	2	3
Andrade et al.[60]	Post-caesarean hemorrhage without previous bleeding	Obstetric Haemorrhage	2	10
	Marginal placenta previa without bleeding	Obstetric Haemorrhage	2	10
	Nulliparous pelvic presentation with stroke	Non-obstetric complications	2	10
	Postoperative pulmonary embolism	Obstetric embolism	1	10
	Disseminated intravascular coagulation with post-hemorrhage surgery	Obstetric Haemorrhage	1	10
	Dead fetus in a patient with stroke	Non-obstetric complications	1	10
	Postoperative paralytic ileus.	Non-obstetric complications	1	10
Chattopadhyay et al.[71]	Haemorrhage	Obstetric Haemorrhage	3	9
	Infection	Pregnancy-related infection	2	9
	Pulmonary embolism	Obstetric embolism	2	9

	Anaesthesia	Unanticipated complications of management	2	9
Krone et al.[3]	Pulmonary embolism	Obstetric embolism	2	10
	Paralytic lleus	Non-obstetric complications	2	10
	Cerebral vein thrombosis	Other obstetric complications	1	10
	Amniotic fluid embolism	Obstetric embolism	1	10
	Incident under anesthesia (placenta increta hysterectomy)	Unanticipated complications of management	1	10
	Heart failure with hypertension	Non-obstetric complications	1	10
	Apoplexy with hemiplegia	Non-obstetric complications	1	10
	Afibrinogeniomy	Non-obstetric complications	1	10
Zahran et al.[13]	Complications after caesarean section	Other obstetric complications	13	26
De Muylder[93]	Septicaemia	Pregnancy-related infection	5	22
	Septic shock	Pregnancy-related infection	1	22
	Anaesthetic problems	Unanticipated complications of management	3	22
	Hemorrhage	obstetric haemorrhage	2	22
	Haemorrhage and coagulation defect	obstetric haemorrhage	1	22
	Haemorrhagic complications	obstetric haemorrhage	1	22
	Post-operative complications	Other obstetric complications	2	22
	Pulmonary embolism	Obstetric embolism	1	22
	Post-operative septicaemia	Pregnancy-related infection	1	22
	Post-operative haemorrhage	obstetric haemorrhage	2	22
	Uterine rupture	obstetric haemorrhage	2	22
	Eclampsia	Hypertensive disorders	1	22
Rojas et al.[20]	Post-operative infection	Pregnancy-related infection	18	18
Campbell[7]	Peritonitis	Pregnancy-related infection	1	29
	Septicaemia	Pregnancy-related infection	13	29
	Pneumonia	Non-obstetric complications	4	29
	Shock, exhaustion	Unknown/undetermined	2	29
	Pre-eclampsia. eclampsia	Hypertensive disorders	3	29
	Pulmonary embolism	Obstetric embolism	3	29
	Cardiac arrest during operation	Other obstetric complications	1	29
	Cor pulmonale	Non-obstetric complications	1	29
	Renal Failure	Non-obstetric complications	1	29
Kamilya et al.[83]	PPH	obstetric haemorrhage	9	27
	Venous thromboembolism	Obstetric embolism	6	27
	Amniotic fluid embolism	Obstetric embolism	3	27
	Puerperal infection	Pregnancy-related infection	5	27
	Anesthetic complications	Unanticipated complications of management	3	27
	Mismatched blood Transfusion	Unanticipated complications of management	1	27

Schuitemaker et al.[80]	Hypovolemic shock, underlying cause postpartum haemorrhage	Obstetric Haemorrhage	3	57
	Ischemia/cerebral death, complication cardiac arrest	Other obstetric complications	1	57
	Sepsis	Pregnancy-related infection	3	57
	Necrotic enterocolitis/ sepsis	Pregnancy-related infection	3	57
	Anemia/ heart failure	Non-obstetric complications	1	57
	Infected hematoma/sepsis	Pregnancy-related infection	1	57
	Unknown	Unknown/undetermined	1	57
	Respiratory arrest (anesthesia complication)	Unanticipated complications of management	1	57
	Mendelssohn syndrome (anesthesia complication)	Unanticipated complications of management	1	57
	Shock (anesthesia complication)	Unanticipated complications of management	1	57
	Cerebral death (anesthesia complication)	Unanticipated complications of management	1	57
	Cerebral bleeding during or shortly after CS (pre-eclampsia)	Hypertensive disorders	8	57
	Embolism	Obstetric embolism	4	57
	Hemorrhage uterine incision	obstetric haemorrhage	1	57
Kallianidis et al.[2]	Preeclampsia (hypertensive disorder)	Hypertensive disorders	12	86
	Eclampsia (hypertensive disorder)	Hypertensive disorders	6	86
	HELLP (hypertensive disorder)	Hypertensive disorders	7	86
	Obstetric Sepsis	Pregnancy-related infection	7	86
	Obstetric hemorrhage	Obstetric haemorrhage	7	86
	Thromboembolism	Obstetric embolism	5	86
	Acute Fatty Liver of Pregnancy (Obstetric causes)	Other obstetric complications	3	86
	Amniotic Fluid Embolism	Obstetric embolism	2	86
	Anesthesiologic complication	Unanticipated complications of management	1	86
	Unknown	Unknown/undetermined	5	86
	Cardiovascular disease (Non-obstetric causes)	Non-obstetric complications	11	86
	Cerebrovascular disease (Non-obstetric causes)	Non-obstetric complications	10	86
	Non-obstetric sepsis (Non-obstetric causes)	Non-obstetric complications	5	86
	Mental disorders (Non-obstetric causes)	Non-obstetric complications	2	86
	Other (Non-obstetric causes)	Non-obstetric complications	3	86
Oladapo et al.[84]	Massive intraperitoneal bleeding following slipped ligature	obstetric haemorrhage	1	1
Armon[62]	Associated medical or surgical conditions	Unanticipated complications of management	6	10
	Anaesthetic accidents	unanticipated complications of management	4	10
Ozumba et al.[86]	Pulmonary embolism	Obstetric embolism	1	26
	Haemorrhage	obstetric haemorrhage	8	26

	Anesthesia	Unanticipated complications of management	2	26
	Sepsis	Pregnancy-related infection	9	26
	Hypertensive disorders of pregnancy	Hypertensive disorders	6	26
Clark et al.[92]	Haemorrhage	obstetric haemorrhage	3	58
	Sepsis	Pregnancy-related infection	1	58
Gebhardt et al.[57]	Non-pregnancy-related infections	Non-obstetric complications	166	1243
	Pre-eclampsia	Hypertensive disorders	68	1243
	Eclampsia	Hypertensive disorders	146	1243
	HELLP syndrome	Hypertensive disorders	44	1243
	Medical and surgical disorders	Unanticipated complications of management	125	1243
	Obstetric haemorrhage (excludes BDACS)	obstetric haemorrhage	147	1243
	Pregnancy-related sepsis	Pregnancy-related infection	100	1243
	Bleeding – CS (BDACS)	obstetric haemorrhage	222	1243
	Miscarriage	Pregnancies with abortive outcome	1	1243
	Unknown	Unknown/undetermined	41	1243
	Coincidental cause	Coincidental causes	20	1243
	Anaesthetic complications	Unanticipated complications of management	79	1243
	Embolism	obstetric embolism	44	1243
	Acute collapse – cause unknown	Unknown/undetermined	27	1243
Briand et al.[76]	Post-partum haemorrhage	Obstetric haemorrhage	63	157
	Hypertensive complications	Hypertensive disorders	39	157
	Obstructed labor	Other obstetric complications	5	157
	Puerperal infection	Pregnancy-related infection	25	157
	Rupture of the uterus	obstetric haemorrhage	1	157
	Other direct obstetric causes	Other obstetric complications	9	157
	Other indirect obstetric causes	Non-obstetric complications	15	157
Wirakusumah[39]	Sepsis	Pregnancy-related infection	2	5
	Cerebral hemorrhage	Non-obstetric complications	1	5
	Anesthesia related	Unanticipated complications of management	1	5
	Embolism	obstetric embolism	1	5
Chi et al.[15]	Sepsis	Pregnancy-related infection	19	31
	Eclampsia	Hypertensive disorders	1	31
	Haemorrhage	obstetric haemorrhage	5	31
	Anesthesia-related	Unanticipated complications of management	3	31
	Pulmonary embolism	obstetric embolism	3	31
Nyamtema et al.[27]	Intraoperative haemorrhage	obstetric haemorrhage	10	18
	Anaesthetic-associated complications	Unanticipated complications of management	3	18
	Puerperal sepsis	Pregnancy-related infection	2	18
	Other complications of CS	Other obstetric complications	3	18

Mukherji et al.[48]	Haemorrhagic shock	obstetric haemorrhage	19	51
	General anesthesia	unanticipated complications of management	10	51
	Septicaemia	Pregnancy-related infection	7	51
	Eclampsia (excluding anaesthetic death)	Hypertensive disorders	3	51
	Hepatic failure	Non-obstetric complications	3	51
	Pulmonary edema	hypertensive disorders	2	51
	Unknown / pulmonary embolism	Unknown/undetermined	7	51
Igberase et al.[54]	Haemorrhage	obstetric haemorrhage	11	25
	Severe preeclampsia/eclampsia	Hypertensive disorders	7	25
	Infections	Pregnancy-related infection	6	25
	Anaesthetic complications	Unanticipated complications of management	1	25
Tsen et al.[91]	Failed intubation	Unanticipated complications of management	1	1
Palanisamy et al.[64]	Anesthesia-related	Unanticipated complications of management	0	0
Enohumah et al.[1]	Aspiration pneumonitis	Unanticipated complications of management	1	5
	Difficulty with airway management	Unanticipated complications of management	2	5
	Difficult airway/failed intubation	Unanticipated complications of management	1	5
	Oesophageal intubation	Unanticipated complications of management	1	5
Nwobodo et al.[79]	Anaphylactic reaction to general anesthetic agent.	Unanticipated complications of management	1	18
Zongo et al.[73]	Haemorrhage	obstetric haemorrhage	109	282
	Pre-eclampsia/eclampsia	Hypertensive disorders	100	282
	Puerperal infection/sepsis	Pregnancy-related infection	23	282
	Uterine rupture	obstetric haemorrhage	36	282
	Obstructed labor	Other obstetric complications	4	282
	Other direct causes (Excluding uterine rupture, ante- or post-partum hemorrhage, pre-eclampsia, obstructed labor and puerperal infection, the complications during surgery or anesthesia, suspected amniotic fluid embolism and thrombo-embolism (not confirmed by autopsy) were the most common direct causes of maternal death)	Other obstetric complications	22	282
	Other indirect causes (Anemia, malaria, HIV/AIDS and cardio-vascular disease were the most common indirect causes of maternal death.)	Non-obstetric complications	48	282
	Unclassified	Unknown/undetermined	2	282
Talebi Doluee et al.[67]	Direct cause	Other obstetric complications	21	44
	Indeterminate cause	Unknown/undetermined	2	44
Löfgren et al.[43]	Sepsis	Pregnancy-related infection	1	4

	Haemorrhage	obstetric haemorrhage	3	4
Maaløe et al.[22]	Related to intrauterine fetal death	Pregnancy with abortive outcome	3	4
	Severe abdominal infection with burst abdomen	Pregnancy-related infection	1	4
Andersgaard et al.[72]	Hypertensive disease of pregnancy	Hypertensive disorders	11	32
	Thromboembolism	obstetric embolism	7	32
	Other direct deaths	Other obstetric complications	6	32
	Amniotic fluid embolism syndrome	obstetric embolism	3	32
Rippmann[66]	Eclampsia	Hypertensive disorders	1	19
	Sepsis	Pregnancy-related infection	4	19
	Pre-eclampsia	Hypertensive disorders	1	19
	Embolism	obstetric embolism	2	19
	Uremia	Non-obstetric complications	1	19
	Air embolism	obstetric embolism	2	19
	Miliary tuberculosis	Non-obstetric complications	1	19
	Tetanus	Pregnancy-related infection	1	19
	Circulatory failure	Non-obstetric complications	1	19
	Pneumonia	Non-obstetric complications	1	19
	Anesthetic complications	Unanticipated complications of management	2	19
	Sinus thrombosis	Other obstetric complications	1	19
	Angioma	Non-obstetric complications	1	19
Bloom et al.[4]	Failed intubation	unanticipated complications of management	1	29
Ojo et al.[65]	Sepsis	Pregnancy-related infection	22	36
	Post partum hemorrhage (primary)	obstetric haemorrhage	1	36
	Post partum hemorrhage (secondary)	obstetric haemorrhage	3	36
	Eclampsia	Hypertensive disorders	1	36
Gundumure[37]	DIC	obstetric haemorrhage	1	7
	Collapse	Unknown/undetermined	1	7
	PPH DIC	obstetric haemorrhage	1	7
	Comatose	Non-obstetric complications	1	7
	Septic shock	Pregnancy-related infection	1	7
	Pneumonia in puerperal, pulmonary TB	Non-obstetric complications	1	7
Sachs et al.[74]	Infection	Pregnancy-related infection	3	27
	Haemorrhage	Obstetric haemorrhage	1	27
	Anesthesia complications	Unanticipated complications of management	1	27
	Pulmonary embolism	Obstetric embolism	2	27
Cisse et al.[52]	Infection	Pregnancy-related infection	15	73
	Haemorrhage	Obstetric haemorrhage	13	73
	complications of dysgravidia	Obstetric haemorrhage	9	73

	Anesthesia-reanimation problems	Unanticipated complications of management	9	73
Evrard et al.[45]	Sepsis	Pregnancy-related infection	7	9
	Haemorrhage	Obstetric haemorrhage	1	9
	Anesthesia	Unanticipated complications of management	1	9
Maswime et al.[18]	Caesarean-related hemorrhage	Obstetric haemorrhage	17	17
Amirikia et al.[82]	Sepsis	Pregnancy-related infection	5	10
	Pulmonary embolism	Obstetric embolism	1	10
	Rheumatic heart disease	Non-obstetric complications	1	10
	Renal failure/ Congenital heart disease	Non-obstetric complications	1	10
	Respiratory failure	Non-obstetric complications	1	10
	Amniotic fluid embolism	Obstetric embolism	1	10
Bolaji et al.[8]	Primary postpartum haemorrhage (PPH), Cardiac arrest	Obstetric haemorrhage	1	4
	Placenta accreta with bladder involvement, Primary PPH, Cardiac arrest	Obstetric haemorrhage	1	4
	Eclampsia (primary cause), Disseminated intravascular coagulopathy (DIC), Cerebral Haemorrhage	Hypertensive disorders	1	4
	Placenta praevia percreta with penetration and invasion of the bladder	Obstetric haemorrhage	1	4
Ikeako et al.[44]	Disseminated intravascular coagulation (DIC)	Obstetric haemorrhage	1	1
Tadesse et al.[24]	Uncontrollable bleeding	Obstetric haemorrhage	5	5
Okonta et al.[31]	Severe pre-eclampsia/ eclampsia	Hypertensive disorders	3	8
	Anaesthesia	Unanticipated complications of management	2	8
	Acute pulmonary embolism	Obstetric embolism	1	8
	Coagulation failure	Obstetric haemorrhage	2	8
Mekbib et al.[5]	Sepsis	Pregnancy-related infection	4	7
	Disseminated intravascular coagulopathy (DIC)	Obstetric haemorrhage	2	7
	Anaesthetic complications	Unanticipated complications of management	1	7
Ezechi et al.[61]	Shock secondary to gram-negative septicaemia and congestive cardiac failure.	Pregnancy-related infection	2	4
	Post-partum haemorrhage	Obstetric haemorrhage	2	4
Daniel et al.[51]	Puerperal sepsis	Pregnancy-related infection	6	10
	Complications of eclampsia	Hypertensive disorders	3	10
	Postpartum hemorrhage	Obstetric haemorrhage	1	10
Bukar et al.[32]	Haemorrhage	Obstetric haemorrhage	1	2

	Eclampsia	Hypertensive disorders	1	2
Njokanma et al.[56]	Aplastic Anaemia	Non-obstetric complications	1	3
	Endotoxic Shock	Pregnancy-related infection	1	3
	ARF/Acute Hepatic Atrophy	Non-obstetric complications	1	3
Etuk et al.[68]	Haemorrhage	Obstetric haemorrhage	11	24
	Sepsis	Pregnancy-related infection	11	24
	Eclampsia [renal failure]	Hypertensive disorders	2	24
Imarengiaye et al.[70]	Anesthesia complications	Unanticipated complications of management	3	11
	Non-anesthetic factors	Other obstetric complications	8	11
Greenhill[41]	Toxemia of pregnancy	Pregnancy-related infection	3	18
	Peritonitis	Pregnancy-related infection	5	18
	Heart disease	Non-obstetric complications	1	18
	Abruptio placentae	Obstetric haemorrhage	1	18
	Pneumonia	Non-obstetric complications	2	18
	Sepsis	Pregnancy-related infection	1	18
	Gangrenous appendicitis	Non-obstetric complications	1	18
	Pulmonary embolism	Obstetric embolism	1	18
	Eclampsia	Hypertensive disorders	2	18
	Tuberculosis meningitis	Non-obstetric complications	1	18
Onoh et al.[29]	Haemorrhage and severe anemia	Obstetric haemorrhage	57	129
	Overwhelming infection	Pregnancy-related infection	41	129
	Hypertensive diseases	Hypertensive disorders	39	129
	Cause of death uncertain	Unknown/undetermined	14	129
Ugwu et al.[69]	Massive intraoperative haemorrhage	Obstetric haemorrhage	5	7
	Cardiopulmonary failure during anaesthesia	Unanticipated complications of management	1	7
	Valvular heart disease	Non-obstetric complications	1	7
Okezie et al.[75]	Haemorrhage	Obstetric haemorrhage	4	7
	Pulmonary oedema	hypertensive disorders	2	7
	Anaesthetic complications	Unanticipated complications of management	1	7
Raphael et al.[25]	Antepartum eclampsia	Hypertensive disorders	2	5
	Intrapartum eclampsia	Hypertensive disorders	2	5
	PPH	Obstetric haemorrhage	1	5
Ijaiya et al.[34]	Sepsis	Pregnancy-related infection	9	29
	Haemorrhage	Obstetric haemorrhage	8	29
	Anaesthesia	Unanticipated complications of management	4	29
	Embolism	Obstetric haemorrhage	4	29
	Cerebrovascular accident (Haemorrhagic)	Non-obstetric complications	1	29
	Acute Renal Failure	Non-obstetric complications	1	29

	Heart Failure	Non-obstetric complications	1	29
	Lobar Pneumonia	Non-obstetric complications	1	29
Krause et al.[42]	Peritonitis (paralytic ileus)	Pregnancy-related infection	1	19
	Afibrinogenemia after ex. Placental removal	Non-obstetric complications	1	19
	Eclampsia	Hypertensive disorders	1	19
	Strangulation Ileus with Peritonitis	Non-obstetric complications	1	19
	Fat embolism	Obstetric embolism	1	19
	Pulmonary edema in severe EPH gestosis	Hypertensive disorders	1	19
	Miliary tuberculosis	Non-obstetric complications	1	19
	Eclampsia	Hypertensive disorders	1	19
	Pulmonary embolism	Obstetric embolism	1	19
	Amniotic fluid embolism	Obstetric embolism	2	19
	Hemascos due to splenic rupture	Non-obstetric complications	1	19
	Heart failure with combined mitral vitium-aortic vitium	Non-obstetric complications	1	19
	Severe edema-proteinuria-hypertension (EPH) gestosis with Kidney failure	Hypertensive disorders	1	19
	Amniotic fluid embolism with coagulation disorder	Obstetric embolism	1	19
	Couvelaire's disease with Coagulation disorder	Obstetric haemorrhage	1	19
	Severe EPH gestosis with Kidney failure	Hypertensive disorders	1	19
	Peritonitis in gallbladder empyema	Pregnancy-related infection	1	19
	Heart failure	Non-obstetric complications	1	19
Alegre Villariz et al.[49]	Sepsis	Pregnancy-related infection	1	1
Muziarelli et al.[47]	anesthesia complications	Unanticipated complications of management	1	2
	failure cardiorespiratory fission from septic shock peritonitic	Pregnancy-related infection	1	2
Pekhlivanov[38]	Cardiac ill (Pathologically anatomical findings of pericarditis, pancreatic heart, decompensation of the liver, coarctation of the aorta were found.)	Non-obstetric complications	1	5
	Cardiac ill	Non-obstetric complications	1	5
	Acute blood loss	Non-obstetric complications	2	5

	Pulmonary embolism	Obstetric embolism	1	5
Poradovsky[94]	Inappropriate/unsuitable indications	Unknown/undetermined	6	60
Imbert et al.[30]	Haemorrhage	Obstetric haemorrhage	2	7
	Multiple organ failure	Pregnancy-related infection	1	7
	Decapsulation of the liver	Non-obstetric complications	2	7
	Cerebral hemorrhage	Non-obstetric complications	1	7
	ARDS (acute respiratory distress syndrome)	Non-obstetric complications	1	7
Picaud et al.[77]	Anesthesia complications	Unanticipated complications of management	4	12
	Coagulation disorders	Obstetric haemorrhage	6	12
	Post-operative infections	Pregnancy-related infection	2	12
Szczepanski et al.[85]	Placental hemorrhage	Obstetric haemorrhage	3	12
	Premature separation of placenta and hemorrhage	Obstetric haemorrhage	1	12
	Amniotic fluid embolism	Obstetric embolism	2	12
	Diathesis hemorrhagic	Non-obstetric complications	2	12
	Bleeding diathesis with hemorrhages to brain tissue and chronic renal failure	Non-obstetric complications	1	12
	Pancreatitis	Non-obstetric complications	1	12
	Heart defects with concomitant active inflammatory process in the myocardium and endocardium	Non-obstetric complications	2	12
Carazzone et al.[26]	Eclampsia	Hypertensive disorders	1	8
	Peritonitis	Pregnancy-related infection	5	8
	Disk clot pathology	Other obstetric complications	1	8
	Rupture uterus	Obstetric haemorrhage	1	8
Georgiades et al.[46]	Heavy bleeding in placenta previa	Obstetric haemorrhage	1	4
	Brain embolism as part of endocarditis	Non-obstetric complications	1	4
	Consumption coagulopathy with an existing mitral vitium	Obstetric haemorrhage	1	4
	Cardiovascular failure with silent peritonitis	Non-obstetric complications	1	4
Chavez Azuela et al.[58]	Renal insufficiency	Non-obstetric complications	7	30
	Stroke	Non-obstetric complications	6	30
	Heart attack	Non-obstetric complications	10	30
	Pulmonary embolism	Obstetric embolism	2	30
	Bacteremic shock	Pregnancy-related infection	2	30
	Acidosis	Non-obstetric complications	1	30
	Hypovolemia	Unknown/undetermined	1	30
	Acute lung edema	Hypertensive disorders	1	30
Kartushina[6]	Peritonitis and sepsis	Pregnancy-related infection	11	30

	Thromboembolism	Obstetric embolism	2	30
	Air embolism	Obstetric embolism	1	30
	Shock and collapse	Unknown/undetermined	1	30
	Labour bleeding and hypo- and atony of the uterus in the early postpartum period	Obstetric haemorrhage	8	30
	Eclampsia	Hypertensive disorders	3	30
	Diseases of the cardiovascular system	Non-obstetric complications	1	30
	Malignant tumors of various organs	Non-obstetric complications	1	30
	Brain hemorrhage	Non-obstetric complications	2	30
Zhu et al.[11]	Pregnancy induced hypertension	Hypertensive disorders	23	150
	Embolism	Obstetric embolism	19	150
	Obstetric hemorrhage	Obstetric haemorrhage	18	150
	Puerperal infection	Pregnancy-related infection	12	150
	Anesthesia complications	Unanticipated complications of management	1	150
	Heart disease	Non-obstetric complications	22	150
	Liver disease	Non-obstetric complications	15	150
	Other indirect	Non-obstetric complications	40	150
Strobel[21]	Pulmonary embolism	Obstetric embolism	4	8
	Vein thrombosis	Other obstetric complications	1	8
Warm et al.[33]	Eclampsia	Hypertensive disorders	14	49
	Septic disorders	Pregnancy-related infection	10	49
	Peritonitis	Pregnancy-related infection	9	49
	Paralytic ileus	Non-obstetric complications	9	49
	Circulatory failure	Non-obstetric complications	4	49
	Heart defect (decompensated)	Non-obstetric complications	3	49
	Embolism	Obstetric embolism	2	49
	Shock	Unknown/undetermined	2	49
	Acute pancreatic necrosis	Non-obstetric complications	1	49
Kambo et al.[120]	Pulmonary embolism	Obstetric embolism	5	21
	Severe anemia	Non-obstetric complications	4	21
	Haemorrhage	Obstetric haemorrhage	4	21
	Amniotic fluid embolism	Obstetric embolism	3	21
	Septicemia	Pregnancy-related infection	2	21
	Eclampsia	Hypertensive disorders	1	21
	Adult respiratory distress syndrome	Non-obstetric complications	1	21
	Anesthetic complication	Unanticipated complications of management	1	21
Fesseha et al.[102]	Sepsis	Pregnancy-related infection	1	2
	Not reported	Unknown/undetermined	1	2
Ojiyi et al.[103]	Difficult intubation	Unanticipated complications of management	1	3

	Intrapartum haemorrhage.	Obstetric haemorrhage	1	3
Garba et al.[104]	Eclampsia	Hypertensive disorders	6	10
	Obstructed labour	Other obstetric complications	2	10
	Antepartum haemorrhage (abruption placentae).	Obstetric haemorrhage	2	10
Kandasamy et al.[110]	Obstructed labor	Other obstetric complications	1	2
	Antepartum hemorrhage	Obstetric haemorrhage	1	2
Kor-Anantakul et al.	Amniotic fluid embolism	Obstetric embolism	1	2
	Intracerebral haemorrhage	Non-obstetric complications	1	2
Yaïch et al.[111]	Uterine rupture	Obstetric haemorrhage	3	5
	Eclampsia	Hypertensive disorders	1	5
	HRP/ postpartum haemorrhage	Obstetric haemorrhage	1	5
Cebekulu et al.[107]	Fatal pulmonary edema	hypertensive disorders	1	1
Diawara et al.[106]	Haemorrhage	Obstetric haemorrhage	3	4
Teguete et al.[116]	Haemorrhage (direct)	Obstetric haemorrhage	45	244
	Hypertension and complications (direct)	Hypertensive disorders	17	244
	Dystocia (direct)	Other obstetric complications	5	244
	Uterine rupture (direct)	Obstetric haemorrhage	101	244
	Postpartum infection (direct)	Pregnancy-related infection	57	244
	Other direct causes	Other obstetric complications	8	244
	Hemoglobinopathy (indirect)	Non-obstetric complications	1	244
	Anemia (indirect)	Non-obstetric complications	1	244
	Cardiac disease (indirect)	Non-obstetric complications	7	244
	Other indirect causes	Non-obstetric complications	2	244
Eshiet et al.[118]	Hypoxia following failed intubation	Unanticipated complications of management	4	5
	Eclampsia - unsuccessful cardiopulmonary resuscitation	Hypertensive disorders	1	5
Goswami et al.[117]	Anesthesia complication.	Unanticipated complications of management	1	50
	Necrotizing fasciitis	Pregnancy-related infection	1	50
Abebe et al.[113]	Respiratory failure	Non-obstetric complications	4	9
	Haemorrhagic shock	Obstetric haemorrhage	2	9
	Disseminated intravascular coagulation	Obstetric haemorrhage	2	9
	Aspiration pneumonia	Unanticipated complications of management	1	9
Rasoarimahandry et al.[126]	Infectious complications (in a context of psychometry and chorioamnionitis or egg opening more than 24 hours)	Pregnancy-related infection	5	11
	Coagulopathy	Obstetric haemorrhage	1	11
	Irreversible hypovolemic shock (haemorrhagic)	Obstetric haemorrhage	1	11

	Eclamptic illness	Hypertensive disorders	2	11
	Retroplacental hematoma [HRP]	Other obstetric complications	1	11
	Anesthetic accident	Unanticipated complications of management	1	11
Okafor et al.[109]	Failure to intubate/ventilate and pulmonary aspiration	Unanticipated complications of management	6	9
	Massive intraoperative haemorrhage (following failure to achieve haemostasis)	Obstetric haemorrhage	1	9
Nelissen et al.[115]	Sepsis	Pregnancy-related infection	1	5
Sekirime et al.[123]	AIDS	Non-obstetric complications	2	7
	Septicemia	Pregnancy-related infection	4	7
	Meningitis	Non-obstetric complications	1	7
Adisso et al.[124]	Cardiac arrest (anesthesia related)	Unanticipated complications of management	2	2
Richard et al.[122]	Anesthesia accident	Unanticipated complications of management	1	50
	Postoperative hemorrhage	Obstetric haemorrhage	1	50
	Infection	Pregnancy-related infection	1	50
	Transfusion accident	Unanticipated complications of management	1	50
	Haemorrhage	Obstetric haemorrhage	1	50
	Eclampsia	Hypertensive disorders	2	50
	Haemorrhage	Obstetric haemorrhage	5	50
Meda et al.[121]	Haemorrhage due to uterine rupture	Obstetric haemorrhage	4	120
	Placenta previa	Obstetric haemorrhage	1	120
	Placental abruption	Obstetric haemorrhage	1	120
	Postoperative complications	Other obstetric complications	3	120
Asıcıoglu et al.[114]	Pulmonary embolism	Obstetric embolism	1	1
Pereira et al.[101]	Post-operative infection	Pregnancy-related infection	11	17
	Coagulopathy	Obstetric haemorrhage	3	17
	Hypertensive complications	Hypertensive disorders	3	17
Khawaja et al.[125]	Pulmonary embolism	Obstetric embolism	1	1
Ouedraogo et al.	Bleeding	Obstetric haemorrhage	18	25
	Infection	Pregnancy-related infection	7	25
Rabiu et al.[105]	Massive obstetric hemorrhage	Obstetric haemorrhage	3	3
Chau-In et al.[81]	Anesthesia complications	Unanticipated complications of management	8	8
MATERNAL AND PERINATAL MORTALITY COMMITTEE[36]	Ruptured splenic artery (unrelated to CS)	Non-obstetric complications	1	7
	Intraventricular hemorrhage (unrelated to CS)	Non-obstetric complications	1	7
	Endotoxic shock related to E.coli septicaemia (unrelated to CS)	Non-obstetric complications	1	7
	Pulmonary embolism	Obstetric embolism	2	7
	Anesthesia complications	Unanticipated complications of management	1	7
	Cardiac arrest	Other obstetric complications	1	7

Moldin et al.[16]	Pulmonary embolism	Obstetric embolism	2	13
	Acute peritonitis + postop. wound infection	Pregnancy-related infection	1	13
	Pulmonary embolism	Obstetric embolism	1	13
	Sub-arachnoid hemorrhage	Non-obstetric complications	1	13
	Pulmonary edema + bronchopneumonia + coagulopathy	Hypertensive disorders + non-obstetric complications + obstetric haemorrhage	1	13
	Amniotic fluid embolism	Obstetric embolism	1	13
	Pulmonary embolism	Obstetric embolism	1	13
	Intra-abdominal hemorrhage	Obstetric haemorrhage	1	13
	Coagulopathy	Obstetric haemorrhage	1	13
	Pulmonary embolism	Obstetric embolism	1	13
	Septicemia+ acute peritonitis	Pregnancy-related infection	1	13
	Amniotic fluid embolism	Obstetric embolism	1	13
	Ablatio placentae premature	Obstetric haemorrhage	1	13
	Cardiac arrest + acute myocarditis	Other obstetric complications	1	13
	Amniotic fluid embolism	Obstetric Embolism	2	13
	Coagulopathy	Obstetric haemorrhage	2	13
Rubin et al.[12]	Pulmonary embolism	Obstetric embolism	6	16
	Cardiorespiratory arrest during general anesthesia	Unanticipated complications of management	3	16
	Profuse bleeding at CSD	Obstetric haemorrhage	1	16
	Bilateral basal pulmonary infiltrates and effusions.	Non-obstetric complications	1	16
	Eclampsia	Hypertensive disorders	1	16
	Cerebral hemorrhage	Non-obstetric complications	1	16
	DIC	Obstetric haemorrhage	1	16
	Cardiorespiratory arrest due to high spinal anesthesia	Unanticipated complications of management	1	16
	Eclampsia	Hypertensive disorders	1	16
	DIC	Obstetric haemorrhage	1	16
	Hepatic necrosis, acute renal tubular necrosis, systemic candidiasis	Non-obstetric complications	1	16
Bruce et al.[35]	Irreversible shock from acute anemia	Non-obstetric complications	3	6
	Irreversible post operative shock (placenta previa)	Obstetric haemorrhage	1	6
	Uterine rupture (pelvic vice)	Obstetric haemorrhage	1	6
	Cardiac arrest (anesthetic shock)	Unanticipated complications of management	1	6
Abbassi et al.[14]	Haemorrhage, uterine inertia	Obstetric haemorrhage	1	9

	Haemorrhagic placenta previa	Obstetric haemorrhage	2	9
	Haemorrhage, CIVD	Obstetric haemorrhage	1	9
	Irreversible hemorrhagic shock (due to the surgical procedure itself)	Obstetric haemorrhage	1	9
	Eclampsia	Hypertensive disorders	1	9
	Haemorrhagic stroke	Non-obstetric complications	1	9
	Eclampsia, HELLP syndrome	Hypertensive disorders	1	9
	eclampsia	Hypertensive disorders	1	9
	HELLP syndrome	Hypertensive disorders	1	9
Pinsker et al.[63]	Toxemia (direct)	Hypertensive disorders	44	102
	Infection (direct)	Pregnancy-related infection	27	102
	Acute anemia (direct)	Non-obstetric complications	10	102
	Anesthetic accidents (direct)	Unanticipated complications of management	9	102
	Thromboembolism (direct)	Obstetric embolism	3	102
	Heart disease (indirect)	Non-obstetric complications	4	102
	Tuberculosis (indirect)	Non-obstetric complications	2	102
	Pericarditis (indirect)	Non-obstetric complications	1	102
	Acute abdomen (indirect)	Non-obstetric complications	1	102
	Fimic meningoencephalitis	Non-obstetric complications	1	102
	Cerebral aneurysm rupture	Non-obstetric complications	1	102
	Allergy to pyrazolone	Non-obstetric complications	1	102
	Pheochromocytoma	Non-obstetric complications	1	102
Beck et al.[10]	Heavy bleeding (atonic bleeding, retroperitoneal bleeding, diffuse intraperitoneal bleeding, coagulation disorder)	Obstetric haemorrhage	18	55
	Pulmonary embolism	Obstetric embolism	7	55
	Anesthetic incidents	Unanticipated complications of management	4	55
	Shock	Unknown/undetermined	1	55
	Rupture	Obstetric haemorrhage	1	55
	Peritonitis	Pregnancy-related infection	1	55
	Suture dehiscence	Other obstetric complications	2	55
	Liver damage	Non-obstetric complications	1	55
	Cerebral complication	Non-obstetric complications	2	55
	Uraemia	Non-obstetric complications	2	55
	Pneumonia	Non-obstetric complications	1	55
	Volvulus	Non-obstetric complications	1	55
	Shock lung	Unknown/undetermined	2	55
	Intraop. cardiac	Unknown/undetermined	1	55
	Cardiac	Non-obstetric complications	1	55

Saving Mothers 2017[99]	Medical and surgical disorders	Unanticipated complications of management	34	362
	Non-pregnancy-related infections	Non-obstetric complications	45	362
	Pregnancy-related sepsis	Pregnancy-related infection	27	362
	Obstetric haemorrhage	Obstetric haemorrhage	100	362
	Hypertension	Hypertensive disorders	95	362
	Anaesthetic complications	Unanticipated complications of management	24	362
	Adverse drug reactions	Non-obstetric complications	1	362
	Embolism	Obstetric embolism	16	362
	Acute collapse - cause unknown	Unknown/undetermined	3	362
	Miscellaneous	Unknown/undetermined	2	362
	Unknown	Unknown/undetermined	9	362
Slaytor et al.[96]	Postpartum haemorrhage (direct COD)	Obstetric haemorrhage	1	34
	Amniotic fluid embolism (direct COD)	Obstetric embolism	4	34
	Pulmonary thromboembolism (direct COD)	Obstetric embolism	2	34
	Ventricular fibrillation (direct COD)	Non-obstetric complications	1	34
	Cerebral haemorrhage (direct COD)	Non-obstetric complications	1	34
	Unascertained (direct COD)	Unknown/undetermined	1	34
	Cerebral infarction (direct COD)	Non-obstetric complications	1	34
	Renal failure (direct COD)	Non-obstetric complications	1	34
	Hypoxia (direct COD) contributory cause: Failed intubation	Unanticipated complications of management	1	34
	Anaphylactic reaction of unknown aetiology (direct COD)	Non-obstetric complications	1	34
	Puerperal cardiomyopathy (direct COD)	Non-obstetric complications	1	34
	Cardiac arrhythmia (indirect COD)	Non-obstetric complications	1	34
	Infective endocarditis (indirect COD)	Non-obstetric complications	1	34
	Aortic valve disease (indirect COD)	Non-obstetric complications	1	34
	Suicide by gunshot wound (indirect COD)	Other obstetric complications	1	34
	Suicide by hanging (indirect COD)	Other obstetric complications	1	34
	Drug overdose (indirect COD)	Other obstetric complications	1	34
	Sub arachnoid haemorrhage (indirect COD)	Non-obstetric complications	1	34
	Retroperitoneal haemorrhage (indirect COD), contributory: Trauma	Non-obstetric complications	1	34
	Pneumonia (indirect COD)	Non-obstetric complications	1	34
	Pulmonary hypertension (indirect COD)	Hypertensive disorders	1	34
	Motor vehicle accident (Incidental COD)	Coincidental causes	1	34
	Glioma (Incidental COD)	Non-obstetric complications	1	34
	Ovarian cancer (Incidental COD)	Non-obstetric complications	1	34
	Metastatic melanoma (Incidental COD)	Non-obstetric complications	1	34

	Hepatic failure (Incidental COD)	Non-obstetric complications	1	34
	E. coli sepsis (Incidental COD)	Non-obstetric complications	1	34
	Meningococcal septicaemia (Incidental COD)	Non-obstetric complications	1	34
	Sub arachnoid haemorrhage (Incidental COD)	Non-obstetric complications	1	34
	Intracerebral haemorrhage (Incidental COD)	Non-obstetric complications	1	34
NCCEMD[97]	Medical and surgical disorders	Unanticipated complications of management	137	1201
	Non-pregnancy-related	Non-obstetric complications	124	1201
	Ectopic pregnancy	Pregnancy with abortive outcome	1	1201
	Pregnancy-related sepsis	Pregnancy-related infection	100	1201
	Obstetric haemorrhage	Obstetric haemorrhage	345	1201
	Hypertension	Hypertensive disorders	297	1201
	Anaesthetic complications	Unanticipated complications of management	64	1201
	Adverse drug reactions	Non-obstetric complications	9	1201
	Embolism	Obstetric embolism	43	1201
	Acute collapse - cause unknown	Unknown/undetermined	23	1201
	Miscellaneous	Unknown/undetermined	3	1201
	Unknown	Unknown/undetermined	38	1201
NCCEMD[98]	Bleeding to death	Obstetric haemorrhage	1	960
	Haemorrhage	Obstetric haemorrhage	1	960
	Abruptio placentae	Obstetric haemorrhage	1	960
	hemoperitoneum from broad ligament bleeding	Obstetric haemorrhage	1	960
	Coagulopathy	Obstetric haemorrhage	1	960
	Pregnancy related sepsis	Pregnancy-related infection	102	960
	Anesthesia complications	Unanticipated complications of management	63	960
	Cardiac arrest	Other obstetric complications	1	960
Maswime et al.[18] 2016	Bleeding during and after caesarean section	Obstetric haemorrhage	26	26
Hogberg et al.[88]	Anesthesia complication	Unanticipated complications of management	2	103
	Postoperative shock (unspecified)	Unknown/undetermined	5	103
	Haemorrhage	Obstetric haemorrhage	9	103
	Peritonitis	Pregnancy-related infection	10	103
	Ileus	Non-obstetric complications	7	103
	Embolism	Obstetric embolism	15	103
Wong, et al.[53]	Pulmonary embolism (direct)	Obstetric embolism	1	8
	Septic shock (following C-section no time provided) (direct)	Pregnancy-related infection	1	8
	Pulmonary edema complicated by adult respiratory distress syndrome (direct)	Hypertensive disorders	1	8
	Cardiac arrest following intubation (indirect)	Unanticipated complications of management	1	8

	Ruptured aortic aneurysm (indirect)	Non-obstetric complications	1	8
	Thrombotic thrombocytopenic purpura (indirect)	Non-obstetric complications	1	8
	Post- C-section hemorrhage (direct)	Obstetric haemorrhage	2	8
Wiebenga[55]	Puerperal Sepsis (after CS)	Pregnancy-related infection	7	10
	Bleeding after caesarean section	Obstetric haemorrhage	2	10
	Peritonitis	Pregnancy-related infection	1	10
Ounsa et al.[112]	Puerperal sepsis and septic shock	Pregnancy-related infection	1	1
Chama et al. [100]	Anaesthetic accident	Unanticipated complications of management	1	2
	Septicaemia	Pregnancy-related infection	1	2
van Ham et al.[127]	Cerebral aneurysm (non-obstetric)	Non-obstetric complications	1	3
	Subarachnoidal bleeding (non-obstetric)	Non-obstetric complications	1	3
	Cryptogenic cirrhosis (non-obstetric)	Non-obstetric complications	1	3
Benaron et al. [128]	Necrosis of abdomen and uterine inc. peritonitis, bacteremia, hemolytic staphyococcus albus	Pregnancy-related infection	1	2
	Eclampsia, endothelial changes of glomeruli, brain hemorrhage	Hypertensive disorders	1	2
Tomta et al. [129]	Inhalation of gastric contents during induction (anesthesia related)	Unanticipated complications of management	3	12
	Post-operative hypoxia (anesthesia related)	Unanticipated complications of management	1	12
	Unrecognized esophageal intubation (anesthesia related)	Unanticipated complications of management	1	12
	Haemorrhage	Obstetric haemorrhage	3	12
	Disseminated intravascular coagulation	Obstetric haemorrhage	3	12
	Acute edema of the lungs	Hypertensive disorders	1	12
Drazancic[130]	Asphyxia fetus	Unknown/undetermined	7	29
	Eclampsia-preeclampsia	Hypertensive disorders	7	29
	Sepsis puerperalis	Pregnancy-related infection	1	29
	Haemorrhage	Obstetric haemorrhage	5	29
	Pulmonary embolism	Obstetric embolism	1	29
	Considerable heart disability	Non-obstetric complications	2	29
	Diabetes mellitus, preeclampsia	Non-obstetric complications	1	29
	Acute liver atrophy	Non-obstetric complications	1	29
	Melanoma neoplasma	Non-obstetric complications	1	29
	As a metastatic mother	Non-obstetric complications	1	29
	Acute meningoencephalitis, Cerebral coma	Non-obstetric complications	1	29
	Hydrocephalus mother	Unknown/undetermined	1	29
Semeshi et al. [131]	Circulatory failure	Non-obstetric complications	2	3
	Vascular embolism	Obstetric embolism	1	3

Table 16: Quality assessment for 131 studies that reported on causes of caesarean-related deaths

Author	1) Is the definition of maternal death reported? (Y/N/Unclear)	2) Is the ascertainment of cause of death conducted through robust approaches? (Y/N/ Unclear)	3) Are causes of death during or after caesarean section reported in at least 95% of cases? (Y/N/ Unclear)	4) Has the study included all women or a random selection of women who have undergone caesarean section? (Y/N/ Unclear)	5) Is the source of information for outcome assessment adequate? (Y/N/ Unclear)	Overall Score
Okafor et al.[90]	N	N	Y	Y	Y	Low quality
Lilford et al.[19]	N	Y	Y	Y	Y	High quality
Holmer et al. [95]	N	N	Y	Y	Y	Low quality
Crichton et al.[23]	N	Y	N	Y	Unclear	Low quality
Anger et al.[50]	N	N	N	Y	Y	Low quality
Nolens et al.[78]	Y	N	Y	N	Y	Low quality
Ekanem et al.[40]	N	Y	Y	N	Y	Low quality
McKenzie[87]	Y	Y	N	Y	Y	High quality
Kuzma[9]	Y	N	Y	Y	Y	High quality
Rutgers et al.[59]	Y	Y	Y	Y	Y	High quality
Remy et al.[17]	Y	Y	Y	Y	Y	High quality
Kalisa et al.[89]	N	Y	N	N	Y	Low quality
Andrade et al.[60]	N	Y	Y	Y	Y	High quality
Chattopadhyay et al.[71]	N	N	Y	Y	Unclear	Low quality
Krone et al. [3]	N	N	Y	Y	Unclear	Low quality
Zahran et al.[13]	Y	Y	N	Y	Y	High quality
De Muylder[93]	N	Y	Y	Y	Y	High quality
Rojas et al.[20]	N	Y	Y	Y	Y	High quality
Campbell[7]	Y	Y	Y	Y	Y	High quality
Kamilya et al.[83]	N	Y	Y	Y	Y	High quality
Schuitemaker et al.[80]	N	Y	Y	Y	Y	High quality
Kallianidis et al.[2]	N	Y	Y	Y	Y	High quality
Oladapo et al.[84]	N	N	Y	N	Y	Low quality
Armon[62]	Y	Y	Y	Y	N	High quality
Ozumba et al.[86]	N	N	Y	Y	Unclear	Low quality
Clark et al.[92]	N	Y	N	Y	Y	Low quality
Gebhardt et al.[57]	N	Y	Y	Y	Y	High quality
Briand et al.[76]	Y	N	Y	N	Y	Low quality

Wirakusumah [39]	Y	N	Y	Y	Y	High quality
Chi et al.[15]	Y	Y	Y	Y	Y	High quality
Nyamtema et al.[27]	N	N	Y	Y	Y	Low quality
Mukherji et al.[48]	N	N	Y	Y	Y	Low quality
Igberase et al.[54]	N	N	Y	Y	Y	Low quality
Tsen et al.[91]	N	N	Y	Y	Y	Low quality
Palanisamy et al.[64]	N	N	Y	N	Y	Low quality
Enohumah et al.[1]	Y	Y	Y	Y	Y	High quality
Nwobodo et al.[79]	N	N	N	Y	Y	Low quality
Zongo et al.[73]	N	Y	Y	Y	Y	High quality
Talebi Doluee et al.[67]	N	Y	N	Y	Y	Low quality
Löfgren et al.[43]	Y	N	Y	Y	Y	High quality
Maaløe et al.[22]	N	N	Y	N	Y	Low quality
Andersgaard et al.[72]	Y	Y	Y	Y	Y	High quality
Rippmann[66]	N	N	Y	Y	Unclear	Low quality
Bloom et al.[4]	N	Y	N	Y	Y	Low quality
Ojo et al.[65]	N	N	N	Y	Y	Low quality
Gundumure[37]	N	N	Y	Y	Y	Low quality
Sachs et al.[74]	N	Y	Y	Y	Y	High quality
Cisse et al.[52]	N	N	N	Y	Y	Low quality
Evrard et al.[45]	N	Y	Y	Y	Y	High quality
Maswime et al.[18]	Y	Y	Y	Y	Y	High quality
Amirikia et al.[82]	N	N	Y	Y	Y	Low quality
Bolaji et al.[8]	N	N	Y	Y	Y	Low quality
Ikeako et al.[44]	N	N	Y	N	Y	Low quality
Tadesse et al.[24]	N	N	Y	Y	Y	Low quality
Okonta et al.[31]	N	N	Y	Y	Y	Low quality
Mekbib et al.[5]	N	N	Y	Y	Y	Low quality
Ezechi et al.[61]	N	N	Y	Y	Y	Low quality
Daniel et al.[51]	N	Y	Y	N	Y	Low quality
Bukar et al.[32]	N	Y	Y	Y	Y	High quality
Njokanma et al.[56] 2002	N	N	Y	N	Y	Low quality
Etuk et al.[68]	N	Y	Y	N	Y	Low quality

Imarengiaye et al.[70]	N	N	N	N	Y	Low quality
Greenhill[41]	N	N	Y	Y	Unclear	Low quality
Onoh et al.[29]	Y	N	Y	Y	Y	High quality
Ugwu et al.[69]	N	N	Y	Y	Y	Low quality
Okezie et al.[75]	N	N	Y	Y	Y	Low quality
Raphael et al.[25]	N	N	Y	Y	Y	Low quality
Ijaiya et al.[34]	N	Y	Y	Y	Y	High quality
Krause et al.[42]	N	N	Y	Y	Unclear	Low quality
Alegre Villariz et al.[49]	N	N	Y	Y	Unclear	Low quality
Muziarelli et al.[47]	N	N	Y	Y	Y	Low quality
Pekhlivanov[38]	N	N	Y	Y	Y	Low quality
Poradovsky[94]	N	N	N	Y	Unclear	Low quality
Imbert et al.[30]	N	N	Y	N	Y	Low quality
Picaud et al.[77]	N	N	Y	Y	Y	Low quality
Szczepanski et al.[85]	N	N	Y	Y	Unclear	Low quality
Carazzone et al.[26]	N	N	Y	Y	Y	Low quality
Georgiades eta al.[46]	N	N	Y	Y	Y	Low quality
Chavez Azuela et al.[58]	N	N	Y	Y	Y	Low quality
Kartushina[6]	N	N	Y	Y	Unclear	Low quality
Zhu et al.[11]	N	Y	Y	Y	Y	High quality
Strobel[21]	N	N	N	Y	Unclear	Low quality
Warm et al.[33]	N	N	N	Y	Unclear	Low quality
Kambo et al.[120]	N	N	Y	Y	Y	Low quality
Fesseha et al.[102]	N	N	N	Y	Y	Low quality
Ojiyi et al.[103]	N	N	N	Y	Y	Low quality
Garba et al.[104]	N	N	Y	Y	Y	Low quality
Kandasamy et al.[110]	Y	N	Y	Y	Y	High quality
Kor-Anantakul et al. [119]	N	N	Y	Y	Y	Low quality
Yaïch et al.[111]	N	N	Y	N	Y	Low quality
Cebekulu et al.[107]	N	N	Y	N	Y	Low quality
Diawara et al.[106]	N	N	N	Y	Y	Low quality
Teguete et al.[116]	N	N	Y	Y	Y	Low quality

Eshiet et al.[118]	Y	Y	Y	N	Y	High quality
Goswami et al.[117]	Y	Y	N	N	Y	Low quality
Abebe et al.[113]	N	N	Y	N	Y	Low quality
Rasoarimahandry et al.[126]	N	N	Y	Y	Y	Low quality
Okafor et al.[109]	Y	Y	Y	Y	Y	High quality
Nelissen et al.[115]	Y	Y	N	Y	Y	High quality
Sekirime et al.[123]	N	N	Y	N	Y	Low quality
Adisso et al.[124]	N	N	Y	Y	Y	Low quality
Richard et al.[122]	N	N	N	Y	Y	Low quality
Meda et al.[121]	N	Y	N	Y	Y	Low quality
Asıcıoglu et al.[114]	N	N	Y	N	Y	Low quality
Pereira et al.[101]	N	N	Y	Y	Y	Low quality
Khawaja et al.[125]	N	N	Y	Y	Y	Low quality
Ouedraogo et al.[108]	N	N	Y	Y	Y	Low quality
Rabiu et al.[105]	N	N	Y	N	Y	Low quality
Chau-In et al.[81]	N	N	Y	Y	Y	Low quality
MATERNAL AND PERINATAL MORTALITY COMMITTEE[36]	N	N	Y	Y	Y	Low quality
Moldin et al.[16]	Y	Y	Y	Y	Y	High quality
Rubin et al.[12]	Y	Y	Y	Y	Y	High quality
Bruce et al.[35]	N	N	Y	Y	Y	Low quality
Abbassi et al.[14]	Y	N	Y	Y	Y	High quality
Pinsker et al.[63]	N	Y	Y	Y	Y	High quality
Beck et al.[10]	N	Y	N	Y	Y	Low quality
Saving Mothers 2017[99]	N	Y	N	Y	Y	Low quality
Slaytor et al.[96]	Y	Y	Y	N	Y	High quality
NCCEMD[97]	N	N	Y	Y	Y	Low quality
NCCEMD[98]	Y	Y	N	Y	Y	High quality
Maswime et al.[18]	N	N	Y	Y	Y	Low quality
Hogberg et al.[88]	N	Y	N	Y	Y	Low quality
Wong, et al. [53]	Y	Y	Y	Y	Y	High quality
Wiebenga[55]	Y	Y	Y	Y	Y	High quality
Ounsa et al.[112]	N	Y	Y	Y	Y	High quality
Chama et al.[100]	N	Y	Y	Y	Y	High quality

van Ham et al.[127]	N	N	Y	Y	Y	Low quality
Benaron et al.[128]	N	Y	Y	Y	Y	High quality
Tomta et al. [129]	Y	Y	Y	Y	Y	High quality
Drazancic[130]	N	Y	Y	Y	Y	High quality
Semeshi et al.[131]	N	N	Y	Y	Unclear	Low quality

Abbreviations:
Y=Yes, N=No

Bibliography of Included Studies

1.Enohumah, K. O., Imarengiaye, C. O., K.O., E., Enohumah, K. O., & Imarengiaye, C. O. (2006). Factors associated with anaesthesia-related maternal mortality in a tertiary hospital in Nigeria. *Acta Anaesthesiologica Scandinavica*, *50*(2), 206–210. https://doi-org.proxy1.lib.uwo.ca/10.1111/j.1399-6576.2006.00945.x

2.Kallianidis, A. F., Schutte, J. M., van Roosmalen, J., van den Akker, T., & Maternal Mortality and Severe Morbidity Audit Committee of the Netherlands Society of Obstetrics and Gynecology (2018). Maternal mortality after cesarean section in the Netherlands. European journal of obstetrics, gynecology, and reproductive biology, 229, 148–152. https://doi.org/10.1016/j.ejogrb.2018.08.586

3.Krone, H. A., & Mattheus, J. (1975). Die mütterliche Mortalität beim Kaiserschnitt im Vergleich zur vaninalen Entbindung [Maternal mortality in cesarean section as compared to vaginal delivery]. *Fortschritte der Medizin*, *93*(27), 1266–1268. . Retrieved from https://www.scopus.com/inward/record.uri?eid=2-s2.0-18144447299&partnerID=40&md5=9b76667f2dbe3624e80cbde23b3c3952

4.Bloom, S. L., Spong, C. Y., Weiner, S. J., Landon, M. B., Rouse, D. J., Varner, M. W., Moawad, A. H., Caritis, S. N., Harper, M., Wapner, R. J., Sorokin, Y., Miodovnik, M., O'Sullivan, M. J., Sibai, B., Langer, O., Gabbe, S. G., & National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network (2005). Complications of anesthesia for cesarean delivery. *Obstetrics and gynecology*, *106*(2), 281–287. http://dx.doi.org/10.1097/01.AOG.0000171105.39219.55

5.Mekbib, T. A., & Teferi, B. (1994). Caesarean section and foetal outcome at Yekatit 12 Hospital, Addis Abeba, Ethiopia, 1987-1992. *Ethiopian Medical Journal*, *32*(3), 173–179. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med3&NEWS=N&AN=7957129

6.Kartushina, L. M. (1972). [Causes of maternal mortality associated with Cesarean section]. *Pediatr Akus Ginekol.*, *5*, 45–47. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med1&NEWS=N&AN=4658820

7.Campbell, G. R. (1974). Maternal mortality at Goroka Base Hospital. *Papua and New Guinea Medical Journal*, *17*(4), 335–341.Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed2&NEWS=N&AN=6511060

8.Bolaji, I. I., & Meehan, F. P. (1993). Caesarean section survey in Galway--1973 through 1987. *European Journal of Obstetrics, Gynecology, and Reproductive Biology*, *48*(1), 1–8. https://doi-org.proxy1.lib.uwo.ca/10.1016/0028-2243(93)90045-e
9.Kuzma, T. (2017). Caesarean Sections in a National Referral Hospital in Addis Ababa, Ethiopia: Trends, Predictors and Outcomes. *Journal of Obstetrics and Gynaecology Canada*, *39*(5), 394.
10.Beck, A., & Vutuc, C. (1984). Die Mortalität und Letalität der Sectio caesarea [Mortality and fatality in cesarean section]. *Geburtshilfe und Frauenheilkunde*, *44*(7), 421–424. https://doi-org.proxy1.lib.uwo.ca/10.1055/s-2008-1036689
11.Zhu, L., Zhou, B., & Qin, M. (2000). [Analysis on maternal deaths of cesarean section in Shanghai]. *Zhonghua fu chan ke za zhi*, *35*(3), 153–156. https://doi.org/10.1017/CBO9781107415324.004
12.Rubin, G. L., Peterson, H. B., Rochat, R. W., McCarthy, B. J., & Terry, J. S. (1981). Maternal death after cesarean section in Georgia. *American journal of obstetrics and gynecology*, *139*(6), 681–685. https://doi-org.proxy1.lib.uwo.ca/10.1016/0002-9378(81)90485-3
13.Zahran, K. M., Fadel, K. A., Ahmed, S. M., & El-Gazzar, A. F. (2017). Maternal mortality in an academic institution in Upper Egypt. *Journal of obstetrics and gynaecology : the journal of the Institute of Obstetrics and Gynaecology*, *37*(3), 315–319. https://dx.doi.org/10.1080/01443615.2016.1242559
14.Abbassi, H., Aboulfalah, A., Morsad, F., Matar, N., Himmi, A., & Mansouri, A. E. (2000). Complications maternelles des césariennes: analyse rétrospective de 3,231 interventions à la maternité universitaire de Casablanca, Maroc [Maternal complications of cesarean section: retrospective analysis of 3,231 interventions at the Casablanca University Hospital, Morocco]. *Sante (Montrouge, France)*, *10*(6), 419–423. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med4&NEWS=N&AN=11226939
15.Chi, I. C., Whatley, A., Wilkens, L., & Potts, M. (1986). In-hospital maternal mortality risk by cesarean and vaginal deliveries in two less developed countries--a descriptive study. *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics*, *24*(2), 121–131. http://dx.doi.org/10.1016/0020-7292%2886%2990006-8
16.Moldin, P., Hokegard, K. H., Nielsen, T. F.(1984). Cesarean section and maternal mortality in Sweden 1973-1979. *Acta Obstetricia et Gynecologica Scandinavica*, *63*(1), 7–11. https://doi-org.proxy1.lib.uwo.ca/10.3109/00016348409156266
17.Remy, N., Jaluvka, V., & Weitzel, H. K. (1993). Mortalität und Letalität nach Schnittentbindung in West-Berlin 1975 bis 1989 [Mortality and fatalities after cesarean section in West Berlin 1975 to 1989]. *Zentralblatt fur Gynakologie*, *115*(1), 7–12. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med3&NEWS=N&AN=8438632

18.Maswime, T.S., & Buchmann, E.J. (2016). Inequities in resources and preparedness for surgical complications of caesarean section in southern gauteng hospitals. *South African Journal of Obstetrics and Gynaecology*, *22*(1), 21–24. https://doi.org/10.7196/SAJOG.2016.v22i1.1039
19.Lilford, R. J., van Coeverden de Groot, H. A., Moore, P. J., & Bingham, P. (1990). The relative risks of caesarean section (intrapartum and elective) and vaginal delivery: a detailed analysis to exclude the effects of medical disorders and other acute pre-existing physiological disturbances. *British Journal of Obstetrics and Gynaecology*, *97*(10), 883–892. https://doi-org.proxy1.lib.uwo.ca/10.1111/j.1471-0528.1990.tb02442.x
20.Rojas, L., Ramirez, R., & Cantillo, J. (1974). Mortalidad materna en el instituto materno infantil de Bogota, Colombia [Maternal mortality at the Mother and Child Institute, Bogota, Colombia]. *Revista Colombiana de Obstetricia y Ginecologia*, *25*(2), 127–149. Retrieved from https://www.scopus.com/inward/record.uri?eid=2-s2.0-0016346194&partnerID=40&md5=e1db4df92479b4ce65c4b11c1ca6da61
21.Strobel E. (1967). Abdominale Schnittentbindung und Geburtshilfliche Ergebnisse [Abdominal surgical delivery and obstetrical results]. *Geburtshilfe und Frauenheilkunde*, *27*(9), 859–868. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med1&NEWS=N&AN=5590982
22.Maaløe, N., Bygbjerg, I. C., Onesmo, R., Secher, N. J., & Sorensen, B. L. (2012). Disclosing doubtful indications for emergency cesarean sections in rural hospitals in Tanzania: a retrospective criterion-based audit. *Acta obstetricia et gynecologica Scandinavica*, *91*(9), 1069–1076. https://doi.org/10.1111/j.1600-0412.2012.01474.x
23.Crichton, D., & Knobel, J. (1973). The principles of prevention of avoidable maternal death. A study of 538 consecutive maternal deaths in the obstetric unit, King Edward 8th Hospital, Durban, 1953-1971. *South African medical journal = Suid-Afrikaanse tydskrif vir geneeskunde*, *47*(42), 2005–2010. . Retrieved from https://www.scopus.com/inward/record.uri?eid=2-s2.0-0015692939&partnerID=40&md5=01abd0aade342350d1af86edf68c7fa0
24.Tadesse, E., Adane, M., & Abiyou, M. (1996). Caesarean section deliveries at Tikur Anbessa Teaching Hospital, Ethiopia. *East African medical journal*, *73*(9), 619–622.
25.Raphael, A. A., Muhammad, Z., & Iman, H. (2015). An audit of caesarean section in a tertiary hospital northwest Nigeria. *Tropical Journal of Obstetrics and Gynaecology*, *32*(2), 6-12.
26.Carazzone, P., Torretta, G. M., Leone, G., & Massano, A. (1978). Il taglio cesareo oggi [Cesarean section today]. *Minerva ginecologica*, *30*(5), 438–442. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med1&NEWS=N&AN=673241
27.Nyamtema, A., Mwakatundu, N., Dominico, S., Mohamed, H., Shayo, A., Rumanyika, R., Kairuki, C., Nzabuhakwa, C., Issa, O., Lyimo, C., Kasiga, I., & van Roosmalen, J. (2016). Increasing the availability and quality of caesarean

section in Tanzania. *BJOG : an international journal of obstetrics and gynaecology*, *123*(10), 1676–1682. https://doi.org/10.1111/1471-0528.14223
28.Maswime, S., & Buchmann, E. (2016). Causes and avoidable factors in maternal death due to cesarean-related hemorrhage in South Africa. *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics*, *134*(3), 320–323. https://doi.org/10.1016/j.ijgo.2016.03.013
29.Onoh, R. C., Eze, J. N., Ezeonu, P. O., Lawani, L. O., Iyoke, C. A., & Nkwo, P. O. (2015). A 10-year appraisal of cesarean delivery and the associated fetal and maternal outcomes at a teaching hospital in southeast Nigeria. *International journal of women's health*, *7*, 531–538. https://doi.org/10.2147/IJWH.S81338
30.Imbert, P., Berger, F., Diallo, N. S., Cellier, C., Goumbala, M., Ka, A. S., & Petrognani, R. (2003). Pronostic maternel et pédiatrique des césariennes en urgence: etude prospective à l'Hôpital Principal de Dakar, Sénégal [Maternal and infant prognosis of emergency cesarean section: prospective study of the Principal Hospital in Dakar, Senegal]. *Medecine tropicale : revue du Corps de sante colonial*, *63*(4-5), 351–357. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med4&NEWS=N&AN=14763288
31.Okonta, P. I., Otoide, V. O., & Okogbenin, S. A. (2003). Caesarean Section at the University of Benin Teaching Hospital Revisited. *Tropical Journal of Obstetrics and Gynaecology*, *20*(1), 63-66. https://doi.org/10.4314/tjog.v20i1.14404
32.Bukar, M., Audu, B. M., & Massa, A. A. (2009). Caesarean delivery at the Federal Medical Centre Gombe: a 3-year experience. *Nigerian journal of medicine : journal of the National Association of Resident Doctors of Nigeria*, *18*(2), 179–183. https://doi-org.proxy1.lib.uwo.ca/10.4314/njm.v18i2.45060
33.Warm, R., & Felker, A. (1966). 25 Jahre Kaiserschnitt (1939 bis 1963). Versuch einer Bilanz an Hand von 2800 Fällen. 2. Untersuchungen über Mortalität und Morbidität [25 years of cesarean section (1939 to 1963). Attempted assessment based on 2,800 cases. 2. A study of mortality and morbidity]. *Zentralblatt fur Gynakologie*, *88*(29), 963–970. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med1&NEWS=N&AN=5998487
34.Ijaiya, M. A., & Aboyeji, P. A. (2001). Caesarean Delivery: The Trend Over a Ten-Year Period at Ilorin, Nigeria. *Nigerian Journal of Surgical Research*, *3*(1), 11-18.
35.Bruce, J., & Mayorga, L. (1966). Estudio crítico de las actuales indicaciones de operación CES'AREA EN Valdivia [Critical study of current indications for cesarean section in Valdivia]. *Revista chilena de obstetricia y ginecologia*, *31*(2), 72–80. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med1&NEWS=N&AN=5997537
36.Maternal and perinatal mortality committee. (1969). Caesarean section in New South Wales, 1966-1967: a mortality and morbidity study. *The Medical journal of Australia*, *1*(7), 319–323. https://doi.org/10.5694/j.1326-5377.1969.tb116960.x

37.Gundumure, G. (2002). Characteristics and determinants of caesarean section and cord prolapse at the University Teaching Hospital, Lusaka.
38.Pekhlivanov K. (1975). Maĭchinata smurtnost pri sectio caesarea [Maternal mortality in sectio caesarea]. *Akusherstvo i ginekologiia*, *14*(3), 182–185. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med2&NEWS=N&AN=7377520
39.Wirakusumah, F. F. (1995). Maternal and perinatal mortality/morbidity associated with cesarean section in Indonesia. *Journal of Obstetrics and Gynaecology (Tokyo, Japan)*, *21*(5), 475–481. https://doi-org.proxy1.lib.uwo.ca/10.1111/j.1447-0756.1995.tb01040.x
40.Ekanem, A. D., Udoma, E. J., Etuk, S. J., & Eshiet, A. I. (2008). Outcome of emergency caesarean sections in Calabar, Nigeria: Impact of the seniority of the medical team. *Journal of Obstetrics and Gynaecology : The Journal of the Institute of Obstetrics and Gynaecology*, *28*(2), 198–201. https://dx.doi.org/10.1080/01443610801912329
41.Greenhill, J. P. (1930). An analysis of 874 cervical cesarean sections performed at the Chicago lying-in hospital. *American Journal of Obstetrics and Gynecology*, *19*(5), 613–632. https://doi.org/10.1016/S0002-9378(30)90502-9
42.Krause, W., Möbius, W., Günther, M., Eichhorn, K. H., Creutzburg, P., Mönch, A., Knappe, M., & Kunath, H. (1979). Die mütterliche und kindliche Mortalität und Morbidität nach Sectio im Zeitraum von 1956--1976 an der Universitäts-Frauenklinik Jena [The maternal and perinatal mortality and morbitity in attendance to Caesarean section in the period from 1956--1976 at the UFK-Jena (author's transl)]. *Zeitschrift fur Geburtshilfe und Perinatologie*, *183*(2), 136–147. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med1&NEWS=N&AN=442730
43.Löfgren, J., Kadobera, D., Forsberg, B. C., Mulowooza, J., Wladis, A., & Nordin, P. (2015). District-level surgery in Uganda: Indications, interventions and perioperative mortality. *Surgery*, *158*(1), 7–16. https://doi.org/10.1016/j.surg.2015.03.022
44.Ikeako, L. C., Nwajiaku, L., & Ezegwui, H. U. (2009). Caesarean section in a Secondary Health Hospital in Awka, Nigeria. *Nigerian Medical Journal*, *50*(3), 64.
45.Evrard, J. R., & Gold, E. M. (1977). Cesarean section and maternal mortality in Rhode Island. Incidence and risk factors, 1965-1975. *Obstetrics and gynecology*, *50*(5), 594–597. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed2&NEWS=N&AN=8223576
46.Georgiades, E., & Reinold, E. (1972). Sectio caesarea an der I. Universitäts-Frauenklinik Wien. Bericht über die Jahre 1959 bis 1970 [Cesarean section in the 1. University Women's Hospital of Vienna. Report on the years 1959-1970]. *Zentralblatt fur Gynakologie*, *94*(23), 737–742. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med1&NEWS=N&AN=5078311

47.Muziarelli, A., Trentadue, R., & Di Masi, M. (1989). Studio retrospettivo sul taglio cesareo negli anni 1974-87 [Retrospective study of cesarean section in the years 1974-87]. *Minerva ginecologica*, *41*(7), 353–358. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med3&NEWS=N&AN=2608205
48.Mukherji, J., & Samaddar, J. C. (1995). How safe is caesarean section. *Journal of obstetrics and gynaecology (Tokyo, Japan)*, *21*(1), 17–21. https://doi-org.proxy1.lib.uwo.ca/10.1111/j.1447-0756.1995.tb00892.x
49.Alegre Villariz, A., Garitano Caballero, C., Gándara Ibarra, A., & Aranguren Duo, G. (1977). Aspectos clínicos y estadísticos de la cesárea (revisión de 1.499 casos) [Statistical and clinical studies on cesarean section (review of 1,499 cases)]. *Acta obstetrica y ginecologica hispano-lusitana*, *25*(8), 459–478. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med1&NEWS=N&AN=607743
50.Anger, H., Frye, L., Burkhardt, G., Ononge, S., Durocher, J., Dabash, R., & Kayaga, J.(2018). Stillbirth, comorbidities and multicausality in maternal deaths with obstetric hemorrhage in uganda. *International Journal of Gynecology and Obstetrics*, *143*(Supplement 3), 286. /http://dx.doi.org/10.1002/ijgo.12582
51.Daniel, C. N., & Singh, S. (2016). Caesarean delivery: An experience from a tertiary institution in north western Nigeria. *Nigerian Journal of Clinical Practice*, *19*(1), 18–24. https://dx.doi.org/10.4103/1119-3077.164350
52.Cisse, C. T., Faye, E. O., de Bernis, L., Dujardin, B., & Diadhiou, F. (1998). Césariennes au Sénégal: couverture des besoins et qualité des services [Cesarean sections in Senegal: coverage of needs and quality of services]. *Sante (Montrouge, France)*, *8*(5), 369–377. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed6&NEWS=N&AN=29472558
53.Wong, A. B., & Etches, D. J. (2006). Maternal mortality in British Columbia, 1987-2004. *British Columbia Medical Journal*, *48*(2), 76–80. Retrieved from https://www.scopus.com/inward/record.uri?eid=2-s2.0-33646702339&partnerID=40&md5=db4ffc996ed7e3d0fa0cf9404981dcab
54.Igberase, G. O., Ebeigbe, P. N., & Andrew, B. O. (2009). High caesarean section rate: a ten year experience in a tertiary hospital in the Niger Delta, Nigeria. *Nigerian Journal of Clinical Practice*, *12*(3), 294–297. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med6&NEWS=N&AN=19803029
55.Wiebenga, J. E. (1992). Maternal mortality at Queen Elizabeth Central Hospital, 1989 to 1990. *Malawi Medical Journal : The Journal of Medical Association of Malawi*, *8*(1), 19–23. Retrieved from https://www.scopus.com/inward/record.uri?eid=2-s2.0-0026854756&partnerID=40&md5=dfa22b7c5045d1d12e7f5f13c9b6034d
56.Njokanma, F. O., Egri-Okwaji, M. T. C., Nwokoro, C. A., Orebamjo, T., & Okeke, G. C. E. (2002). Birth Asphyxia, Perinatal and Maternal Mortality Associated With Caesarean Section. *Tropical Journal of Obstetrics and Gynaecology*, *19*(1), 25-29. https://doi.org/10.4314/tjog.v19i1.14364

57.Gebhardt, G. S., Fawcus, S., Moodley, J., & Farina, Z. (2015). Maternal death and caesarean section in South Africa: Results from the 2011-2013 Saving Mothers Report of the National Committee for Confidential Enquiries into Maternal Deaths. *South African Medical Journal = Suid-Afrikaanse Tydskrif Vir Geneeskunde*, *105*(4), 287–291. /http://dx.doi.org/10.7196/SAMJ.9351
58.Chavez Azuela, J., Soberon Acevedo, J., & Castelazo Ayala, L. (1967). Operación cesárea y mortalidad materna. Factores predisponentes [Cesarean section and maternal mortality. Predisposing factors]. *Ginecologia y obstetricia de Mexico*, *22*(127), 163–172. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed1&NEWS=N&AN=89035909
59.Rutgers, R., Van Eygen, L. (2008). Mortality related to caesarean section in rural Matebeleland North Province, Zimbabwe. *The Central African Journal of Medicine*, *54*(5/8), 24–28. https://doi-org.proxy1.lib.uwo.ca/10.4314/cajm.v54i5-8.62623
60.Andrade, A. T. L., Guerra, M. D. O., De Andrade, G. N., Araujo, D. A. D. C. A., & De Souza, J. P. (2006). Maternal mortality: 75 years of observations in a teaching maternity hospital. *Revista Brasileira de Ginecologia e Obstetricia*, *28*(7), 380–387. https://doi.org/10.1590/S0100-72032006000700002
61.Ezechi, C.O., Nwokoro, A. C., Kalu, K. E. B., Njokanma, O. F., & Okeke, C. E. G. (2002). Caesarean Morbidity and Mortality in a Private Hospital in Lagos, Nigeria. *Tropical Journal of Obstetrics and Gynaecology*, *19*(2), 97-100.
62.Armon, P. J. (1979). Maternal deaths in the Kilimanjaro region of Tanzania. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, *73*(3), 284–288. https://doi.org/10.1016/0035-9203(79)90083-X
63.Shor Pinsker, V., Chávez Azuela, J., Castelazo, E., Rivero, E., & Karchmer, S. (1982). Mortalidad materna asociada a la operación cesárea [Maternal mortality associated with cesarean operations]. *Ginecologia y obstetricia de Mexico*, *50*(303), 189–195. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med2&NEWS=N&AN=7182234
64.Palanisamy, A., Mitani, A. A., & Tsen, L. C. (2011). General anesthesia for cesarean delivery at a tertiary care hospital from 2000 to 2005: a retrospective analysis and 10-year update. *International Journal of Obstetric Anesthesia*, *20*(1), 10–16. https://doi.org/10.1016/j.ijoa.2010.07.002
65.Ojo, V. A., Adetoro, O. O., & Okwerekwu, F. E. O. (1988). Characteristics of maternal deaths following cesarean section in a developing country. *International Journal of Gynecology and Obstetrics*, *27*(2), 171–176. https://doi.org/10.1016/0020-7292(88)90003-3
66.Rippmann E. T. (1965). Die mütterliche Mortalität der Jahre 1940-1963 im Frauenspital Basel [Maternal mortality of the years 1940-1963 in Frauenspital Basel]. *Gynaecologia. International monthly review of obstetrics and gynecology. Revue internationale mensuelle d'obstetrique et de gynecologie. Monatsschrift fur Geburtshilfe und Gynakologie*, *160*(2), 117–128. https://doi.org/10.1159/000303368

67.Talebi Doluee, M., Zabihi, H., Rezvani, B., Zarmehri, B., Najaf Najafi, M. (2018). Downward Trend in Maternal Mortality Ratio in Khorasan Razavi Province, Iran. *Journal of Midwifery & Reproductive Health*, *6*(1), 1179–1185. https://doi.org/10.22038/jmrh.2017.9967
68.Etuk, S. J., Udoma, E. J., & Ekott, M. I. (2001). Avoidable factors in maternal mortality following caesarean section (excluding ruptured uterus) in Calabar, Nigeria. *Tropical Doctor*, *31*(2), 108–109. https://doi.org/10.1177/004947550103100221
69.Ugwu, E. O., Obioha, K. C., Okezie, O. A., & Ugwu, A. O. (2011). A five-year survey of caesarean delivery at a Nigerian tertiary hospital. *Annals of medical and health sciences research*, *1*(1), 77–84. https://doi.org/10.4103/tjog.tjog_59_17
70.Imarengiaye, C. O., Otoide, V. O., Ande, A. B., & Obiaya, M. O. (2001). Anaesthesia related complications following caesarean delivery necessitating intensive care unit admissions in a tertiary centre. *African Journal of Medicine and Medical Sciences*, *30*(3), 229–232. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed7&NEWS=N&AN=37333444
71.Chattopadhyay, S. K., Sengupta, B. S., Chattopadhyay, C., Zaidi, Z., & Showail, H. (1983). Maternal mortality in Riyadh, Saudi Arabia. *British journal of obstetrics and gynaecology*, *90*(9), 809–814. https://doi.org/10.1111/j.1471-0528.1983.tb09320.x
72.Andersgaard, A. B., Langhoff-Roos, J., & Øian, P. (2008). Direct maternal deaths in Norway 1976-1995. *Acta obstetricia et gynecologica Scandinavica*, *87*(8), 856–861. https://doi.org/10.1080/00016340802237067
73.Zongo, A., Dumont, A., Fournier, P., Traore, M., Kouanda, S., & Sondo, B. (2015). Effect of maternal death reviews and training on maternal mortality among cesarean delivery: post-hoc analysis of a cluster-randomized controlled trial. *European journal of obstetrics, gynecology, and reproductive biology*, *185*, 174–180. https://doi.org/10.1016/j.ejogrb.2014.12.023
74.Sachs, B. P., Yeh, J., Acker, D., Driscoll, S., Brown, D. A., & Jewett, J. F. (1988). Cesarean section-related maternal mortality in Massachusetts, 1954-1985. *Obstetrics and Gynecology*, *71*(3 Pt 1), 385–388. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med3&NEWS=N&AN=3347424
75.Okezie, A. O., Oyefara, B., & Chigbu, C. O. (2007). A 4-year analysis of caesarean delivery in a Nigerian teaching hospital: one-quarter of babies born surgically. *Journal of Obstetrics and Gynaecology*, *27*(5), 470–474. https://doi.org/10.1080/01443610701405945
76.Briand, V., Dumont, A., Abrahamowicz, M., Sow, A., Traore, M., Rozenberg, P., Watier, L., & Fournier, P. (2012). Maternal and perinatal outcomes by mode of delivery in senegal and mali: a cross-sectional epidemiological survey. *PloS one*, *7*(10), e47352. https://doi.org/10.1371/journal.pone.0047352

77.Picaud, A., Nlome-Nze, A. R., Kouvahe, V., Faye, A., & Ondo-Mve, R. (1990). Les indications de césarienne et leur évolution au Centre Hospitalier de Libreville [Indications for cesarean section and their outcome at the Hospital Center in Libreville]. *Revue francaise de gynecologie et d'obstetrique*, *85*(6), 393–398. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med3&NEWS=N&AN=2202041
78.Nolens, B., Namiiro, F., Lule, J., van den Akker, T., van Roosmalen, J., & Byamugisha, J. (2018). Prospective cohort study comparing outcomes between vacuum extraction and second-stage cesarean delivery at a Ugandan tertiary referral hospital. *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics*, *142*(1), 28–36. https://doi.org/10.1002/ijgo.1250
79.Nwobodo, E. I., Isah, A. Y., & Panti, A. (2011). Elective caesarean section in a tertiary hospital in Sokoto, north western Nigeria. *Nigerian medical journal : journal of the Nigeria Medical Association*, *52*(4), 263–265. https://doi.org/10.4103/0300-1652.93801
80.Schuitemaker, N., van Roosmalen, J., Dekker, G., van Dongen, P., van Geijn, H., & Gravenhorst, J. B. (1997). Maternal mortality after cesarean section in The Netherlands. *Acta obstetricia et gynecologica Scandinavica*, *76*(4), 332–334. http://dx.doi.org/10.1111/j.1600-0412.1997.tb07987.x
81.Chau-in, W., Hintong, T., Rodanant, O., Lekprasert, V., Punjasawadwong, Y., Charuluxananan, S., & Tanudsintum, S. (2010). Anesthesia-related complications of caesarean delivery in Thailand: 16,697 cases from the Thai Anaesthesia Incidents Study. *Journal of the Medical Association of Thailand = Chotmaihet thangphaet*, *93*(11), 1274–1283. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med7&NEWS=N&AN=21114206
82.Amirikia, H., Zarewych, B., & Evans, T. N. (1981). Caesarean section: a 15-year review of changing incidence, indications, and risks. *American Journal of Obstetrics and Gynecology*, *140*(1), 81–90. https://dx.doi.org/10.1016/0002-9378(81)90261-1
83.Kamilya, G., Seal, S. L., Mukherji, J., Bhattacharyya, S. K., & Hazra, A. (2010). Maternal mortality and cesarean delivery: an analytical observational study. *The Journal of Obstetrics and Gynaecology Research*, *36*(2), 248–253. https://dx.doi.org/10.1111/j.1447-0756.2009.01125.x
84.Oladapo, O. T., Lamina, M. A., & Sule-Odu, A. O. (2007). Maternal morbidity and mortality associated with elective Caesarean delivery at a university hospital in Nigeria. *The Australian & New Zealand journal of obstetrics & gynaecology*, *47*(2), 110–114. https://dx.doi.org/10.1111/j.1479-828X.2007.00695.x
85.Szczepanski, J., Krywko, A., Arustowicz, Z., Mierzejewski, W., & Wszelaki-Lass, E. (1975). Ciaze o wysokim ryzyku w materiale cieć cesarskich w okresie 14 lat [High-risk pregnancies in the archives of cesarean section during a 14-year period]. *Wiadomosci lekarskie (Warsaw, Poland : 1960)*, *28*(11), 929–932. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med1&NEWS=N&AN=1136456

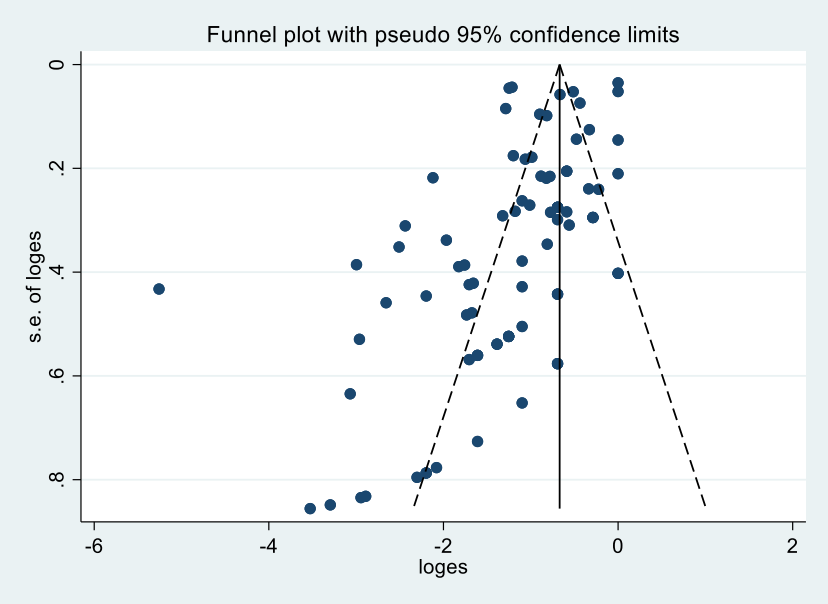
86.Ozumba, B. C., & Anya, S. E. (2002). Maternal deaths associated with cesarean section in Enugu, Nigeria. *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics*, *76*(3), 307–309. https://doi.org/http://dx.doi.org/10.1016/S0020-7292%2801%2900501-x
87.McKenzie A. G. (1998). Operative obstetric mortality at Harare Central Hospital 1992-1994: an anaesthetic view. *International journal of obstetric anesthesia*, *7*(4), 237–241. http://dx.doi.org/10.1016/S0959-289X%2898%2980045-9
88.Högberg U. (1989). Maternal deaths related to cesarean section in Sweden, 1951-1980. *Acta obstetricia et gynecologica Scandinavica*, *68*(4), 351–357. http://dx.doi.org/10.3109/00016348909028671
89.Kalisa, R., Rulisa, S., van den Akker, T., & van Roosmalen, J. (2016). Maternal Near Miss and quality of care in a rural Rwandan hospital. *BMC pregnancy and childbirth*, *16*(1), 324. http://dx.doi.org/10.1186/s12884-016-1119-1
90.Okafor, U. V., Ezegwui, H. U., & Ekwazi, K. (2009). Trends of different forms of anaesthesia for caesarean section in South-eastern Nigeria. *Journal of Obstetrics and Gynaecology*, *29*(5), 392–395. http://dx.doi.org/10.1080/01443610902932390
91.Tsen, L. C., Pitner, R., & Camann, W. R. (1998). General anesthesia for cesarean section at a tertiary care hospital 1990-1995: Indications and implications. *International Journal of Obstetric Anesthesia*, *7*(3), 147–152. https://doi.org/10.1016/S0959-289X(98)80001-0
92.Clark, S. L., Belfort, M. A., Dildy, G. A., Herbst, M. A., Meyers, J. A., & Hankins, G. D. (2008). Maternal death in the 21st century: causes, prevention, and relationship to cesarean delivery. *American journal of obstetrics and gynecology*, *199*(1), 36.e1–e11. http://dx.doi.org/10.1016/j.ajog.2008.03.007
93.De Muylder X. (1990). Maternal mortality audit in a Zimbabwean province. *Archives of Gynecology and Obstetrics*, *247*(3), 131–138. http://dx.doi.org/10.1007/BF02390861
94.Poradovský, K., & Sedová, A. (1968). Materská umrtnost v súvislosti s pôrodníckymi opráciami [Maternal mortality in connection with obstetrical surgery]. *Ceskoslovenska gynekologie*, *33*(8), 602–605. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med1&NEWS=N&AN=5702985
95.Holmer, H., Kamara, M. M., Bolkan, H. A., van Duinen, A., Conteh, S., Forna, F., Hailu, B., Hansson, S. R., Koroma, A. P., Koroma, M. M., Liljestrand, J., Lonnee, H., Sesay, S., & Hagander, L. (2019). The rate and perioperative mortality of caesarean section in Sierra Leone. *BMJ global health*, *4*(5), e001605.https://doi.org/10.1136/bmjgh-2019-001605
96.Slaytor, E. K., King, J. F., & Sullivan, E. A. (2004). Maternal deaths in Australia, 1997-1999. *AIHW Cat. No. PER 24. Sydney: AIHW National Perinatal Statistics Unit. (Maternal Deaths Series No.1)*
97.NCCEMD. (2014). Saving Mothers 2011-2013: Sixth report on confidential enquiries into maternal deaths in South Africa, Short report. *Pretoria: Department of Health*, *35*(6), 1–365. https://doi.org/10.2337/dc14-S014

98.NCCEMD. (2012). Saving mothers 2008–2010: fifth report on the confidential enquiries into maternal deaths in South Africa. *Department of Health Republic of South Africa*, 1–365. https://doi.org/10.2337/dc14-S014
99.National committee on confidential enquiries into maternal deaths. (2017). Saving Mothers 2017: Annual Report on Confidential inquiries into maternal death in South Africa. *Department of Health RSA*, 1–97. Retrieved from http://www.health.gov.za/index.php/shortcodes/2015-03-29-10-42-47/2015-04-30-08-18-10/2015-04-30-08-24-27/category/559-saving-mothers#
100.Chama, C. M., El-Nafaty, A. U., & Idrisa, A. (2000). Caesarean morbidity and mortality at Maiduguri, Nigeria. *Journal of Obstetrics and Gynaecology*, *20*(1), 45–48. https://doi.org/10.1080/01443610063453
101.Pereira, C., Bugalho, A., Bergström, S., Vaz, F., & Cotiro, M. (1996). A comparative study of caesarean deliveries by assistant medical officers and obstetricians in Mozambique. *BJOG: An International Journal of Obstetrics and Gynaecology*, *103*(6), 508–512. https://doi.org/10.1111/j.1471-0528.1996.tb09797.x
102.Fesseha, N., Getachew, A., Hiluf, M., Gebrehiwot, Y., & Bailey, P. (2011). A national review of cesarean delivery in Ethiopia. *International Journal of Gynecology and Obstetrics*, *115*(1), 106–111. https://doi.org/10.1016/j.ijgo.2011.07.011
103.Ojiyi, E.E., Dike, E., Anolue, F., & Chukwulebe, A.E. (2012). Appraisal Of Caesarean Section At The Imo State University Teaching Hospital, Orlu, Southeastern Nigeria. *The Internet Journal of Gynecology and Obstetrics*, *16*(2).
104.Garba, N. A.., & Muhammed, Z. (2011). Caesarean Morbidity and Mortality at Aminu Kano Teaching Hospital, Kano-a Two-Year Review. *Borno Medical Journal*, *8*(1), 10-14.
105.Rabiu, K. A., Adewunmi, A. A., Akinola, O. I., Eti, A. E., & Tayo, A. O. (2011). Comparison of maternal and neonatal outcomes following caesarean section in second versus first stage of labour in a Tertiary Hospital in Nigeria. *The Nigerian Postgraduate Medical Journal*, *18*(3), 165–171.
106.Diawara, A., Sangho, H., Tangara, I., Cisse, M.O., Traore, M.N., & Konate, S. (2014). Complications post cesarienne et gratuite de la cesarienne au Mali = cas d'un centre de sante de district. *Mali Medical*, *29*(1), 40-43.
107.Cebekulu, L., & Buchmann, E. J. (2006). Complications associated with cesarean section in the second stage of labor. *International Journal of Gynecology and Obstetrics*, *95*(2), 110–114. https://doi.org/10.1016/j.ijgo.2006.06.026
108.Ouédraogo, C. M., Ouédraogo, A., Ouattara, A., & Lankoandé, J. (2015). La pratique de la césarienne dans un hôpital de district à Ouagadougou Aspects épidémiologiques, cliniques et pronostiques à propos de 3 381 cas. *Medecine et Sante Tropicales*, *25*(2), 194–199. https://doi.org/10.1684/mst.2015.0443
109.Okafor, U., Ezegwui, H. (2008). Maternal Deaths During Caesarean Delivery In A Developing Country-Perspective From Nigeria. *The Internet Journal of Third World Medicine*, *8*(1).

110. Kandasamy, T., Merialdi, M., Guidotti, R. J., Betrán, A. P., Harris-Requejo, J., Hakimi, F., Van Look, P. F., & Kakar, F. (2009). Cesarean delivery surveillance system at a maternity hospital in Kabul, Afghanistan. *International Journal of Gynecology and Obstetrics*, *104*(1), 14–17. https://doi.org/10.1016/j.ijgo.2008.08.024
111. Yaïch, P., Ouattara, A., Koffi, N., Chiaké, A., Sanou, J., Itéké, F., & Kane, M. (2012). Césariennes en urgence : pronostic materno-foetal au CHU de Cocody D'Abidjan. *Revue Africaine d'Anesthésiologie et de Médecine d'Urgence*, *17*(1).
112. Ounsa, M.A.A.E., & Mohamed, E. Y. (2011). Maternal Mortality in Ribat University Hospital, Khartoum, Sudan: Seven years of experience. *Sudan Journal of Medical Sciences*, *6*(4), 277-280
113. Abebe, F. E., Gebeyehu, A. W., Kidane, A. N., & Eyassu, G. A. (2016). Factors leading to cesarean section delivery at Felegehiwot referral hospital, Northwest Ethiopia: A retrospective record review. *Reproductive Health*, *13*(1), 6. https://doi.org/10.1186/s12978-015-0114-8
114. Asicioglu, O., Güngördük, K., Yildirim, G., Asicioglu, B. B., Güngördük, C. O., Ark, C., Günay, T., & Yenigül, N. (2014). Second-stage vs first-stage caesarean delivery: Comparison of maternal and perinatal outcomes. *Journal of Obstetrics and Gynaecology*, *34*(7), 598–604. https://doi.org/10.3109/01443615.2014.920790
115. Nelissen, E. J., Mduma, E., Ersdal, H. L., Evjen-Olsen, B., van Roosmalen, J. J. M., & Stekelenburg, J. (2013). Maternal near miss and mortality in a rural referral hospital in northern Tanzania: A cross-sectional study. *BMC Pregnancy and Childbirth*, *13*, 141. https://doi.org/10.1186/1471-2393-13-141
116. Teguete, I., Traore, Y., Sissoko, A., Djire, M.Y., Thera, A., Dolo, T., Mounkoro, N., Traore, M., & Dolo, A. (2012). Determining Factors of Cesarean Delivery Trends in Developing Countries: Lessons from Point G National Hospital (Bamako - Mali). *Cesarean Delivery*, *Raed Salim*, *IntechOpen*, 161-200. https://doi.org/10.5772/47914
117. Goswami, D., Rathore, A. M., Batra, S., Dubey, C., Tyagi, S., & Wadhwa, L. (2013). Facility-based review of 296 maternal deaths at a tertiary centre in India: Could they be prevented? *Journal of Obstetrics and Gynaecology Research*, *39*(12), 1569–1579. https://doi.org/10.1111/jog.12099
118. Eshiet, A. I., Udoma, E. J., Ekanem, A. D., & Dada, A. (2003). Effect Of Anaesthesia On Morbidity And Mortality In Emergency Caesarean Section Patients In Calabar, Nigeria. *Nigerian Journal of Physiological Sciences*, *18*(1-2), 77-81. https://doi.org/10.4314/njps.v18i1.32624
119. Kor-Anantakul, O., Suwanrath, C., Lim, A., & Chongsuviwatwong, V. (2008). Comparing complications in intended vaginal and caesarean deliveries. *Journal of obstetrics and gynaecology : the journal of the Institute of Obstetrics and Gynaecology*, *28*(1), 64–68. https://doi.org/10.1080/01443610701812207
120. Kambo, I., Bedi, N., Dhillon, B. S., & Saxena, N. C. (2002). A critical appraisal of cesarean section rates at teaching hospitals in India. *International Journal of Gynecology and Obstetrics*, *79*(2), 151–158. https://doi.org/10.1016/S0020-7292(02)00226-6

121. Meda, I. B., Millogo, T., Baguiya, A., Ouédraogo/Nikiema, L., Coulibaly, A., & Kouanda, S. (2016). Rate of and factors associated with indications for cesarean deliveries: Results of a national review in Burkina Faso. *International Journal of Gynecology and Obstetrics*, *135*, S51–S57. https://doi.org/10.1016/j.ijgo.2016.08.010
122. Richard, F., Ouédraogo, C., & De Brouwere, V. (2008). Quality cesarean delivery in Ouagadougou, Burkina Faso: A comprehensive approach. *International Journal of Gynecology and Obstetrics*, *103*(3), 283–290. https://doi.org/10.1016/j.ijgo.2008.08.008
123. Sekirime, W. K., & Lule, J. C. (2009). Outcome of cesarean section in asymptomatic HIV-1 infection in Kampala, Uganda. *Journal of Obstetrics and Gynaecology Research*, *35*(4), 679–688. https://doi.org/10.1111/j.1447-0756.2008.01002.x
124. Adisso, S., Takpara, I., Teguete, I., Gbegnide, H., Chobli, M., & Alihonou, E. (2006). Pronostic maternel selon le type d'anesthésie pour la césarienne en milieu urbain au Bénin. *Fondation Genevoise pour la Formation et la Recherche Médicales.*
125. Khawaja, N. P., Yousaf, T., & Tayyeb, R. (2004). Analysis of caesarean delivery at a tertiary care hospital in Pakistan. *Journal of obstetrics and gynaecology : the journal of the Institute of Obstetrics and Gynaecology*, *24*(2), 139–141. https://doi-org.proxy1.lib.uwo.ca/10.1080/01443610410001645415
126. Andriamady Rasoarimahandry, C. L., Andrianarivony, M. O., & Ranjalahy, R. J. (2001). Indications et pronostic de l'opération césarienne là maternitée de Befelatanana - CHU d'Antananarivo (à propos de 529 cas, durant l'année 1998). *Gynecologie Obstetrique et Fertilite*, *29*(12), 900–904. https://doi.org/10.1016/S1297-9589(01)00240-5
127. van Ham, M. A., van Dongen, P. W., & Mulder, J. (1997). Maternal consequences of caesarean section. A retrospective study of intra-operative and postoperative maternal complications of caesarean section during a 10-year period. *European journal of obstetrics, gynecology, and reproductive biology*, *74*(1), 1–6. https://doi.org/10.1016/s0301-2115(97)02725-5
128. Benaron, H. W., & Tucker, B. E. (1971). The effect of obstetric management and factors beyond clinical control on maternal mortality rates at the Chicago Maternity Center from 1959 to 1963. *American journal of obstetrics and gynecology*, *110*(8), 1113–1118. https://doi.org/10.1016/0002-9378(71)90310-3
129. Tomta, K., Maman, F. O., Agbétra, N., Baeta, S., Ahouangbévi, S., & Chobli, M. (2003). Mortalité maternelle: implication anesthésique au CHU de Lomée (Togo) [Maternal deaths and anesthetics in the Lomé (Togo) University Hospital]. *Sante (Montrouge, France)*, *13*(2), 77–80.
130. Drazancic, A. (2005). Maternal mortality. *Gynaecologia et Perinatologia*, *14*(1), 7–17. Retrieved from http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=emed9&NEWS=N&AN=40593029
131. Semeshi, I., Chepli, I., Khed'i, R., Fupnik, P., Shikloshi, D., Sani, L., & Sekeĭ, L. (1970). Analiz 1000 operatsiĭ kesareva secheniia [Analysis of 1000 cesarean sections]. *Akusherstvo i ginekologiia*, *46*(1), 55–57.

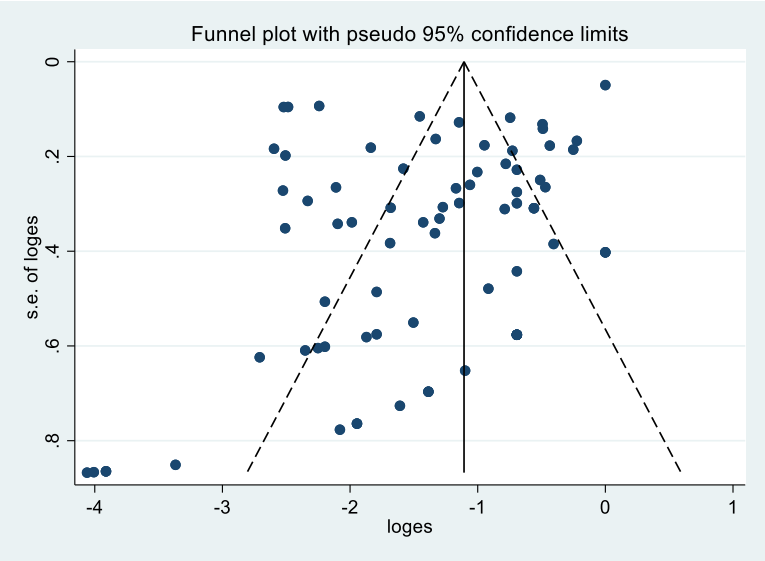
APPENDIX H: RESULTS OF PUBLICATION BIAS ASESSMENT AND SENSITIVITY ANALYSES




```
Egger's test for small-study effects:
Regress standard normal deviate of intervention
effect estimate against its standard error
Number of studies =  82                                 Root MSE      =   3.954
------------------------------------------------------------------------------
     Std_Eff |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
       slope |  -.4719492   .0818677    -5.76   0.000    -.6348711   -.3090273
        bias |  -2.115164   .5851248    -3.61   0.001      -3.2796   -.9507289
------------------------------------------------------------------------------
```

```
Test of H0: no small-study effects          P = 0.001
```

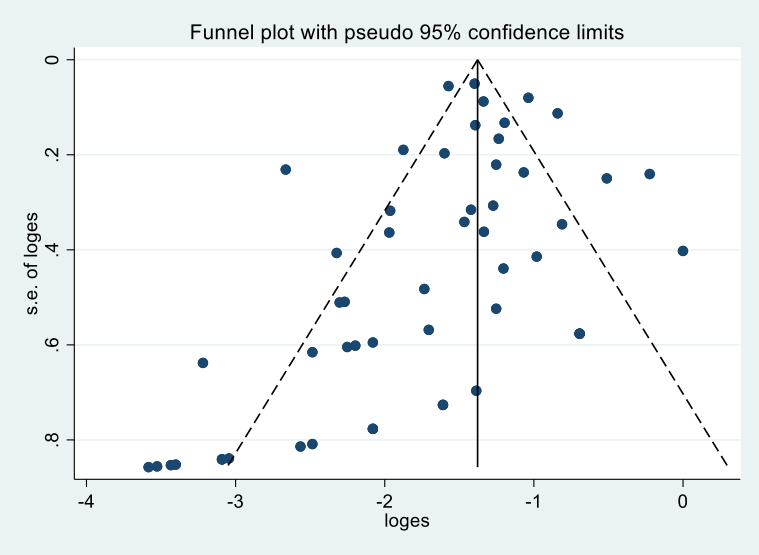
Figure 8: Publication bias for studies reporting the prevalence of caesarean-related deaths due to obstetric haemorrhage




```
Egger's test for small-study effects:
Regress standard normal deviate of intervention
effect estimate against its standard error
Number of studies =  75                                  Root MSE      =   4.502
------------------------------------------------------------------------------
     Std_Eff |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
       slope |  -.8128753   .1728592    -4.70   0.000    -1.157383   -.4683675
```

```
        bias |  -1.817758   .8361596    -2.17   0.033    -3.484222   -.1512944
------------------------------------------------------------------------------
Test of H0: no small-study effects          P = 0.033
```

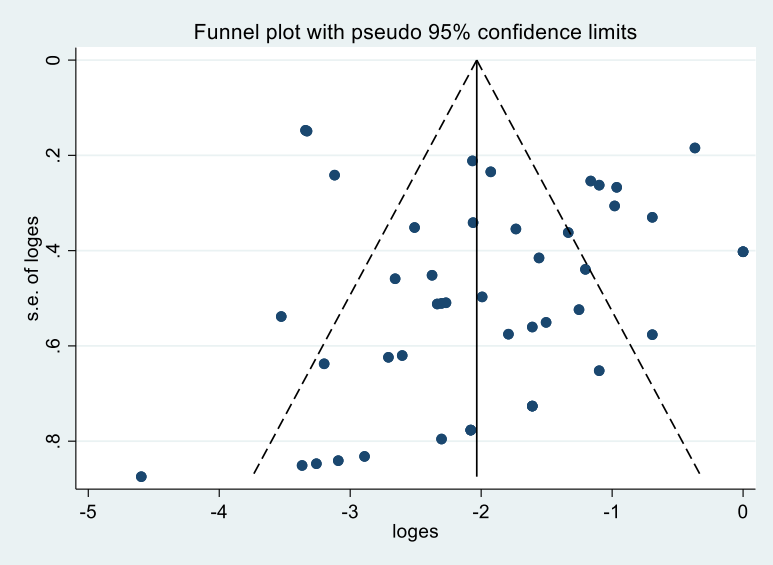
Figure 9: Publication bias for studies reporting the prevalence of caesarean-related deaths due to pregnancy-related infectio




```
Egger's test for small-study effects:
Regress standard normal deviate of intervention
effect estimate against its standard error
Number of studies =  53                                 Root MSE      =   2.046
------------------------------------------------------------------------------
     Std_Eff |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
```

```
-------------+----------------------------------------------------------------
       slope |  -1.278919   .0717473   -17.83   0.000    -1.422957    -1.13488
        bias |  -.7725242   .3848404    -2.01   0.050    -1.545124    .0000751
------------------------------------------------------------------------------
Test of H0: no small-study effects          P = 0.050
```

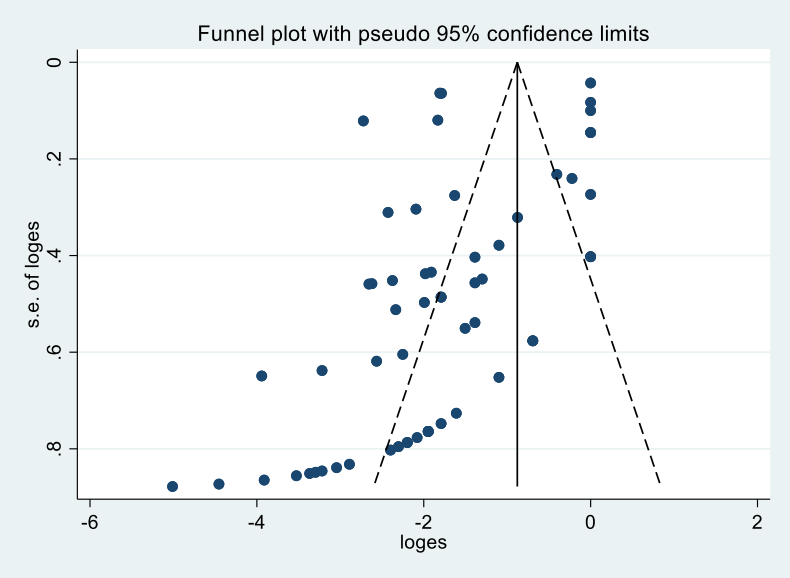
Figure 10: Publication bias for studies reporting the prevalence of caesarean-related deaths due to hypertensive disorders




```
Egger's test for small-study effects:
Regress standard normal deviate of intervention
effect estimate against its standard error
Number of studies =  45                                 Root MSE      =   3.133
------------------------------------------------------------------------------
```

```
     Std_Eff |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+------------------------------------------------------------------
       slope |  -2.324209     .33898    -6.86   0.000    -3.007827   -1.640591
        bias |   .9484609   .9692658     0.98   0.333     -1.00625    2.903172
------------------------------------------------------------------------------
Test of H0: no small-study effects          P = 0.333
```

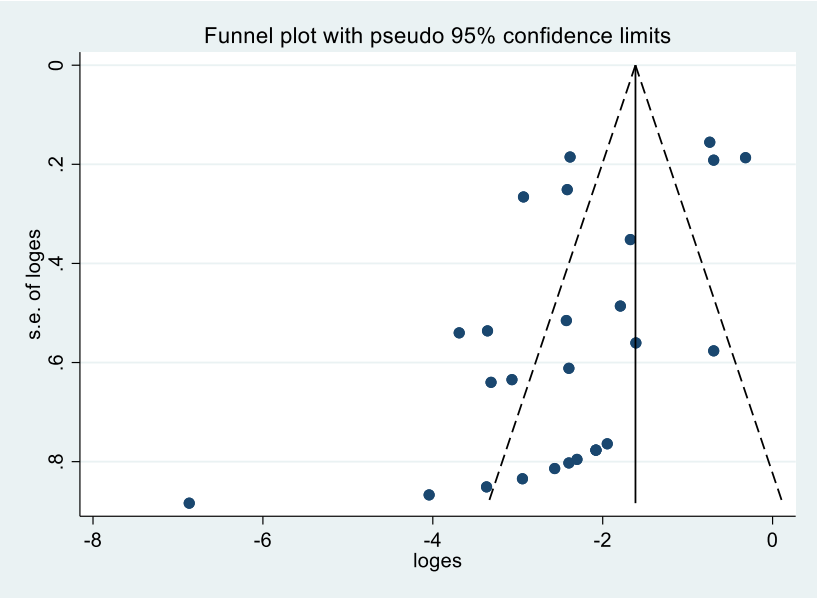
Figure 11: Publication bias for studies reporting the prevalence of caesarean-related deaths due to obstetric embolism




```
Egger's test for small-study effects:
Regress standard normal deviate of intervention
```

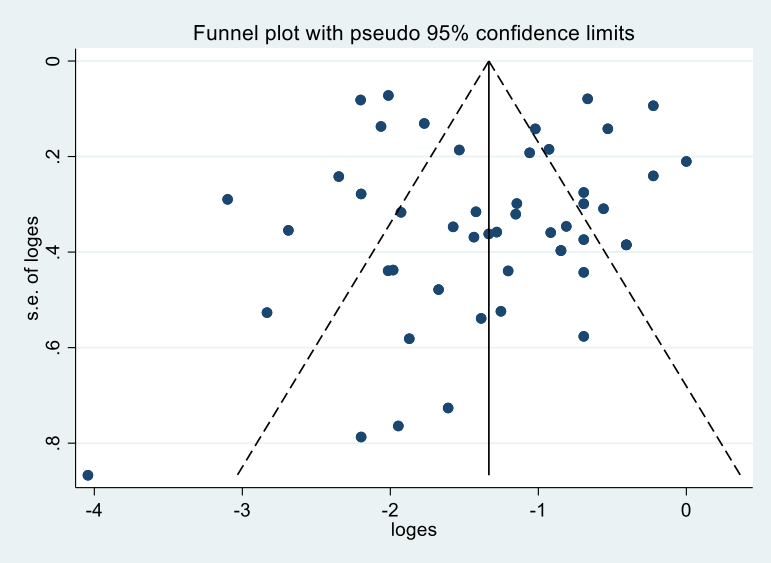
```
effect estimate against its standard error


Number of studies =  60                                 Root MSE      =   5.083
------------------------------------------------------------------------------
     Std_Eff |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
       slope |  -.5835422    .158536    -3.68   0.001    -.9008865   -.2661979
        bias |  -2.484751   .8524509    -2.91   0.005    -4.191117   -.7783854
------------------------------------------------------------------------------
Test of H0: no small-study effects          P = 0.005
```

Figure 12: Publication bias for studies reporting the prevalence of caesarean-related deaths due to unanticipated complications of management




```
Egger's test for small-study effects:
Regress standard normal deviate of intervention
effect estimate against its standard error
Number of studies =  26                                 Root MSE      =   2.662
------------------------------------------------------------------------------
     Std_Eff |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
       slope |  -.6631705   .3327432    -1.99   0.058    -1.349919    .0235777
        bias |  -3.233813   .9421178    -3.43   0.002    -5.178248   -1.289377
------------------------------------------------------------------------------
Test of H0: no small-study effects          P = 0.002
```

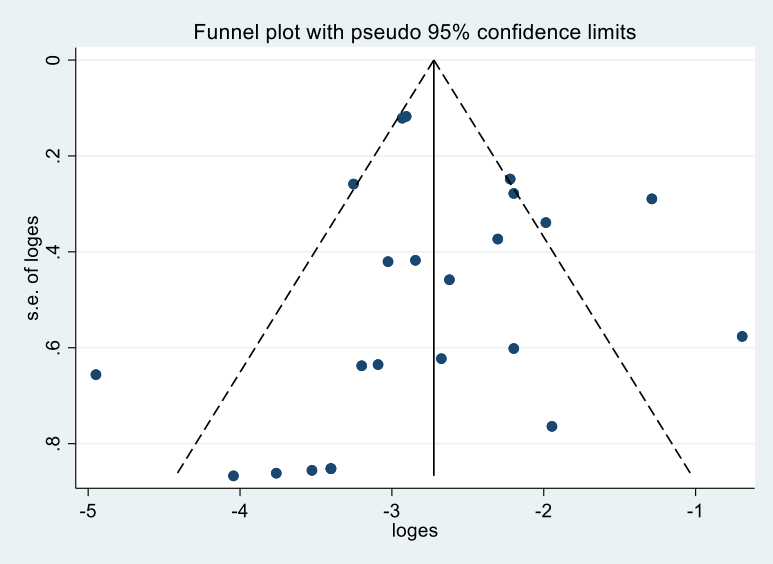
Figure 13: Publication bias for studies reporting the prevalence of caesarean-related deaths due to other obstetric complications




```
Egger's test for small-study effects:
Regress standard normal deviate of intervention
effect estimate against its standard error
Number of studies =  49                                   Root MSE      =   3.885
------------------------------------------------------------------------------
     Std_Eff |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
       slope |  -1.359577   .1881579    -7.23   0.000    -1.738102   -.9810519
        bias |   .1559392   .9336535     0.17   0.868    -1.722329    2.034208
```

```
------------------------------------------------------------------------------
Test of H0: no small-study effects          P = 0.868
```

Figure 14: Publication bias for studies reporting the prevalence of caesarean-related deaths due to non-obstetric complications




```
Egger's test for small-study effects:
Regress standard normal deviate of intervention
effect estimate against its standard error
Number of studies =  23                                 Root MSE      =    1.96
------------------------------------------------------------------------------
     Std_Eff |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
```

```
       slope |  -2.770755   .2062644   -13.43   0.000    -3.199706   -2.341805
        bias |   .1951574   .6835452     0.29   0.778    -1.226353    1.616667
------------------------------------------------------------------------------
Test of H0: no small-study effects            P = 0.778
```

Figure 15: Publication bias for studies reporting the prevalence of caesarean-related deaths due to unknown/undetermined causes

	Number of Studies	Events	Proportion of All Deaths (%; 95% CI)	p value for subgroup interaction	
				By HDI	By decade
Obstetric haemorrhage					
Pre-1970s	9	33/229	16.37 (6.79-28.33)		<0.00001
High HDI	4	12/167	6.53 (2.87-11.23)	<0.00001	
Low HDI	5	21/62	32.82 (20.52-46.19)		
1970s-1980s	17	91/504	20.06 (12.97-28.05)		
High HDI	5	18/117	17.28 (6.02-31.91)	0.575	
Low HDI	12	73/387	21.59 (12.59-31.94)		
1990s-2000s	44	631/2622	34.77 (22.81-47.57)		
High HDI	4	13/186	5.68 (1.93-10.76)	<0.00001	
Low HDI	40	618/2436	38.94 (25.43-53.19)		
2010s-2020s	12	961/3023	55.88 (44.35-67.14)		
High HDI	NR	NR	NR	N/A	
Low HDI	12	961/3023	55.88 (44.35-67.14)		
Overall	82	1716/6378	32.60 (26.11-39.38)		
Pregnancy-related infection					
Pre-1970s	12	131/422	34.27 (18.26-52.09)		<0.00001
High HDI	7	49/237	21.92 (8.96-37.76)	0.128	
Low HDI	5	82/185	49.34 (20.33-78.58)		
1970s-1980s	20	148/604	33.12 (20.69-46.60)		
High HDI	5	27/111	32.06 (12.02-55.77)	0.834	
Low HDI	15	121/493	33.84 (18.44-50.80)		
1990s-2000s	33	369/2449	17.17 (12.06-22.80)		
High HDI	3	9/152	4.29 (0.15-11.69)	0.0006	
Low HDI	30	360/2297	19.21 (13.56-25.41)		
2010s-2020s	10	252/2947	5.91 (2.94-9.51)		
High HDI	NR	NR	NR	N/A	

Low HDI	10	252/2947	5.91 (2.94-9.51)		
Overall	75	900/6422	22.87 (18.63-27.33)		
Hypertensive disorders					
Pre-1970s	8	31/196	12.54 (5.51-21.27)		0.085
High HDI	5	24/107	19.05 (9.99-29.66)	0.011	
Low HDI	3	7/89	7.55 (2.53-14.42)		
1970s-1980s	13	101/536	13.05 (6.18-21.57)		
High HDI	5	23/140	14.42 (5.86-25.42)	0.844	
Low HDI	8	78/396	12.35 (3.21-25.05)		
1990s-2000s	25	280/1253	19.23 (12.40-26.89)		
High HDI	3	27/128	13.44 (0.10-38.07)	0.467	
Low HDI	22	253/1125	20.36 (12.74-28.94)		
2010s-2020s	7	675/2922	20.53 (17.82-23.35)		
High HDI	NR	NR	NR	N/A	
Low HDI	7	675/2922	20.53 (17.82-23.35)		
Overall	53	1087/4907	16.44 (13.20-19.90)		
Obstetric embolism					
Pre-1970s	16	51/379	11.92 (7.35-17.19)		<0.00001
High HDI	9	38/260	14.97 (7.60-23.89)	0.348	
Low HDI	7	13/119	8.57 (3.19-15.50)		
1970s-1980s	14	74/567	14.82 (8.41-22.41)		
High HDI	6	34/150	26.62 (10.55-46.22)	0.027	
Low HDI	8	40/417	8.00 (4.01-12.90)		
1990s-2000s	11	37/243	12.69 (2.88-26.02)		
High HDI	3	14/128	9.92 (4.10-17.42)	0.123	
Low HDI	8	23/115	18.36 (1.61-42.67)		
2010s-2020s	4	104/2905	3.45 (2.80-4.17)		
High HDI	NR	NR	NR	N/A	
Low HDI	4	104/2905	3.45 (2.80-4.17)		
Overall	45	266/4094	10.09 (6.88-13.68)		
Unanticipated complications of management					
Pre-1970s	6	8/172	4.11 (0.18-10.96)		0.0082
High HDI	5	7/166	3.62 (0.11-9.93)	0.271	
Low HDI	1	1/6	16.67 (3.01-56.35)		
1970s-1980s	15	52/530	15.61 (6.49-26.98)		
High HDI	3	9/82	11.47 (2.08-25.33)	0.459	
Low HDI	12	43/448	16.99 (5.74-31.47)		
1990s-2000s	34	171/1630	21.32 (12.42-31.42)		
High HDI	6	5/158	0.05 (0.00-6.79)	0.00031	
Low HDI	28	166/1472	26.23 (15.41-38.34)		
2010s-2020s	6	472/2838	15.70 (11.62-20.18)		

High HDI	NR	NR	NR	N/A	
Low HDI	6	472/2838	15.70 (11.62-20.18)		
Overall	61	703/5170	15.58 (11.40-20.14)		
Other obstetric complications					
Pre-1970s	5	5/73	5.48 (0.57-13.26)		
High HDI	4	4/44	8.21 (0.81-19.84)	0.279	
Low HDI	1	1/29	3.45 (0.61-17.18)		
1970s-1980s	7	15/230	5.71 (1.83-11.00)		
High HDI	3	8/102	7.60 (0.00-23.10)	0.643	
Low HDI	4	7/128	4.33 (0.92-9.30)		0.0025
1990s-2000s	11	75/1917	6.77 (1.41-14.52)		
High HDI	2	6/120	4.58 (1.27-9.38)	0.220	
Low HDI	9	69/1797	7.56 (1.12-17.28)		
2010s-2020s	3	37/88	38.90 (20.71-58.72)		
High HDI	NR	NR	NR	N/A	
Low HDI	3	37/88	38.90 (20.71-58.72)		
Overall	26	132/2308	10.03 (4.96-16.25)		
Non-obstetric complications					
Pre-1970s	16	103/354	37.38 (23.24-52.53)		
High HDI	7	48/225	27.83 (13.45-44.65)	0.164	
Low HDI	9	55/129	46.84 (24.50-69.74)		
1970s-1980s	11	144/476	25.96 (12.74-41.45)		
High HDI	6	19/121	23.85 (4.68-49.52)	0.755	
Low HDI	5	125/355	29.59 (13.93-47.88)		
1990s-2000s	17	160/983	21.17 (12.45-31.13)		<0.00001
High HDI	3	53/128	42.18 (24.52-60.84)	0.0069	
Low HDI	14	107/855	14.43 (7.68-22.39)		
2010s-2020s	5	360/2914	11.63 (9.50-13.93)		
High HDI	NR	NR	NR	N/A	
Low HDI	5	360/2914	11.63 (9.50-13.93)		
Overall	49	767/4727	24.35 (19.46-29.53)		
Pregnancy with abortive outcome					
Pre-1970s	NR	NR	NR		
High HDI	NR	NR	NR	N/A	
Low HDI	NR	NR	NR		
1970s-1980s	NR	NR	NR		
High HDI	NR	NR	NR	N/A	0.00005
Low HDI	NR	NR	NR		
1990s-2000s	1	3/4	75.00 (30.06-95.44)		
High HDI	NR	NR	NR	N/A	
Low HDI	1	3/4	75.00 (30.06-95.44)		

2010s-2020s	2	2/2444	0.08 (0.00-0.26)		
High HDI	NR	NR	NR	N/A	
Low HDI	2	2/2444	0.08 (0.00-0.26)		
Overall	3	5/2448	N/A*		
Unknown/undetermined					
Pre-1970s	6	17/301	5.28 (2.81-8.34)		
High HDI	2	7/152	4.52 (1.58-8.63)	0.393	
Low HDI	4	10/149	6.37 (2.67-11.22)		
1970s-1980s	3	6/155	3.55 (0.92-7.39)		
High HDI	1	1/57	1.75 (0.31-9.29)	0.322	
Low HDI	2	5/98	4.84 (1.16-10.33)		0.395
1990s-2000s	9	41/638	7.30 (1.30-16.12)		
High HDI	2	6/120	4.79 (1.40-9.66)	0.157	
Low HDI	7	35/518	9.72 (0.91-23.51)		
2010s-2020s	5	159/2949	5.16 (3.98-6.48)		
High HDI	NR	NR	NR	N/A	
Low HDI	5	159/2949	5.16 (3.98-6.48)		
Overall	23	223/4043	4.61 (3.01-6.44)		
Coincidental causes					
Pre-1970s	NR	NR	NR		
High HDI	NR	NR	NR	N/A	
Low HDI	NR	NR	NR		
1970s-1980s	2	2/65	2.83 (0.00-9.09)		
High HDI	1	1/22	4.55 (0.81-21.80)	0.581	
Low HDI	1	1/43	2.33 (0.41-12.06)		
1990s-2000s	1	1/34	2.94 (0.52-14.92)		0.321
High HDI	1	1/34	2.94 (0.52-14.92)	N/A	
Low HDI	NR	NR	NR		
2010s-2020s	1	20/1243	1.61 (1.04-2.47)		
High HDI	NR	NR	NR	N/A	
Low HDI	1	20/1243	1.61 (1.04-2.47)		
Overall	4	23/1342	0.81 (0.27-1.55)		

***Analysis produced effect estimates with values of zero. HDI=human development index. NR=not reported. N/A=not available.**

Table 17: Sensitivity analysis for the prevalence of causes of caesarean-related deaths in low and high HDI countries with random effects model

	Number of Studies	Proportion of All Deaths (%; 95% CI)	p value for heterogeneity between sub-groups	
			By HDI	By decade
Obstetric haemorrhage				
Pre-1970s	9	11.01 (6.66-16.06)		
High HDI	4	6.53 (2.87-11.23)	<0.00001	
Low HDI	5	32.82 (20.52-46.19)		
1970s-1980s	17	15.33 (11.96-18.97)		
High HDI	5	13.30 (7.16-20.67)	0.446	
Low HDI	12	15.94 (12.03-20.19)		
1990s-2000s	37	12.32 (10.75-13.96)		<0.00001
High HDI	4	5.64 (2.32-9.94)	0.00008	
Low HDI	33	13.00 (11.32-14.75)		
2010s-2020s	10	30.28 (28.53-32.04)		
High HDI	NR	NR	N/A	
Low HDI	10	30.28 (28.53-32.04)		
Overall	73	20.63 (19.49-21.78)		
Pregnancy-related infection				
Pre-1970s	12	28.78 (24.22-33.52)		
High HDI	7	16.94 (11.76-22.68)	<0.00001	
Low HDI	5	44.89 (37.61-52.28)		
1970s-1980s	20	19.13 (15.55-22.92)		
High HDI	5	22.03 (14.22-30.80)	0.741	
Low HDI	15	18.31 (14.33-22.57)		
1990s-2000s	27	9.75 (8.25-11.33)		<0.00001
High HDI	3	4.16 (1.03-8.61)	0.00086	
Low HDI	24	10.20 (8.61-11.88)		
2010s-2020s	10	3.74 (2.80-4.77)		
High HDI	NR	NR	N/A	
Low HDI	10	3.74 (2.80-4.77)		
Overall	69	8.75 (7.88-9.65)		
Hypertensive disorders				
Pre-1970s	8	12.86 (7.82-18.68)		
High HDI	5	19.59 (11.45-28.89)	0.005	
Low HDI	3	7.55 (2.53-14.42)		
1970s-1980s	13	16.18 (12.91-19.69)		
High HDI	5	15.07 (9.22-21.88)	0.611	
Low HDI	8	16.51 (12.66-20.69)		0.0039
1990s-2000s	21	18.33 (15.83-20.96)		
High HDI	3	18.45 (11.72-26.13)	0.874	
Low HDI	18	18.30 (15.62-21.11)		

2010s-2020s	6	20.54 (18.89-22.23)		
High HDI	NR	NR	N/A	
Low HDI	6	20.54 (18.89-22.23)		
Overall	48	19.45 (18.21-20.71)		
		Obstetric embolism		
Pre-1970s	16	10.92 (7.48-14.79)		
High HDI	9	12.32 (8.15-17.07)	0.575	
Low HDI	7	8.57 (3.19-15.50)		
1970s-1980s	14	10.52 (7.84-13.47)		
High HDI	6	20.08 (13.63-27.28)	0.0004	
Low HDI	8	7.62 (4.90-10.75)		<0.00001
1990s-2000s	9	4.93 (1.26-10.06)		
High HDI	3	9.43 (4.40-15.73)	0.559	
Low HDI	6	4.60 (0.02-13.72)		
2010s-2020s	4	3.45 (2.80-4.17)		
High HDI	NR	NR	N/A	
Low HDI	4	3.45 (2.80-4.17)		
Overall	43	2.08 (1.47-2.76)		
		Unanticipated complications of management		
Pre-1970s	6	2.03 (0.05-5.72)		
High HDI	5	2.11 (0.07-5.78)	0.196	
Low HDI	1	16.67 (3.01-56.35)		
1970s-1980s	15	5.22 (2.99-7.85)		
High HDI	3	9.19 (3.14-17.26)	0.357	
Low HDI	12	4.49 (2.21-7.27)		
1990s-2000s	27	4.40 (3.06-5.90)		<0.00001
High HDI	4	1.27 (0.00-4.47)	0.00071	
Low HDI	23	4.84 (3.35-6.50)		
2010s-2020s	5	15.43 (14.04-16.86)		
High HDI	NR	NR	N/A	
Low HDI	5	15.43 (14.04-16.86)		
Overall	53	9.03 (8.08-10.03)		
		Other obstetric complications		
Pre-1970s	5	5.48 (0.57-13.26)		
High HDI	4	8.21 (0.81-19.84)	0.279	
Low HDI	1	3.45 (0.61-17.18)		
1970s-1980s	7	4.94 (2.08-8.63)		
High HDI	3	5.76 (1.54-11.74)	0.761	
Low HDI	4	4.33 (0.92-9.30)		<0.00001
1990s-2000s	9	N/A*		
High HDI	2	4.58 (1.27-9.38)	0.028	

Low HDI	7	N/A*		
2010s-2020s	3	41.54 (31.18-52.25)		
High HDI	NR	NR	N/A	
Low HDI	3	41.54 (31.18-52.25)		
Overall	24	0.87 (0.35-1.54)		
		Non-obstetric complications		
Pre-1970s	16	25.48 (20.58-30.66)		
High HDI	7	18.32 (13.13-24.07)	<0.00001	
Low HDI	9	41.14 (31.87-50.68)		
1970s-1980s	11	27.02 (22.78-31.46)		
High HDI	6	10.42 (4.65-17.58)	<0.00001	
Low HDI	5	33.82 (28.74-39.07)		<0.00001
1990s-2000s	13	13.01 (10.46-15.74)		
High HDI	3	41.02 (32.26-50.05)	<0.00001	
Low HDI	10	8.75 (6.34-11.42)		
2010s-2020s	5	11.45 (10.25-12.70)		
High HDI	NR	NR	N/A	
Low HDI	5	11.45 (10.25-12.70)		
Overall	45	12.85 (11.75-13.98)		
		Pregnancy with abortive outcome		
Pre-1970s	NR	NR		
High HDI	NR	NR	N/A	
Low HDI	NR	NR		
1970s-1980s	NR	NR		
High HDI	NR	NR	N/A	
Low HDI	NR	NR		N/A
1990s-2000s	NR	NR		
High HDI	NR	NR	N/A	
Low HDI	NR	NR		
2010s-2020s	2	0.08 (0.00-0.26)		
High HDI	NR	NR	N/A	
Low HDI	2	0.08 (0.00-0.26)		
Overall	2	0.08 (0.00-0.26)		
		Unknown/undetermined		
Pre-1970s	6	5.28 (2.81-8.34)		
High HDI	2	4.52 (1.58-8.63)	0.393	
Low HDI	4	6.37 (2.67-11.22)		
1970s-1980s	3	3.55 (0.94-7.35)		0.843
High HDI	1	1.75 (0.31-9.29)	0.322	
Low HDI	2	4.84 (1.16-10.33)		
1990s-2000s	9	2.07 (0.73-3.85)		

High HDI	2	4.79 (1.40-9.66)	0.821	
Low HDI	7	1.50 (0.26-3.40)		
2010s-2020s	5	5.09 (4.30-5.94)		
High HDI	NR	NR	N/A	
Low HDI	5	5.09 (4.30-5.94)		
Overall	23	3.59 (2.92-4.32)		
Coincidental causes				
Pre-1970s	NR	NR		0.321
High HDI	NR	NR	N/A	
Low HDI	NR	NR		
1970s-1980s	2	2.83 (0.00-9.09)		
High HDI	1	4.55 (0.81-21.80)	0.581	
Low HDI	1	2.33 (0.41-12.06)		
1990s-2000s	1	2.94 (0.52-14.92)		
High HDI	1	2.94 (0.52-14.92)	N/A	
Low HDI	NR	NR		
2010s-2020s	1	1.61 (1.04-2.47)		
High HDI	NR	NR	N/A	
Low HDI	1	1.61 (1.04-2.47)		
Overall	4	0.81 (0.27-1.55)		

***Analysis produced effect estimates with values of zero. HDI=human development index. NR=not reported. N/A=not available.**

Table 18: Sensitivity analysis for the prevalence of causes of caesarean-related deaths involving studies without a specific subgroup of patients

	Number of Studies	Proportion of All Deaths (%; 95% CI)	p value for heterogeneity between sub-groups	
			By HDI	By decade
Obstetric haemorrhage				
Pre-1970s	7	7.74 (3.58-12.88)		<0.00001
High HDI	4	6.53 (2.87-11.23)	<0.00001	
Low HDI	3	44.87 (21.73-68.98)		
1970s-1980s	14	14.50 (11.13-18.16)		
High HDI	5	13.30 (7.16-20.67)	0.653	
Low HDI	9	14.87 (10.96-19.17)		
1990s-2000s	34	6.95 (5.49-8.53)		
High HDI	4	5.64 (2.32-9.94)	0.020	
Low HDI	30	7.13 (5.55-8.83)		
2010s-2020s	9	30.24 (28.51-32.00)		
High HDI	NR	NR	N/A	
Low HDI	9	30.24 (28.51-32.00)		
Overall	64	18.65 (17.47-19.85)		
Pregnancy-related infection				
Pre-1970s	8	20.60 (15.18-26.49)		<0.00001
High HDI	5	10.35 (5.21-16.53)	<0.00001	
Low HDI	3	45.61 (34.34-57.09)		
1970s-1980s	16	17.93 (14.28-21.83)		
High HDI	5	28.78 (20.97-37.20)	0.013	
Low HDI	11	14.35 (10.35-18.73)		
1990s-2000s	22	10.96 (9.19-12.82)		
High HDI	3	4.16 (1.03-8.61)	0.00010	
Low HDI	19	11.71 (9.80-13.74)		
2010s-2020s	6	4.93 (3.94-5.98)		
High HDI	NR	NR	N/A	
Low HDI	6	4.93 (3.94-5.98)		
Overall	52	7.94 (7.04-8.88)		
Hypertensive disorders				
Pre-1970s	5	8.24 (2.42-16.07)		0.00011
High HDI	3	16.52 (4.26-32.67)	0.048	
Low HDI	2	6.40 (1.07-14.67)		
1970s-1980s	12	16.37 (13.09-19.90)		
High HDI	5	15.07 (9.22-21.88)	0.603	
Low HDI	7	16.80 (12.94-21.00)		
1990s-2000s	18	14.58 (11.69-17.69)		
High HDI	3	18.45 (11.72-26.13)	0.433	
Low HDI	15	13.77 (10.62-17.19)		

2010s-2020s	6	20.12 (18.46-21.83)		
High HDI	NR	NR	N/A	
Low HDI	6	20.12 (18.46-21.83)		
Overall	41	18.68 (17.37-20.02)		
		Obstetric embolism		
Pre-1970s	8	10.94 (6.83-15.70)		
High HDI	4	12.86 (7.87-18.71)	0.494	
Low HDI	4	7.87 (1.83-16.38)		
1970s-1980s	12	10.43 (7.76-13.39)		
High HDI	5	20.24 (13.63-27.65)	0.0005	
Low HDI	7	7.60 (4.91-10.72)		<0.00001
1990s-2000s	7	9.87 (5.81-14.67)		
High HDI	3	9.43 (4.40-15.73)	0.789	
Low HDI	4	10.56 (4.39-18.45)		
2010s-2020s	4	3.45 (2.80-4.17)		
High HDI	NR	NR	N/A	
Low HDI	4	3.45 (2.80-4.17)		
Overall	31	3.50 (2.82-4.23)		
		Unanticipated complications of management		
Pre-1970s	3	0.92(0.00-4.38)		
High HDI	2	1.90 (0.03-5.46)	0.129	
Low HDI	1	16.67 (3.01-56.35)		
1970s-1980s	12	3.32 (1.44-5.69)		
High HDI	3	9.19 (3.14-17.26)	0.101	
Low HDI	9	2.26 (0.57-4.66)		
1990s-2000s	25	2.36 (1.21-3.79)		<0.00001
High HDI	5	N/A*	N/A	
Low HDI	20	3.38 (1.99-5.03)		
2010s-2020s	5	15.43 (14.04-16.86)		
High HDI	NR	NR	N/A	
Low HDI	5	15.43 (14.04-16.86)		
Overall	45	7.83 (6.86-8.84)		
		Other obstetric complications		
Pre-1970s	1	3.45 (0.61-17.18)		
High HDI	NR	NR	N/A	
Low HDI	1	3.45 (0.61-17.18)		
1970s-1980s	6	5.12 (2.25-8.80)		
High HDI	3	5.76 (1.54-11.74)	0.640	<0.00001
Low HDI	3	4.66 (1.23-9.61)		
1990s-2000s	9	N/A*		
High HDI	2	4.58 (1.27-9.38)	N/A	

Low HDI	7	N/A*		
2010s-2020s	3	41.54 (31.18-52.25)		
High HDI	NR	NR	N/A	
Low HDI	3	41.54 (31.18-52.25)		
Overall	19	0.48 (0.09-1.09)		
		Non-obstetric complications		
Pre-1970s	9	22.73 (16.86-29.08)		
High HDI	3	10.76 (5.77-16.84)	<0.00001	
Low HDI	6	51.38 (39.64-63.05)		
1970s-1980s	10	26.99 (22.70-31.46)		
High HDI	5	8.94 (3.34-16.15)	<0.00001	
Low HDI	5	33.82 (28.74-39.07)		<0.00001
1990s-2000s	10	11.92 (8.90-15.25)		
High HDI	3	41.02 (32.26-50.05)	<0.00001	
Low HDI	7	4.91 (2.49-7.87)		
2010s-2020s	5	11.45 (10.25-12.70)		
High HDI	NR	NR	N/A	
Low HDI	5	11.45 (10.25-12.70)		
Overall	34	12.42 (11.30-13.59)		
		Pregnancy with abortive outcome		
Pre-1970s	NR	NR		
High HDI	NR	NR	N/A	
Low HDI	NR	NR		
1970s-1980s	NR	NR		
High HDI	NR	NR	N/A	
Low HDI	NR	NR		
1990s-2000s	1	75.00 (30.06-95.44)		0.00005
High HDI	NR	NR	N/A	
Low HDI	1	75.00 (30.06-95.44)		
2010s-2020s	2	0.08 (0.00-0.26)		
High HDI	NR	NR	N/A	
Low HDI	2	0.08 (0.00-0.26)		
Overall	3	N/A*		
		Unknown/undetermined		
Pre-1970s	3	4.58 (1.58-8.70)		
High HDI	1	4.85 (2.09-10.86)	0.780	
Low HDI	2	4.96 (0.41-12.64)		
1970s-1980s	3	3.55 (0.94-7.35)		0.0023
High HDI	1	1.75 (0.31-9.29)	0.322	
Low HDI	2	4.84 (1.16-10.33)		
1990s-2000s	8	7.58 (4.46-11.24)		

High HDI	2	4.79 (1.40-9.66)	0.0079	
Low HDI	6	10.34 (5.93-15.49)		
2010s-2020s	5	5.09 (4.30-5.94)		
High HDI	NR	NR	N/A	
Low HDI	5	5.09 (4.30-5.94)		
Overall	19	3.84 (3.10-4.64)		
		Coincidental causes		
Pre-1970s	NR	NR		0.321
High HDI	NR	NR	N/A	
Low HDI	NR	NR		
1970s-1980s	2	2.83 (0.00-9.09)		
High HDI	1	4.55 (0.81-21.80)	0.581	
Low HDI	1	2.33 (0.41-12.06)		
1990s-2000s	1	2.94 (0.52-14.92)		
High HDI	1	2.94 (0.52-14.92)	N/A	
Low HDI	NR	NR		
2010s-2020s	1	1.61 (1.04-2.47)		
High HDI	NR	NR	N/A	
Low HDI	1	1.61 (1.04-2.47)		
Overall	4	0.81 (0.27-1.55)		

***Analysis produced effect estimates with values of zero. HDI=human development index. NR=not reported. N/A=not available.**

Table 19: Sensitivity analysis for the prevalence of causes of caesarean-related deaths for studies with retrospective data collection

	Number of Studies	Proportion of All Deaths (%; 95% CI)	p value for heterogeneity between sub-groups	
			By HDI	By decade
Obstetric haemorrhage				
Pre-1970s	NR	NR		<0.00001
High HDI	NR	NR	N/A	
Low HDI	NR	NR		
1970s-1980s	2	42.79 (21.47-65.39)		
High HDI	NR	NR	N/A	
Low HDI	2	42.79 (21.47-65.39)		
1990s-2000s	10	40.50 (36.39-44.66)		
High HDI	NR	NR	N/A	
Low HDI	10	40.50 (36.39-44.66)		
2010s-2020s	3	86.67 (72.46-96.98)		
High HDI	NR	NR	N/A	
Low HDI	3	86.67 (72.46-96.98)		
Overall	15	43.35 (39.36-47.38)		
Pregnancy-related infection				
Pre-1970s	1	47.44 (36.74-58.38)		<0.00001
High HDI	NR	NR	N/A	
Low HDI	1	47.44 (36.74-58.38)		
1970s-1980s	2	18.91 (3.81-39.75)		
High HDI	NR	NR	N/A	
Low HDI	2	18.91 (3.81-39.75)		
1990s-2000s	11	8.73 (6.28-11.45)		
High HDI	NR	NR	N/A	
Low HDI	11	8.73 (6.28-11.45)		
2010s-2020s	4	45.01 (22.23-68.67)		
High HDI	NR	NR	N/A	
Low HDI	4	45.01 (22.23-68.67)		
Overall	18	12.11 (9.48-14.95)		
Hypertensive disorders				
Pre-1970s	NR	NR		0.709
High HDI	NR	NR	N/A	
Low HDI	NR	NR		
1970s-1980s	NR	NR		
High HDI	NR	NR	N/A	
Low HDI	NR	NR		
1990s-2000s	7	22.75 (18.61-27.11)		

High HDI	NR	NR	N/A	
Low HDI	7	22.75 (18.61-27.11)		
2010s-2020s	1	30.00 (10.78-60.32)		
High HDI	NR	NR	N/A	
Low HDI	1	30.00 (10.78-60.32)		
Overall	8	23.04 (18.96-27.34)		
Obstetric embolism				
Pre-1970s	1	28.57 (8.22-64.11)		0.469
High HDI	1	28.57 (8.22-64.11)	N/A	
Low HDI	NR	NR		
1970s-1980s	1	22.22 (6.32-54.74)		
High HDI	NR	NR	N/A	
Low HDI	1	22.22 (6.32-54.74)		
1990s-2000s	4	42.82 (16.48-70.80)		
High HDI	NR	NR	N/A	
Low HDI	4	42.82 (16.48-70.80)		
2010s-2020s	NR	NR		
High HDI	NR	NR	N/A	
Low HDI	NR	NR		
Overall	6	33.62 (15.31-53.95)		
Unanticipated complications of management				
Pre-1970s	1	14.29 (2.57-51.31)		<0.00001
High HDI	1	14.29 (2.57-51.31)	N/A	
Low HDI	NR	NR		
1970s-1980s	3	57.29 (38.59-75.10)		
High HDI	NR	NR	N/A	
Low HDI	3	57.29 (38.59-75.10)		
1990s-2000s	8	14.64 (10.31-19.49)		
High HDI	1	3.45 (0.61-17.18)	0.027	
Low HDI	7	16.45 (11.64-21.81)		
2010s-2020s	1	100.00 (56.55-100.00)		
High HDI	NR	NR	N/A	
Low HDI	1	100.00 (56.55-100.00)		
Overall	13	18.93 (14.31-23.95)		
Other obstetric complications				
Pre-1970s	1	14.29 (2.57-51.31)		0.471
High HDI	1	14.29 (2.57-51.31)	N/A	
Low HDI	NR	NR		
1970s-1980s	NR	NR		
High HDI	NR	NR	N/A	
Low HDI	NR	NR		

1990s-2000s	2	9.10 (6.55-12.00)		
High HDI	NR	NR	N/A	
Low HDI	2	9.10 (6.55-12.00)		
2010s-2020s	NR	NR		
High HDI	NR	NR	N/A	
Low HDI	NR	NR		
Overall	3	7.51 (4.91-10.49)		
		Non-obstetric complications		
Pre-1970s	1	42.86 (15.82-74.95)		
High HDI	1	42.86 (15.82-74.95)	N/A	
Low HDI	NR	NR		
1970s-1980s	NR	NR		
High HDI	NR	NR	N/A	
Low HDI	NR	NR		0.092
1990s-2000s	7	11.12 (7.70-14.93)		
High HDI	NR	NR	N/A	
Low HDI	7	11.12 (7.70-14.93)		
2010s-2020s	NR	NR		
High HDI	NR	NR	N/A	
Low HDI	NR	NR		
Overall	8	11.59 (8.15-15.40)		
		Pregnancy with abortive outcome		
Pre-1970s	NR	NR		
High HDI	NR	NR	N/A	
Low HDI	NR	NR		
1970s-1980s	NR	NR		
High HDI	NR	NR	N/A	
Low HDI	NR	NR		N/A
1990s-2000s	NR	NR		
High HDI	NR	NR	N/A	
Low HDI	NR	NR		
2010s-2020s	NR	NR		
High HDI	NR	NR	N/A	
Low HDI	NR	NR		
Overall	NR	NR		
		Unknown/undetermined		
Pre-1970s	NR	NR		
High HDI	NR	NR	N/A	
Low HDI	NR	NR		N/A
1970s-1980s	NR	NR		
High HDI	NR	NR	N/A	

Low HDI	NR	NR		
1990s-2000s	1	0.71 (0.01-2.13)		
High HDI	NR	NR	N/A	
Low HDI	1	0.71 (0.01-2.13)		
2010s-2020s	NR	NR		
High HDI	NR	NR	N/A	
Low HDI	NR	NR		
Overall	1	0.71 (0.01-2.13)		
		Coincidental causes		
Pre-1970s	NR	NR		
High HDI	NR	NR	N/A	
Low HDI	NR	NR		
1970s-1980s	NR	NR		
High HDI	NR	NR	N/A	
Low HDI	NR	NR		N/A
1990s-2000s	NR	NR		
High HDI	NR	NR	N/A	
Low HDI	NR	NR		
2010s-2020s	NR	NR		
High HDI	NR	NR	N/A	
Low HDI	NR	NR		
Overall	NR	NR		

***Analysis produced effect estimates with values of zero. HDI=human development index. NR=not reported. N/A=not available.**

Table 20: Sensitivity analysis for the prevalence of causes of caesarean-related deaths for studies with prospective data collection

	Number of Studies	Proportion of All Deaths (%; 95% CI)	p value for heterogeneity between sub-groups	
			By HDI	By decade
Obstetric haemorrhage				
Pre-1970s	8	11.54 (6.91-16.92)		
High HDI	3	6.79 (2.93-11.79)	<0.00001	
Low HDI	5	32.82 (20.52-46.19)		
1970s-1980s	17	15.33 (11.96-18.97)		
High HDI	5	13.30 (7.16-20.67)	0.446	
Low HDI	12	15.94 (12.03-20.19)		<0.00001
1990s-2000s	44	13.80 (12.20-15.45)		
High HDI	4	5.64 (2.32-9.94)	<0.00001	
Low HDI	40	14.62 (12.91-16.38)		
2010s-2020s	12	30.65 (28.89-32.44)		
High HDI	NR	NR	N/A	
Low HDI	12	30.65 (28.89-32.44)		
Overall	81	21.29 (20.15-22.45)		
Pregnancy-related infection				
Pre-1970s	9	26.34 (21.34-31.62)		
High HDI	4	6.41 (1.98-12.33)	<0.00001	
Low HDI	5	44.89 (37.61-52.28)		
1970s-1980s	20	19.13 (15.55-22.92)		
High HDI	5	22.03 (14.22-30.80)	0.741	
Low HDI	15	18.31 (14.33-22.57)		<0.00001
1990s-2000s	33	10.36 (8.90-11.89)		
High HDI	3	4.16 (1.03-8.61)	0.0005	
Low HDI	30	10.85 (9.31-12.47)		
2010s-2020s	10	3.74 (2.80-4.77)		
High HDI	NR	NR	N/A	
Low HDI	10	3.74 (2.80-4.77)		
Overall	72	8.62 (7.76-9.51)		
Hypertensive disorders				
Pre-1970s	5	7.89 (2.46-15.12)		
High HDI	2	25.03 (5.32-50.21)	0.020	
Low HDI	3	7.55 (2.53-14.42)		
1970s-1980s	13	16.18 (12.91-19.69)		0.0013
High HDI	5	15.07 (9.22-21.88)	0.611	
Low HDI	8	16.51 (12.66-20.69)		
1990s-2000s	25	18.03 (15.60-20.57)		

High HDI	3	18.45 (11.72-26.13)	0.720	
Low HDI	22	17.97 (15.39-20.67)		
2010s-2020s	7	20.22 (18.56-21.92)		
High HDI	NR	NR	N/A	
Low HDI	7	20.22 (18.56-21.92)		
Overall	50	18.98 (17.73-20.26)		
Obstetric embolism				
Pre-1970s	12	11.70 (7.62-16.34)		<0.00001
High HDI	5	14.49 (8.99-20.83)	0.313	
Low HDI	7	8.57 (3.19-15.50)		
1970s-1980s	14	10.52 (7.84-13.47)		
High HDI	6	20.08 (13.63-27.28)	0.0004	
Low HDI	8	7.62 (4.90-10.75)		
1990s-2000s	11	7.34 (3.10-12.64)		
High HDI	3	9.43 (4.40-15.73)	0.104	
Low HDI	8	10.27 (3.27-19.40)		
2010s-2020s	4	3.45 (2.80-4.17)		
High HDI	NR	NR	N/A	
Low HDI	4	3.45 (2.80-4.17)		
Overall	41	1.81 (1.22-2.48)		
Unanticipated complications of management				
Pre-1970s	5	1.25 (0.00-4.83)		<0.00001
High HDI	4	1.32 (0.00-4.88)	0.167	
Low HDI	1	16.67 (3.01-56.35)		
1970s-1980s	15	5.22 (2.99-7.85)		
High HDI	3	9.19 (3.14-17.26)	0.357	
Low HDI	12	4.49 (2.21-7.27)		
1990s-2000s	34	4.40 (3.05-5.91)		
High HDI	6	N/A*	N/A	
Low HDI	28	5.60 (4.07-7.28)		
2010s-2020s	6	14.72 (13.30-16.19)		
High HDI	NR	NR	N/A	
Low HDI	6	14.72 (13.30-16.19)		
Overall	60	8.77 (7.81-9.77)		
Other obstetric complications				
Pre-1970s	3	4.89 (0.00-14.81)		<0.00001
High HDI	2	11.55 (0.01-33.30)	0.229	
Low HDI	1	3.45 (0.61-17.18)		
1970s-1980s	7	4.94 (2.08-8.63)		
High HDI	3	5.76 (1.54-11.74)	0.761	
Low HDI	4	4.33 (0.92-9.30)		

1990s-2000s	11	0.19 (0.00-0.66)		
High HDI	2	4.58 (1.27-9.38)	0.078	
Low HDI	9	0.02 (0.00-0.33)		
2010s-2020s	3	41.54 (31.18-52.25)		
High HDI	NR	NR	N/A	
Low HDI	3	41.54 (31.18-52.25)		
Overall	24	1.29 (0.69-2.03)		
Non-obstetric complications				
Pre-1970s	13	23.73 (18.18-29.67)		
High HDI	4	11.22 (5.80-17.76)	<0.00001	
Low HDI	9	41.14 (31.87-50.68)		
1970s-1980s	11	27.02 (22.78-31.46)		
High HDI	6	10.42 (4.65-17.58)	<0.00001	
Low HDI	5	33.82 (28.74-39.07)		<0.00001
1990s-2000s	17	11.65 (9.33-14.13)		
High HDI	3	41.02 (32.26-50.05)	<0.00001	
Low HDI	14	8.01 (5.83-10.42)		
2010s-2020s	5	11.45 (10.25-12.70)		
High HDI	NR	NR	N/A	
Low HDI	5	11.45 (10.25-12.70)		
Overall	46	12.08 (11.00-13.20)		
Pregnancy with abortive outcome				
Pre-1970s	NR	NR		
High HDI	NR	NR	N/A	
Low HDI	NR	NR		
1970s-1980s	NR	NR		
High HDI	NR	NR	N/A	
Low HDI	NR	NR		
1990s-2000s	1	75.00 (30.06-95.44)		0.00005
High HDI	NR	NR	N/A	
Low HDI	1	75.00 (30.06-95.44)		
2010s-2020s	2	0.08 (0.00-0.26)		
High HDI	NR	NR	N/A	
Low HDI	2	0.08 (0.00-0.26)		
Overall	3	N/A*		
Unknown/undetermined				
Pre-1970s	5	5.53 (2.79-8.96)		
High HDI	1	4.85 (2.09-10.86)	0.465	
Low HDI	4	6.37 (2.67-11.22)		0.799
1970s-1980s	3	3.55 (0.94-7.35)		
High HDI	1	1.75 (0.31-9.29)	0.322	

Low HDI	2	4.84 (1.16-10.33)		
1990s-2000s	9	2.07 (0.73-3.85)		
High HDI	2	4.79 (1.40-9.66)	0.821	
Low HDI	7	1.50 (0.26-3.40)		
2010s-2020s	5	5.09 (4.30-5.94)		
High HDI	NR	NR	N/A	
Low HDI	5	5.09 (4.30-5.94)		
Overall	22	3.56 (2.88-4.29)		
		Coincidental causes		
Pre-1970s	NR	NR		0.321
High HDI	NR	NR	N/A	
Low HDI	NR	NR		
1970s-1980s	2	2.83 (0.00-9.09)		
High HDI	1	4.55 (0.81-21.80)	0.581	
Low HDI	1	2.33 (0.41-12.06)		
1990s-2000s	1	2.94 (0.52-14.92)		
High HDI	1	2.94 (0.52-14.92)	N/A	
Low HDI	NR	NR		
2010s-2020s	1	1.61 (1.04-2.47)		
High HDI	NR	NR	N/A	
Low HDI	1	1.61 (1.04-2.47)		
Overall	4	0.81 (0.27-1.55)		

***Analysis produced effect estimates with values of zero. HDI=human development index. NR=not reported. N/A=not available.**

Table 21: Sensitivity analysis for the prevalence of causes of caesarean-related deaths involving studies after the 1960s

Curriculum Vitae

Name:	Areej Hezam
Post-secondary Education and Degrees:	University of Toronto Toronto, Ontario, Canada 2012-2016 HBSc. The University of Western Ontario London, Ontario, Canada 2018-2020 MSc.
Honours and Awards:	Western Graduate Research Scholarship 2018-2020
Related Work Experience	Teaching Assistant The University of Western Ontario 2020