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The impact of quality improvement processes, interventions and structure on maternal and perinatal mortality in low-and middle-income countries: a systematic review and meta-analysis.

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ABSTRACT:

Background: Maternal and perinatal mortality remain high in low and middle-income countries (LMICs) compared to high income countries. We aim to summarise obstetric quality improvement (QI) processes, interventions and structure that have a measurable impact on mortality measures.

Methods: A systematic review and meta-analysis of interventional studies assessing quality improvement processes, interventions, and structure in developing country obstetric systems was conducted from according to the Preferred Reporting Items of Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Studies were included if they were conducted in a LMIC according to the World Bank Income Classification, occurred in an obstetric setting and measured the effect of an implementation on maternal or perinatal mortality.

Results: Of 42,145 search results, 46 studies were included in a qualitative synthesis, and 14 articles included for a meta-analysis. Upgrading facilities to be capable of providing emergency obstetric care improved maternal mortality by RR 0.60 (95%CI 0.40 to 0.89). Obstetric education and training, implementing community-based programs, using QI programs and eliminating user fees improved maternal and perinatal mortality.

Conclusion: There is evidence multiple QI interventions can improve maternal and perinatal mortality in an LMIC setting. These implementations should be considered by policy-makers when aiming to improve maternal outcomes.

Key words: Quality Improvement, Global Surgery, Obstetric, Maternal, Perinatal, Low- and Middle-Income Countries, Outcomes, Mortality

BACKGROUND

High maternal and perinatal mortality is a significant global health burden. An estimated 300 000 women worldwide die from complications of pregnancy and childbirth each year.[1] It is thought that the majority of these deaths could be prevented or avoided through actions that have been proven to be effective and affordable.[2,3] Millennium Development Goal 5, which aimed to reduce maternal mortality by

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75% between 1990 and 2015, was difficult to attain for a number of reasons, including inadequate access to quality care.[4,5]

Quality improvement approaches have been integrated into routine health care in high-resource settings, but not in low-resource settings. These methods include the identification of quality gaps and the assessment of strategies to overcome barriers to quality. The poor quality of care received by mothers and babies in many limited resource countries contributes to high maternal and new-born mortality levels.[6,7] Quality improvement approaches include the identification of quality gaps and the assessment of strategies to overcome barriers to quality. The limited quality of care received by mothers and babies in many limited resource countries contributes to high maternal and new-born mortality levels.[6,7] Previous studies have demonstrated quality improvement interventions could improve the process of maternal and perinatal care in developing countries.[8,9] Systematic reviews have reported that the impact of interventions was measured by an improvement in process indicators such as service utilisation, clinical knowledge, and practice, but few of these studies report the effect of quality improvement interventions on maternal and perinatal mortality.[4,5,8,10,11]

The study forms a part of a series of systematic reviews and meta-analyses conducted by the Global Alliance for Surgical, Obstetric, Trauma, and Anesthesia Care (G4 Alliance) International Standards and Guidelines for Quality Safe Surgery and Anesthesia (ISG-QSSA) Working Group using the GRADE methodology geared towards determining optimal guidelines for quality improvement initiatives in developing countries. In this systematic review, we aim to assess and quantify the effect of quality improvement processes and structure in obstetric systems on maternal and perinatal mortality. These findings can form the basis of evidence-based policy implementation recommendations that seek to increase the quality, access, and safety of obstetric systems in LMICs.

METHODS

The G4 Alliance is a 60+ member organisation representing over 300 international federations, societies, academia, and non-governmental organizations in 160 countries worldwide. In partnership with the International Society of Surgery (ISS), the Alliance formed the ISG-QSSA Working Group which is comprised of 13 members from surgical, anesthesia, government, and public health specialties with the goal of summarizing the existing evidence base regarding optimal surgical, obstetric, trauma, and anesthesia systems quality improvement interventions in order to arrive at global policy recommendations for LMICs. The steering group was charged with identifying relevant research questions and PICO considerations that formed the basis of this systematic review.

Database search

A systematic review of the literature was performed following PRISMA guidelines. The search included five databases: Medline, CINAHL, SCOPUS, CENTRAL and EMBASE and incorporated four domains: 1. LMICs, 2. Obstetric 3. Interventions 4. Mortality. (search terms in **Appendix 1**.). A Grey Literature search was performed using the Open Grey Database, Google Scholar, and WHO regional databases for Africa and Asia. Reference lists of included full-text reports and systematic reviews were cross-checked for relevant records. Date restriction was applied from January 1st, 1989. The search started in February 2020; the date of the last search was 18th August 2020. Results were restricted to English-language full-text articles. PROSPERO registration: CRD42020171542

Inclusion Criteria

Interventional study designs from LMICs that fell under the predefined World Bank Income Classification for low and middle-income countries published in English that assessed any kind of quality improvement process with a corresponding formal maternal or perinatal mortality outcome assessment were included.

Exclusion criteria

Studies were excluded if they did not involve an obstetric system or was not conducted in an LMIC setting. Studies were excluded if they did not include implementing a particular process, intervention or structure, or if they did not report outcomes as morbidity or mortality. Studies were excluded if they focused on a disease-specific intervention. Conference abstracts were not included. Review articles were not included, but all relevant reviews were examined for citations of reports that are not already found in our

search. The retrieved records from the database were imported into Endnote® and duplicates were removed. According to the inclusion and exclusion criteria, the results were screened by two independent authors (JJ and SA). If there were disagreements, consensus was reached by discussion according to the exclusion and inclusion criteria, and by a third reviewer.

Data extraction was done using a predefined form, which included information on study setting, study population, sample size, method of quality improvement intervention, and the comparison group and mortality outcome data.

Risk of Bias Analysis

For observational studies, including before and after studies, the risk of bias was assessed using the ROBINS-I Tool.[12] For randomised studies, the risk of bias was assessed with the ROB 2.0 Cluster risk of bias tool.[13] A detailed description of risk of bias judgements are included in **Appendix 2**.

Meta-Analysis

Meta-analysis was conducted when the interventions and outcomes were determined to be combinable. Meta-analysis was performed in R using the "meta" Package.[14,15] The relative risk (RR, 95% confidence interval [CI]) of the primary outcome mortality using original data from the studies was calculated by dividing the probability of death given the presence of an intervention by the probability of death given the absence of an intervention. Relative risks greater than 1 signified an increased risk of mortality in the presence of an intervention, whereas less than 1 signified a reduction of mortality of the given intervention. The Mantel-Hanzel method was used as the weighing method across studies. The I2 statistic for each analysis was calculated to estimate the fraction of variation in the effect estimate (i.e., RR of mortality) caused by heterogeneity. Significant heterogeneity was established when the I2 test statistic was greater than 50%. Random effects were chosen as the analysis moderator if significant heterogeneity among studies were found. Publication bias was assessed using a funnel plot of the effect sizes. No publication bias was noted when the effect sizes were noted to have an even dispersion around the pooled effect estimate.

RESULTS

Initial search results returned 42,145 articles. After duplicate removal, 36,133 were screened and 36,015 articles were excluded after title and abstract screening. 98 full-text articles were screened for eligibility. A total of 46 studies were included in the qualitative synthesis. Fourteen studies were included in a quantitative synthesis for meta-analysis. Studies were from 27 different countries, with 77% of included studies from Africa.

Results show a variety of studies, including randomised studies, controlled before and after studies, uncontrolled before-and-after studies, and retrospective studies. The risk of bias for observational studies and cluster-randomised studies is summarised in **Figure 2**.

In March 2020, an international group of experts from G4 and the International Society of Surgery (ISS-SIC) met in Suva, Fiji, at the Ministry of Health and reviewed the preliminary results and agreed the results were heterogeneous, and the risk of bias was inherently high due to a large number of uncontrolled before and after observational studies.

Strengthening of Maternal Facilities to be capable of Emergency Obstetric Care

Fifteen studies evaluated the effectiveness of strengthening facilities in their capabilities in providing emergency obstetric care.[16-30] There were substantial variations in the implementation scope, depending on the setting. These ranged from upgrading the clinical setting, improving staff capacity, building competence, and introducing quality improvement measures. The data extracted reported maternal deaths over the total number of deliveries, which gives a maternal mortality ratio specific to the study populations involved. A meta-analysis was performed on 14 studies which included data sufficient to calculate this outcome, one study was not included in the analysis as it had only reported obstetric case fatality rates.

The weighted pooled Risk Ratio was 0.60 (0.40-0.89) across the analysed studies. On average, the upgrading of maternal facilities to be capable of emergency obstetric care reduces mortality by 40% compared to the population without the intervention. The I2 statistic was 84%, meaning that 84% of the variance of the observed effect

reflects variance in true effects rather than sampling error.

Figure 1: PRISMA flow diagram of included studies

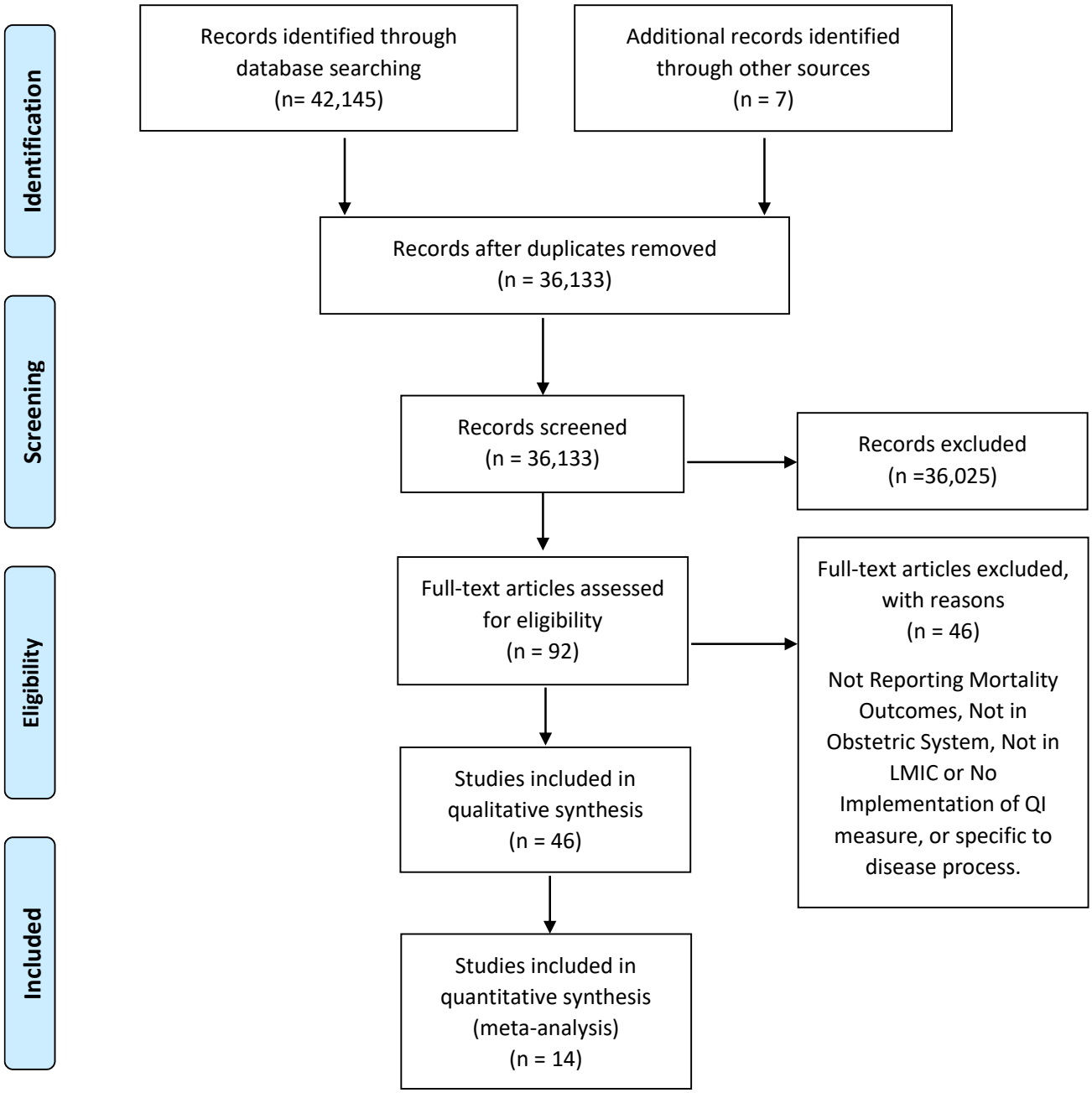


Figure 2: Risk of Bias Summary chart of included studies according to A) ROBINS-I for observational studies and B) Cochrane Risk of Bias 2.0 (Custer) for Cluster RCTs

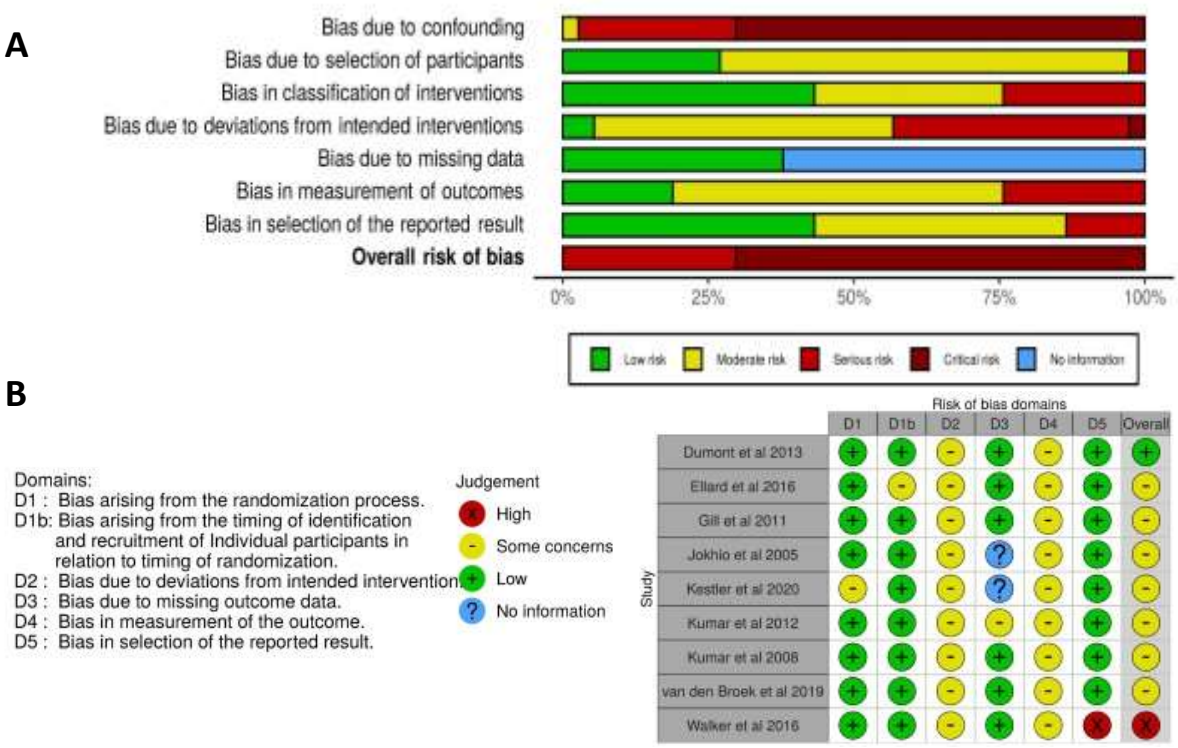
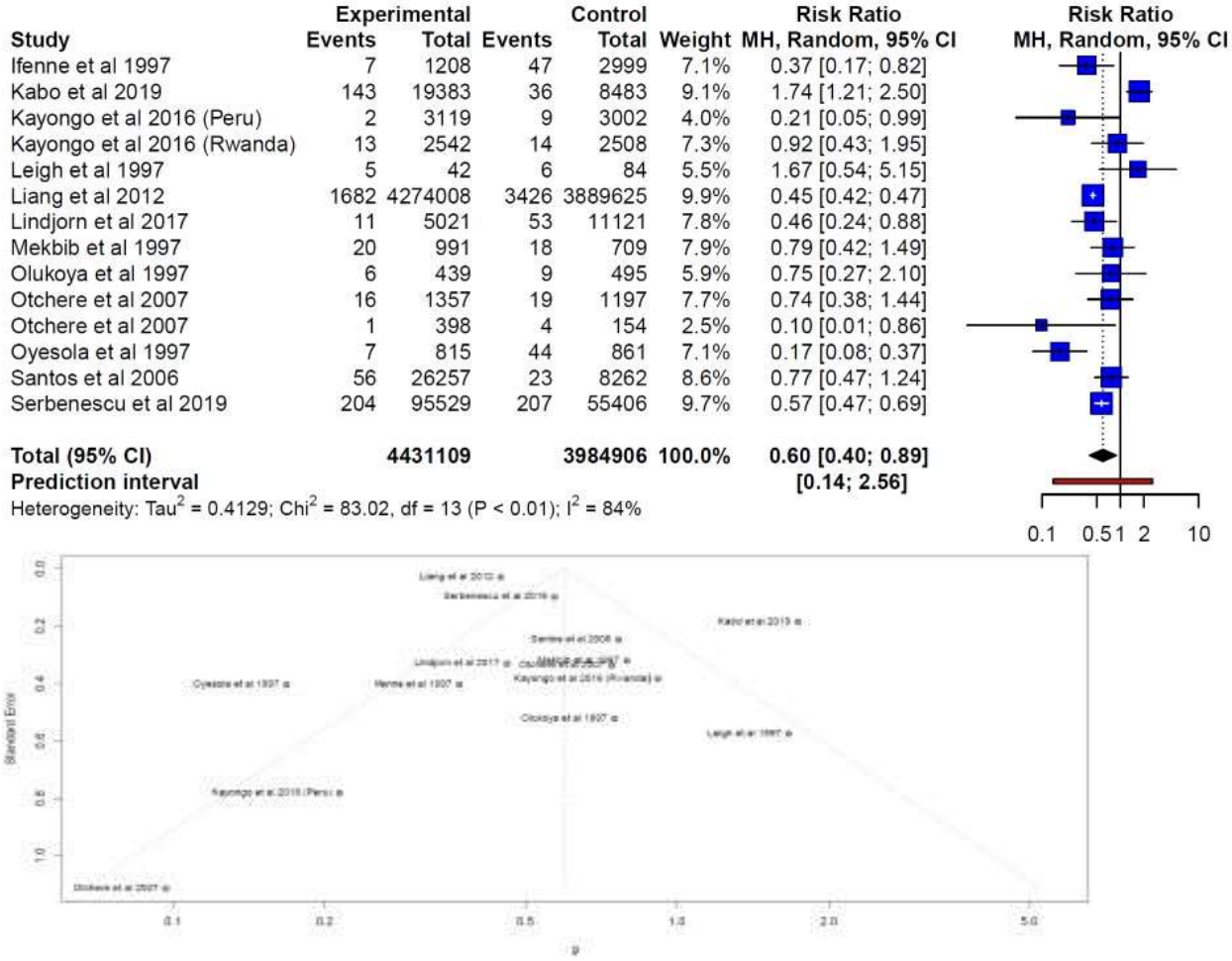


Table 1: Summary of interventions on upgrading maternal facilities to be capable of emergency obstetric care. Description of intervention, study design and outcome measured.

Study	Intervention	Location	Study Type	Time-frame	Effect Size (RR, 95%CI)	Overall Risk of Bias
Kabo et al 2019[17]	Provision of essential equipment and supplies, capacity building, supportive supervision.	Nigeria, multicentre	Prospective Before and After Study	3 years	1.74 (1.21-2.50)	Critical
Kayongo et al 2006 [18](Rwanda)	Upgrading of clinical setting. Improving staff capacity, building competence, quality improvement	Rwanda, Single centre.	Prospective Before and After Study	4 years	0.92 (0.43-1.95)	Critical
Kayongo et al 2006 (Peru) [19]	Upgrading infrastructure and facility setup; data collection and information systems; staff development and supervision.	Peru, multi-centre, Urban	Prospective Before and After Study	5 years	0.21 (0.05-0.99)	Critical
Kayongo et al 2006 (Africa)[20]	Creation of functional health facilities with trained and competent staff, enabling EmOC service delivery.	Tanzania, Rwanda, Ethiopia, Multi-Centre, Rural and Urban	Prospective before and after study.	4 years	Reported as case fatality rates	Critical

Liang et al 2012 [22]	Improving facilities, establish emergency centres, extend hospital delivery to rural areas, health education, supervision and guidance.	China, Multi-centre, Urban and Rural	Retrospective Study, Interrupted Time Series	8 years	0.45 (0.42-0.47)	Critical
Otchere et al 2007 [27] (Mali)	Preparation stage involving facility setup, training, staffing, EmOC provision. Service provision phase involving 24/7 EmOC availability, external supervision and QI processes.	Mali, Multi-Centre, Urban	Interrupted Time Series	4 years	0.74 (0.38-1.44)	Critical
Lindtjorn et al 2017 [23]	Ministry of Health lead upgrading existing instututions to carry out EmOC. Systematic audits and QI programs.	Ethiopia, Multi-Centre	Interrupted Time Series	4 years	0.46 (0.24-0.88)	Critical
Serbenescu et al 2019 [30]	Saving Mothers, giving lives approach. Community engagement, improving access to facilities	Uganda and Zambia, multi-centre.	Prospective before and after study	5 years	0.57 (0.47-0.69)	Critical
Ifenne et al 1997 [16]	Upgrading of facilities, training of staff to provide EmOC	Nigeria, single centre, Tertiary.	Prospective before and after study	6 years	0.37 (0.17-0.82)	Critical
Leigh et al 1997 [21]	Comission of facilities, training of staff.	Sierra Leone, Single Centre, District	Prospective before and after study	6 years	1.67 (0.54-5.15)	Critical
Mekbib et al 2003 [24]	Management and coordination, upgrade of facilities, training of service providers.	Ethiopia, single centre.	Prospective before and after study	3 years	0.79 (0.42-1.49)	Critical
Olukoya et al 1997[25]	Training of staff to perform EmOC, upgrade of theatre facilities.	Nigeria, Single Centre, Secondary Referral Hospital	Prospective before and after study	3 years	0.75 (0.27-2.10)	Critical
Otchere et al 2007 (Vietnam)[26]	Infrastructure improvements including equipment and supplies	Vietnam, multi centre (2 sites), district hospitals.	Prospective before and after study	4 years	0.10 (0.01-0.86)	Critical
Oyesola et al 1997 [28]	Training for in staff, provision of emergency packs for obstetric care.	Nigeria, Single centre, Tertiary	Prospective before and after study	6 years	0.17 (0.08-0.37)	Critical
Santos et al 2006 [29]	Improvements in infrastructure, EmOC facilities improved from 4 to 18. Human resource development, referral system and QI activities.	Mozambique, multi centre, district hospitals	Prospective before and after study	5 years	0.77 (0.47-1.24)	Critical

Figure 3. A meta-analysis on the effect of upgrading obstetric facilities to be capable of emergency obstetric care.



Eliminating User Fees

Four studies reported the effect of eliminating user fees to improve access to obstetric facilities. These are before-and-after studies that measured maternal and perinatal mortality before and after introducing a state-wide policy of eliminating user fees. Overall, the studies found that the state-wide elimination of user fees effectively reduced maternal and perinatal mortality. The risk of bias was critical. The results were heterogeneous in terms of study design and outcome reporting, so a meta-analysis was not performed.[31-34]

Obstetric Education and Training

Nine studies investigated the impact of an intervention based on obstetric education and training of associate clinicians and junior medical personnel. These studies reported a heterogeneous mix of interventions, study designs, and outcome reporting, so a meta-analysis was not performed.[35-43]

Overall, there are 3 cluster RCTs and 6 before and after studies. The interventions vary from short courses of 1-2 days duration consisting of skills and drills training to long-term interventions such as postgraduate training. Other quality improvement interventions include the WHO package in effective perinatal care on infant mortality.[43] Overall, the studies reported a reduction for maternal mortality ranging from RR 0.20-0.79 (95%CI 0.09-1.20), and perinatal mortality RR 0.50- 0.59 (95%CI 0.38- 0.71). The summary of the studies is displayed in **Table 3**.

Table 2: Summary of studies showing the effect of elimination of user fees and education and training in obstetric systems. Description of intervention, study design and outcome measured.

Summary of studies showing the effect of eliminating user fees.					
Study	Intervention	Location, Study Type	Study Type	Effect Size	Overall Risk of bias
Ebrahim et al 2000 [31]	Free antenatal care across the region.	South Africa, Single centre, tertiary.	Retrospective study	PMR decreased from 26/1000 to 22.7/1000 births.	Critical
Johri et al 2014 [32]	Eliminating user fees for pregnant women and children under 5	Burkina Faso, Multi-centre, district level.	Interrupted time-series study	Under 5 mortality decreased from 235 per 1000 births to 210 per 1000 births.	Critical
Lang'at et al 2019 [33]	Free maternity Service Policy	Kenya, Multi-centre, county level.	Retrospective study	No significant change in stillbirth rate or C-section rate.	Critical
Zhou et al 2012 [34]	Integrated approach including elimination of user fees, health promotion. Training of health-care providers.	China, Multi-centre, County level.	Prospective before and after study	MMR decreased from 45.5/100,000 births to 32.7/100,000.	Critical
Summary of Education and Training in Obstetric systems.					
Ellard et al 2016 [35]	Upskilling of Associate Clinicians	Malawi, Community based	Cluster RCT	RR for Control 1.31 (0.97, 1.77) RR Intervention Group 0.67 (0.55 to 0.81)	Some concerns
van den Broek et al 2019 [36]	Training on Emergency Obstetric Care	South Africa, multicentre, district based.	Stepped-Wedge Cluster RCT,	RR Before and after 1.17 (0.94, 1.46)	Some concerns
Walker et al 2016 [37]	Simulation Based Training in Obstetric Emergencies	South Africa	Cluster RCT	Maternal Complication Index reported, no maternal deaths reported.	High
Chang et al 2019 [38]	Training on teamwork protocols, skills and drills	Malawi, multicentre, district based.	Before and After study	RR Before and after 0.18 (0.04 to 0.84)	Serious
Crofts et al 2015 [39]	Onsite Emergency Obstetric Training	Zimbabwe, multicentred	Before and After Study,	RR Before and after 0.69 (0.47 to 1.00)	Serious
Martley et al 1995 [40]	Postgraduate Training in Obstetrics and Gynaecology	Ghana, single centre.	Before and After Study	Maternal Mortality Ratio Reduction 7.0 per 1000 deliveries to 4.2 per 1000	Critical
Pattinson et al 2019 [41]	Skills and Drills Training in Emergency Obstetrics	South Africa, multicentre	Before and After Study	RR Before and After 0.71 (0.65, 0.77)	Critical
Shikuku et al 2019 [42]	High Frequency Clinical Mentorship Program	Kenya, multi-centre.	Controlled Before and After Study	No maternal deaths reported in both groups	Serious
Berglund et al 2010 [43]	Training using 'Effective Perinatal Care', (EPC) approach.	Ukraine, multicentre,	Before and after study,	No effect on early perinatal mortality.	Critical

Table 3: Summary of community-based programs on the training of traditional birth attendants (TBAs). Description of intervention, study design and outcome measured.

Author	Intervention	Study Type, Location	Quantitative outcome	Overall risk of bias
Kestler et al 2020 [50]	Multifaceted intervention Skills and drills training of obstetric teams, Training of TBAs involving workshops with pregnant women, obstetric and neonatal emergency simulations, and a social marketing campaign.	Stepped wedge cluster RCT, Guatemala	Maternal Mortality Adjusted RR 0.78 (0.60-1.02). Perinatal Mortality Adjusted 0.84(-.68-1.05)	Some concerns
Kumar et al 2012 [51]	Community based Essential maternal and new-born care comprised of birth preparedness, including preparation of the delivery room, prior identification of birth attendant, and emergency preparedness; hygienic delivery and immediate newborn care; post-partum care; and care seeking from trained providers.	Cluster RCT, India,	Maternal Mortality RR 0.50, (95% CI 0.22 to 1.15)	Some concerns
Kumar et al 2008 [52]	Community based Essential maternal and new-born care, including skin-to-skin care between the infant and a family member, promoted through behaviour change management, layered on existing services available to the control groups.	Cluster RCT, India	Perinatal Mortality RR 0.48, (95% CI 0.34 to 0.66)	Some concerns
Fauveau et al 1991 [45]	Community Care program with trained Midwives equipped to treat immediate obstetric complications at onset, backed up by effective chain of referral.	Controlled Before and After Study, Bangladesh	Change in MMR -3.04 per 1000 intervention vs -0.02 per 1000 control.	Critical
Broughton et al 2006 [44]	Integration of traditional birth attendants in community and outreach involving service reorganization, integration of TBAs with formal supervision, community outreach and education, and health worker technical training.	Controlled Before and After Study, Ethiopia	Perinatal Mortality Change in PNR -1.3 per 1000 intervention vs +0.2 per 1000 control	Serious
Schaider et al 1999 [54]	Traditional Birth Attendant Training: intensive 38-hr training course on skills for safe prenatal, delivery, and postnatal care.	Before and After Study, Angola	Maternal Mortality, 1241 per 100,000 Before to 293 per 100,000 After	Critical
Satischandra et al 2013 [53]	Traditional Birth Attendant Training, 2 days intensive training programme with, topics on antenatal care, safe delivery practices, postnatal care and family planning practices.	Before and after Study, India	Maternal mortality, 11 deaths preintervention period to 3 deaths post intervention period.	Serious
Gill et al 2011 [47]	Traditional Birth Attendant training in a modified version of the neonatal resuscitation protocol, and single dose amoxicillin coupled with facilitated referral of infants to a health centre.	Cluster RCT, Zambia	Maternal Mortality Risk Ratio 0.57, (95% CI 0.38 to 0.83)	Some concerns
Jokhio et al 2005 [49]	Training of Traditional Birth Attendant involving use of picture cards containing advice on antepartum, intrapartum, and post-partum care; how to	Cluster RCT, Pakistan	Maternal Mortality, Risk Ratio 0.74 (95% CI 0.45 to 1.23)	Some concerns

	conduct a clean delivery; use of the disposable delivery kit; when to refer women for emergency obstetrical care; and care of the newborn.			
Huoy et al 2017 [48]	Training of emergency obstetric care focusing on resuscitation of blue babies and obstetric emergencies. A core group of 27 experienced midwives and trauma paramedics were trained as instructors to conduct two-day courses	Interrupted Time Series, Cambodia	Maternal Mortality RR 0.51 (95% CI 0.27 to 0.98)	Serious
Garces et al 2012 [46]	Training of Traditional Birth Attendants on WHO essential new-born care focusing on practice and acquisition of skills with one-on-one monitoring and follow-up in clinical contexts in the field.	Before and after study, Guatemala	Perinatal Mortality Risk Ratio 0.72 (0.54, 0.97)	Serious

Implementation of Community-Based Programs on training Traditional Birth Attendants

Eleven studies investigated the effect of community-based interventions in reducing maternal mortality.[44-54] These studies all implemented training and education of traditional birth attendants (TBAs) in the community setting, these included skills courses taken by TBAs in providing evidence-based pre-natal, safe delivery and post-natal care and recognition and management of emergencies and prompt referral for emergency care.

These studies report a mix of mortality measures and some studies had a randomised allocation with the presence of a control group and measured outcomes before and after the intervention. Other studies (before-and-after studies) were uncontrolled and only measured the effect at two different time points. Hence a meta-analysis was not undertaken in these studies due to the variation in study design and data reporting.

Overall, these studies indicate a measurable effect on maternal mortality or perinatal mortality when measured before and after the intervention and between randomised control and intervention groups. The RR for maternal mortality ranged from 0.48 (0.34 to 0.66) to 0.74 (0.45 to 1.23).

Multifaceted Maternal Quality Improvement Measures

Seven studies measured the impact of multifaceted maternal quality improvement programs.[55-61] These implementations were heterogeneous, and the studies reported the outcomes as a mix of improvement in maternal mortality, case fatality rates and perinatal mortality. Some studies also had control groups, and others were uncontrolled. The results were not able to be pooled with a meta-analysis. The quality improvement packages described were varied; these included monitoring and evaluating hospital outputs, quarterly meetings on continuous quality improvement, improved hospital governance, and management. Cavallin *et al*. assessed the changes based on the World Health Organisation's maternal and neonatal quality of hospital care assessment tool and measured outcomes was perinatal mortality rates were demonstrated to be RR 0.50 (0.38 to 0.66).[55] Dumont et al. undertook a cluster RCT to assess the impact of a multifaceted intervention involving establishing a multidisciplinary audit committee trained in undertaking maternal death reviews and providing feedback. The study compared the maternal mortality ratio between intervention and controlled districts and found the RR 0.85 (0.73-0.98).[56] Srofenyoh *et al.* investigated the effect of bundled continuous quality improvement interventions on case fatality rates using a before and after study model in Ghana, which was accompanied by a 22.4% reduction in maternal mortality from 2007 to 2011.[61]

Table 4: Maternal Quality Improvement Programs. Description of Intervention, Study design, and outcome measured.

Study	Intervention	Study type and location	Effect size RR, 95%CI	Overall risk of bias
Dumont et al 2013 [56]	"Quality of Care, Risk Management and Technology implementation"- Includes best practices training, Maternal Death Reviews, Audit cycles and training.	Cluster RCT, Senegal and Mali	Maternal Mortality RR in Intervention arm 0.66 (0.57 - 0.76) compared to Control arm 0.88(0.76-1.02)	Low
Pattinson et al 2006 [58]	Cycle of audit, identification of problems, strategies to solve those problems, implementation of those strategies and audit to evaluate the results of the new strategies	Retrospective Review, South Africa	Maternal Mortality RR 0.79 (95%CI 0.52-1.20)	Critical
Sarin et al 2017 [60]	Training of Implementation of a QI intervention guide. Interventions covered systemic and process changes including facility improvement, supplies of medicines, improved record keeping and so on depending on the nature of the problem identified.	Interrupted Time Series, India	Perinatal Mortality Rate 26.7 before to 22.9 after per 1000 births.	Serious
Cavallin et al 2019 [55]	The implementation included: provision of experienced health care staff; participation in hospital governance; training of local staff; quarterly meeting on continuous quality improvement; monitoring and evaluation of hospital outputs.	Interrupted Time Series, India	Perinatal Mortality Relative Risk 0.50 (0.38-0.66)	Serious
Srofenyoh et al 2016 [61]	Interventions based on three themes (Personnel (P) Quality (Q) System (S) P1 Leadership and organizational development. P2 Motivation, empowerment, responsibility, and accountability of staff. P3 Improvement of knowledge and skills Q1 Improvement of service quality and standards of clinical care Q2 Facilitation of communication between and within departments. Q3 Improvement of communication and feedback with referring institutions S1 Improvement of patient flow processes and timeliness of care S2 Improvement of physical workspace and maximization of capacity S3 Improvement of resources (staffing and equipment) and logistics supplies.	Interrupted Time Series, Ghana	Maternal Mortality RR 0.76 (0.47-1.23)	Serious
Mbaruku et al 1996 [57]	Attention to professional responsibilities with regular audit-oriented meetings, utilization of local material resources, schedules for regular maintenance of equipment, maintenance of working skills by regular on-the-job training of staff, norms for patient management, provision of blood, norms for referral of severely ill patients.	Retrospective Review, Tanzania	Maternal Mortality RR 0.20 (0.09-0.44)	Critical
Rudge et al 2011 [59]	Creation a health system structure based on the exchange of patients from the Level II to the Level III hospital appropriate to the	Interrupted Time Series, Brazil	Perinatal Mortality 0.59 (0.49-0.71)	Serious

level of care required, including the provision of effective
transport from one hospital to the other.

Other interventions not further classified

Several studies reported the effect of disease-specific interventions that may impact maternal mortality; These are specific interventions that target a particular condition, so they were not included in the review. Interventions included the evaluation of the effect of evidence-based guidelines and standardised protocols on maternal mortality, and these included post-partum haemorrhage, eclampsia, and vacuum extraction guidelines.[62-65] Two studies investigated the effect of chlorhexidine cleaning of the umbilical stump and found no change in perinatal mortality.[66-67] Three studies also described a modified WHO safe childbirth checklist which were specific interventions and did not report an improvement in maternal outcomes.[68-70] Other studies included implementing the non-pneumatic-anti-shock garment aimed to reduce the morbidity and mortality following post-partum haemorrhage.

DISCUSSION

Improving maternal mortality remains a key priority in the Asia-Pacific region. An estimated 85,000 women die from pregnancy and childbirth in Asia and the Pacific every year. An extreme disparity in maternal mortality outcomes is seen in this region; the maternal mortality ratio (MMR) averaged around 140 deaths per 100,000 live births in lower-middle- and low-income countries in the Asia Pacific region in 2017. This ratio is more than fourteen times the average for high-income Asia Pacific countries, thus highlighting the inequalities in access to quality health services.[71] (Reference #74) The leading causes of maternal deaths are severe bleeding after childbirth, infections, hypertension in pregnancy, and unsafe abortion, the majority of which can be prevented through quality antenatal, obstetric and perinatal care. Reductions in MMRs have been achieved in certain countries over the last two decades; however, a significant gap still remains in resource-poor regions.[71] (Reference #74) Global action is urgently required to address the disparities of and burden of maternal mortality.

This systematic review has described a number of interventions that reduce maternal mortality and perinatal mortality when implemented in an LMIC setting. Several interventions focused on improving access; this includes implementing community-based programs and training and upskilling of traditional birth attendants. Also, there is evidence that strengthening facilities' capability to provide emergency obstetric care and eliminating user fees can reduce maternal mortality. Although previous systematic reviews have outlined similar quality improvement interventions that may be effective, however, they did not focus on interventions specifically targeting maternal or perinatal mortality.[5,8,9,72]

Significant improvements in maternal mortality are not feasible without improving access. Despite achieving access, the quality of care and availability of services can be varied in these institutions.[9] Institutional quality improvement measures such as departmental education, maternal death reviews, and audits with feedback have been shown to be effective. These quality improvement interventions have been highlighted in previous systematic reviews that measure health care utilisation or compliance outcomes, but not mortality.[5,9] Other specific interventions examples include the adoption of evidence-based guidelines in the hospital could reduce mortality associated with certain conditions.[62-65]

There is evidence that the training and upskilling of care providers can improve maternal and perinatal mortality.[35-42] Many obstetric care providers lack formal training, and there are often not enough medically trained obstetricians in low resource settings. Health care workers, known as "Associate Clinicians" are usually trained in primary diagnosis and treatment. Many are trained in providing obstetric care and are the frontline in delivering babies.[73] Training these skilled attendants to prevent, detect, and manage obstetric complications and perform emergency C-sections is essential in reducing maternal mortality.[11,35] Although these interventions are considered effective, economic evaluations of emergency obstetric training is limited, and further studies are required to standardise scale-

up and economic evaluation of these interventions.[74]

Complex interventions, such as strengthening facilities in providing emergency obstetrics, showed a significant improvement in mortality of RR 0.60 (0.40-0.89). Several studies of this nature targeted individual referral hospitals and upgraded clinical capacity in Africa during the 1990s; the project was titled PMM (Preventing Maternal Mortality).[16,21,25,28] In the 2000s, a number of projects known as AMDD (Averting Maternal Death and Disability) covered a diverse range of sites and upgraded facilities through a district-based approach.[18-20,27,29] These quasi-experimental studies tend to integrate multiple interventions and for more extended periods, compared to randomised studies. These studies had the disadvantage that confounding was not able to be controlled, which lead to the appraisal of a critical risk of bias according to ROBINS-I.

Eliminating user fees is also an important measure in improving access, thereby associated with reducing maternal mortality.[33] There is no high-quality evidence that removing user fees can reduce mortality. Still, four studies show that the elimination of user fees has resulted in increased utilisation of health-care services, including in-hospital deliveries.[31-34] However, there could be many uncontrolled confounding factors that may lead to spurious results. Furthermore, the mortality rate measured as in-hospital maternal mortality did not reflect deaths occurring outside of a hospital setting; therefore, the reported results may not be accurate for an entire district.

Traditional birth attendants are an essential source of obstetric care in resource-poor settings, particularly in rural areas with limited health care.[49] Several studies show that the implementation of community-based programs such as training traditional birth attendants improve maternal mortality and perinatal mortality.[44-49,51-54] The studies show training of birth providers results in increased regular antenatal care and increased referrals for complications. The studies show that primary obstetric care and life support reduces the risk of maternal and perinatal death if provided timely and appropriately. There are multiple cluster-RCTs therefore, high quality evidence exists for these interventions.

The risk of bias for observational studies was appraised with ROBINS-I, and the cluster-RCTs were appraised with ROB 2.0 with additional considerations for cluster-RCTs.[12,13] Overall we found ROBINS-I was adequate for use. There were limitations in its application in the appraisal of confounding in before-and-after studies, which is inherently unable to be controlled resulting in critical risk of bias. Several studies attempted to control known confounders through statistical measures; despite this, a serious risk of bias remains from residual confounding. Overall, the cluster-RCTs were similar in study design. The main risk of bias arose from the domain of deviation in intended interventions and measurement of the outcome as a result of participants and assessors being aware of the interventions provided.

This systematic review's limitations are that it focused our inclusion and exclusion criteria on a set of studies that reported mortality outcomes. Studies that did not include mortality outcomes were excluded; therefore, descriptions of quality improvement programs that report process outcomes, clinical care, and service utilisation are not described in this review. Examples include using vital interventions, compliance with various protocols, and the percentage of c-sections. Other limitations of this systematic review are the broad scope of the review and the search strategy, resulting in missing studies. Future reviews should focus on the effect of individual quality improvement interventions. There is also a high probability of publication bias affecting our results. The majority of papers report positive findings, which could be likely due to quality improvement studies failing to publish the results if there were negative findings.

CONCLUSION

In conclusion, this systematic review shows many quality improvement interventions that effectively reduce maternal and perinatal mortality in the LMIC setting. These include upgrading facilities to provide emergency obstetric care, implementing clinical guidelines and protocols in obstetric care, education and training of associate clinicians and traditional birth attendants in institutions, and community-based approaches as methods to improve maternal mortality. Although most of the studies were before and after design, there were several cluster-RCTs, indicating the potential for

conducting future well-designed trials, contributing a high level of evidence.

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CONFLICTS OF INTEREST

None declared

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APPENDIX 1: Study Protocol Based on PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist.

Section and topic	Item No	Checklist item
ADMINISTRATIVE INFORMATION		
Title:		
Identification	1a	This report is a systematic review protocol.
Update	1b	No update available.
Registration	2	CRD42020171542
Authors:		
Contact	3a	James Jin, corresponding author. James.jin@auckland.ac.nz , South Auckland Clinical Campus, University of Auckland, PO Box 93311, Otahuhu 1640, Auckland, New Zealand.
Contributions	3b	James Jin- database searching, screening of results, data extraction, data analysis, write up of manuscript, original draft, review and editing. Salesi 'Akau'ola: second reviewer for screening of results, data curation. Cheng-Har Yip: review of manuscript and editing, data validation, conceptualisation of ideas. Emmanuel A. Ameh: review of manuscript and editing, data validation conceptualisation of ideas. Peter Nthumba: review of manuscript and editing, methodology,conceptualisation of ideas. Stijn de Jong, review of manuscript, advice on methodology. Mira Mehes: project administration, conceptualisation of ideas, review of manuscript. Iferemi Waiqanabete: conceptualisation of ideas, review of manuscript Jaymie Henry: supervision, review of manuscript and editing, data validation, conceptualisation of ideas. Andrew Hill: supervision, review of manuscript and editing, conceptualisation of ideas.
Amendments	4	No amendments.
Support:		
Sources	5a	No financial support.
Sponsor	5b	No sponsor.
Role of sponsor or funder	5c	No role of funder or sponsor.
INTRODUCTION		
Rationale	6	The Lancet Commission has highlighted inequity in the burden of obstetric mortality in LMICs compared to High Income Countries. Quality improvement processes are integral in reducing morbidity and mortality in Obstetric systems. There is limited knowledge on the effectiveness of such interventions in LMIC. We aimed to establish an evidence base for Quality Improvement interventions in Obstetric systems in LMIC that have a clear outcome on maternal or perinatal mortality.
Objectives	7	Research question: What are quality improvement processes, interventions and structure of obstetric systems in low- and middle-income settings that can improve maternal and perinatal mortality? Population: Low- and middle-income countries according to World Bank criteria. All study settings must include a Low- or Middle-Income setting. We will classify

		the setting according to country, if the study takes place in a single-centre or multi-centre, and level of setting, i.e. Urban or rural, primary vs tertiary etc. Intervention: Interventions, structure, processes that improve morbidity and mortality in the above settings. These are specific interventions which have been implemented, and the effect of the implementation measured. ie, implementation of a guideline, checklist, quality improvement program which shows an improvement in morbidity or mortality. Comparator: Comparator is the non-exposed control group; this includes study population before intervention. Outcome: Maternal or Perinatal Mortality measures.
METHODS		
Eligibility criteria	8	Studies to be included: Studies that satisfy the PICO criteria as above. Studies that show the effect of a specific process, structure, or intervention on morbidity or mortality in obstetric care systems, in a low-middle-income-country setting. Studies to be excluded are: 1. Studies not on Obstetrics or maternity systems. 2. Studies that do not mention the implementation of a specific process, structure, or intervention. 3. Studies that do not report data on morbidity or mortality. 4. Studies that do not involve a low-middle-income-country setting. Years to be considered- 1989, final search of database 18th August 2020. Studies in English language. Only full text studies are included.
Information sources	9	MEDLINE, Embase, Cochrane controlled register of clinical trials (CENTRAL), CINAHL, Scopus, WHO regional databases- Africa and Asia, Grey Literature, Open Grey. Final search of database on 18th August 2020.
Search strategy	10	See appendix.
Study records:		
Data management	11a	Studies are imported into Endnote for screening and review.
Selection process	11b	At least two independent reviewers will screen the titles and abstracts using the relevant inclusion and exclusion criteria. If there are any disagreements, the titles and abstracts will be assessed by agreement.
Data collection process	11c	Data will be obtained from reviewing the full-text paper. The data extraction table will be made on Microsoft Excel. The reviewers will then add the relevant data to the tables.
Data items	12	Percentage reduction in mortality, Odds ratio, Risk ratio, Study characteristics, number of participants, country, duration of study.
Outcomes and prioritization	13	Percentage reduction in mortality, Odds ratio, Risk ratio, Risk difference, in Mortality. Additional outcome is cost effectiveness. Cost of interventions measured in dollar amount if appropriate.
Risk of bias in individual studies	14	Risk of bias analysed for individual studies using the ROBBINS-I and ROB 2.0 depending on the studies.
Data synthesis	15a	Data will be synthesised if the studies in question describes a similar intervention of a quality improvement intervention, structure or process.

	15b	Meta-analysis will be conducted when the interventions and outcomes were determined to be combinable. Meta-analysis will be performed using appropriate software. The relative risk (RR, 95% confidence interval [CI]) of the primary outcome mortality using original data from the studies was calculated by dividing the cumulative incidence of mortality given the presence of an intervention by the cumulative incidence of mortality given the absence of an intervention. Relative risks greater than 1 signified an increased risk of mortality in the presence of an intervention, whereas less than 1 signified a reduction of mortality of the given intervention. The Mantel-Hanzel method will be used as the weighing method across studies. The effect size chosen was the risk ratio RR. Random effects will be chosen as the analysis moderator. A funnel plot will be used to assess the publication bias. Heterogeneity will be measured using the I2 ¬statistic.
	15c	No sensitivity analyses will be undertaken.
	15d	We will summarise the nature and the relative effect of the interventions if the intervention cannot be quantitatively synthesised.
Meta-bias(es)	16	Meta-biases will be assessed at the individual study level using Cochrane Risk of bias tool.
Confidence in cumulative evidence	17	We will not further synthesise the strength of the body of evidence in this review.

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.

Search Strategy:

Database search conducted by Author J.J. with assistance from Counties Manukau District Health Board Library, Middlemore Hospital, Auckland, New Zealand. Date of last search conducted 18th August 2020.

Medline and EMBASE:

Ovid MEDLINE(R) Epub Ahead of Print, In Process & Other Non-Indexed Citations, Ovid MEDLINE (R) Daily, and Ovid MEDLINE (R) 1946-Present

1 Global Health/ or Developing Countries/ or Poverty/ 152988
2 (("low-and-middle-income" or "third-world" or "3rd world" or developing or underdeveloped or "under-developed" or "less-developed" or "least-developed") adj3 (countr* or nation* or state* or region* or world*)).ti,ab,kw. 97904
3 ("low-and-middle-income" or "third-world" or "3rd world" or "developing countr*" or "developing nation*" or "developing state*" or "developing region*" or "underdeveloped countr*" or "underdeveloped nation*" or "underdeveloped state*" or "underdeveloped region*" or "under-developed countr*" or "under-developed nation*" or "under-developed state*" or "under- developed region*" or "less-developed countr*" or "less-developed nation*" or "less-developed state*" or "less-developed region*" or "least-developed countr*" or "least-developed nation*" or "least-developed state*" or "least-developed region*").kw. 33756
4 LMIC*.ti,ab,kw. 5619
5 exp Afghanistan/ or exp Albania/ or exp Algeria/ or exp American Samoa/ or exp Angola/ or exp Argentina/ or exp Armenia/ or exp Azerbaijan/ or exp Bangladesh/ or exp Belarus/ or exp Belize/ or exp Benin/ or exp Bhutan/ or exp Bolivia/ or exp "Bosnia and Herzegovina"/ or exp Botswana/ or exp Brazil/ or exp Bulgaria/ or exp Burkina Faso/ or exp Burundi/ or exp Cabo Verde/ or exp Cambodia/ or exp Cameroon/ or exp Central African Republic/ or exp Chad/ or exp China/ or exp Colombia/ or exp Comoros/ or exp "Democratic

Republic of the Congo"/ or exp Congo/ or exp Costa Rica/ or exp Cote d'Ivoire/ or exp Cuba/ or exp Djibouti/ or exp Dominica/ or exp Dominican Republic/ or exp Ecuador/ or exp Egypt/ or exp El Salvador/ or exp Equatorial Guinea/ or exp Eritrea/ or exp Ethiopia/ or exp Fiji/ or exp Gabon/ or exp Gambia/ or exp "Georgia (Republic)"/ or exp Ghana/ or exp Grenada/ or exp Guatemala/ or exp Guinea/ or exp Guinea-Bissau/ or exp Guyana/ or exp Haiti/ or exp Honduras/ 452884

6 exp India/ or exp Indonesia/ or exp Iran/ or exp Iraq/ or exp Jamaica/ or exp Jordan/ or exp Kazakhstan/ or exp Kenya/ or exp Kiribati/ or exp "Democratic People's Republic of Korea"/ or exp Kosovo/ or exp Kyrgyzstan/ or exp Laos/ or exp Lebanon/ or exp Lesotho/ or exp Liberia/ or exp Libya/ or exp Madagascar/ or exp Malawi/ or exp Malaysia/ or exp Maldives/ or exp Mali/ or exp Marshall Islands/ or exp Mauritania/ or exp Mauritius/ or exp Mexico/ or exp Micronesia/ or exp Moldova/ or exp Mongolia/ or exp Montenegro/ or exp Morocco/ or exp Mozambique/ or exp Myanmar/ or exp Namibia/ or exp Nauru/ or exp Nepal/ or exp Nicaragua/ or exp Niger/ or exp Nigeria/ or exp "Macedonia (Republic)"/ or exp Pakistan/ or exp Papua New Guinea/ or exp Paraguay/ or exp Peru/ or exp Philippines/ 348526

7 exp Romania/ or exp Russia/ or exp Rwanda/ or exp Samoa/ or exp "Independent State of Samoa"/ or American Samoa/ or Samoa/ or exp "Sao Tome and Principe"/ or exp Senegal/ or exp Serbia/ or exp Sierra Leone/ or exp Solomon Islands/ or exp Somalia/ or exp South Africa/ or exp South Sudan/ or exp Sri Lanka/ or exp Saint Lucia/ or exp "Saint Vincent and the Grenadines"/ or exp Sudan/ or exp Suriname/ or exp Syria/ or exp Tajikistan/ or exp Tanzania/ or exp Thailand/ or exp Timor-Leste/ or exp Togo/ or exp Tonga/ or exp Tunisia/ or exp Turkey/ or exp Turkmenistan/ or exp Tuvalu/ or exp Uganda/ or exp Ukraine/ or exp Uzbekistan/ or exp Vanuatu/ or exp Venezuela/ or exp Vietnam/ or exp Yemen/ or exp Zambia/ or exp Zimbabwe/ 283823

8 (Afghanistan* or Albania* or Algeria* or "American Samoa*" or Angola* or Argentina* or Armenia* or Azerbaijan* or Bangladesh* or Belarus* or Belize* or Benin* or Bhutan* or Bolivia* or Bosnia* or Herzegovina* or Botswana* or Brazil* or Bulgaria* or "Burkina Faso*" or Burundi* or "Cabo Verde*" or Cambodia* or Cameroon* or "Central African Republic*" or Chad* or China* or Colombia* or Comoros* or Congo* or "Costa Rica*" or "Cote d'Ivoire*" or "Ivory Coast*" or Cuba* or Djibouti* or Dominica* or "Dominican Republic*" or Ecuador* or Egypt* or "El Salvador*" or "Equatorial Guinea*" or Eritrea* or Ethiopia* or Fiji* or Gabon* or Gambia* or Georgia* or Ghana* or Grenada* or Guatemala* or Guinea* or "Guinea-Bissau*" or Guyana* or Haiti* or Honduras*).ti,ab,kw. 640807

9 (India* or Indonesia* or Iran* or Iraq* or Jamaica* or Jordan* or Kazakhstan* or Kenya* or Kiribati* or Korea* or Kosovo* or Kyrgyzstan* or Laos* or Lebanon* or Lesotho* or Liberia* or Libya* or Madagascar* or Malawi* or Malaysia* or Maldives* or Mali* or "Marshall Islands*" or Mauritania* or Mauritius* or Mexico* or Micronesia* or "Micro-nesia*" or Moldova* or Mongolia* or Montenegro* or Morocco* or Mozambique* or Myanmar* or Namibia* or Nauru* or Nepal* or Nicaragua* or Niger* or Nigeria* or Macedonia* or Pakistan* or "Papua New Guinea*" or Paraguay* or Peru* or Philippines*).ti,ab,kw. 1164680

10 (Romania* or Russia* or Rwanda* or Samoa* or "Sao Tome*" or Principe* or Senegal* or Serbia* or "Sierra Leone*" or "Solomon Islands*" or Somalia* or "South Africa*" or Sudan* or "Sri Lanka*" or "Saint Lucia*" or "St Lucia*" or "Saint Vincent*" or "St Vincent*" or Grenadines* or Suriname* or Syria* or Tajikistan* or Tanzania* or Thailand* or "Timor-Leste*" or Togo* or Tonga* or Tunisia* or Turkey* or Turkmenistan* or Tuvalu* or Uganda* or Ukraine* or Uzbekistan* or Vanuatu* or Venezuela* or Vietnam* or Yemen* or Zambia* or Zimbabwe*).ti,ab,kw. 293655

11 surg*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] 3214114

12 obstet*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] 188008

13 Obstetrics/ 22984

14 quality improvement.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] 56001

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17 guideline*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] 490839

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21 exp morbidity/ or exp basic reproduction number/ or exp mortality/ or exp "cause of death"/ or exp child mortality/ or exp fatal outcome/ or exp fetal mortality/ or exp hospital mortality/ or exp infant mortality/ or exp maternal mortality/ or exp mortality, premature/ or exp survival rate/ 921070
22 mortality.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] 1188099
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24 adverse event*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] 169825
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26 structure.mp. 1560148
27 14 or 15 or 16 or 17 or 18 or 19 or 26 4025250
28 11 or 12 or 13 or 20 3437110
29 21 or 22 or 23 or 24 2047783
30 25 and 27 and 28 and 29 17907

SCOPUS

(TITLE-ABS-KEY (obstetric AND mortality)) AND (quality)

4,373 Results

CINAHL Plus

ALL fields “Obstetric” AND “Mortality”

4943 Results

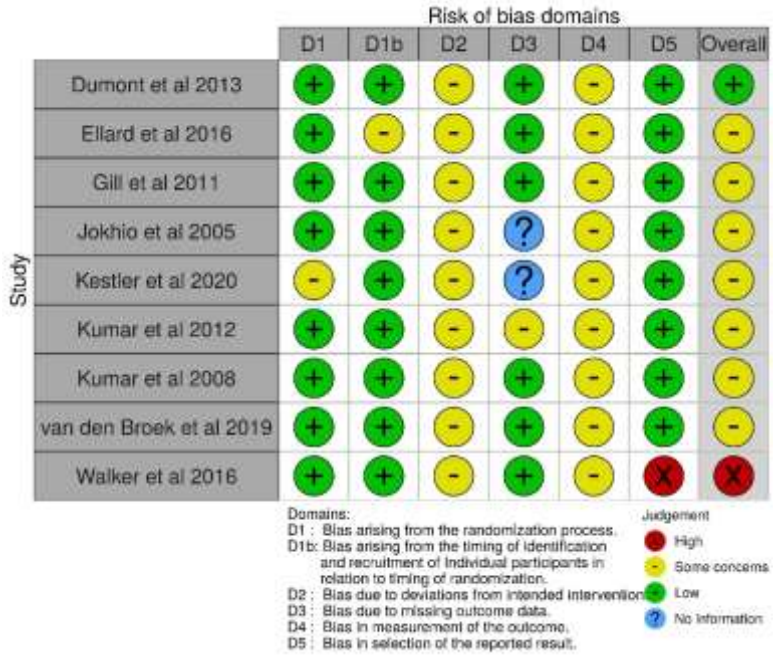
CENTRAL

ALL Text “Obstetric” AND “Mortality”

727 Results

APPENDIX 2: Risk of Bias Assessment

Risk of Bias for Cluster-Randomised Controlled Trials- ROB 2.0



Risk of bias summary chart according to ROB 2.0 (Cluster)

Dumont et al 2013	
Randomisation Process	Low
Allocation Sequence was random, was concealed and no difference in baseline characteristics. "Within each stratum blocked randomisation was used, with each block including two hospitals of similar size. Investigators were informed of the allocation status of the individual hospitals only after the collection Hospitals were stratified by country and hospital type (hospitals in the capital, regional hospitals, and district hospitals outside the capital). To ensure balance in size (number of deliveries per year) between hospitals assigned to the two groups, of baseline data was completed and immediately before the first workshop, as per protocol."	
Bias arising from the timing of identification and recruitment of individual participants in relation to timing of randomization.	Low
Participants were identified and recruited before randomisation. Therefore there is no potential for identification/recruitment bias because randomization happens after.	
Deviations from Intended Interventions	Low
The organisations themselves were not blinded to the intervention. No evidence that there were deviations. "We used a stratified cluster-randomised parallel-group trial design. The hospital was the unit of randomisation to avoid contamination between practitioners in the same service, since the intervention directly targeted teams of professionals."	
Missing outcome data	Low
"There were no missing data for hospital characteristics, whereas for patient characteristics the proportion of missing data varied from 0% for parity to a maximum of 1% for age (1910 of 191 167 patients)."	
Measurement of the outcome	Low

Outcome assessors were aware of interventions received by study participants, and there is no information if the outcome is likely to be influenced by knowledge of the intervention received. "A system of data collection, independent of the intervention process, was set up in all participating hospitals."… "The organisations were not blinded with respect to randomisation but they were not involved in the assessment of the outcome." … "All deliveries that took place in participating centres were registered by local data collectors (appropriately trained nurses or midwives). They completed a standard form for each eligible patient that included information on maternal characteristics, prenatal care, labour and delivery, diagnosed complications, and vital status of both mother and child at hospital discharge. This information was extracted from the hospital registers and from available medical records whose quality and archiving procedures were regularly monitored by the country-level study coordinators."	
Selection in the reported result	Low
No evidence of selection bias in reporting of favourable results. "The intervention effect on the primary outcome was estimated as the difference between the allocation groups in the change of individual mothers' risk of hospital-based mortality from the baseline (year 1) to the postintervention (year 4) periods. Primary intention-to-treat analyses used hospital-based death of individual mothers as the binary individual-level outcome and relied on the generalised estimating equations.	
Overall	**Low**

Ellard et al 2016	
Randomisation Process	Low
Although there was no mention on how randomisation was done, the allocation sequence was random, was concealed and no difference in baseline characteristics. "Following randomisation, ACs within the intervention districts were invited to enrol on the ETATMBA training programme."	
Bias arising from the timing of identification and recruitment of individual participants in relation to timing of randomization.	Some concerns
"Following randomisation, ACs within the intervention districts were invited to enrol on the ETATMBA training programme." There is no information whether randomisation occurred after or before selection of cluster regions. There is potential for identification/recruitment bias although this could be avoided through trial design.	
Deviations from Intended Interventions	Some concerns
Although participants were probably aware of the interventions during the trial, due to the nature of the study. There was low chance that there was deviation of intended interventions as a result.	
Missing outcome data	Low
Data for outcome measurements were available for most participants. Missing data unlikely to have affected results. "There were missing data from one district and for reasons unknown, in 2011, Dowa appears to have 8000 more births (these data were checked and verified)." … "While we do have missing data (and report this), we are confident that the data collected are an accurate reflection of events in all of the districts included in the trial.	
Measurement of the outcome	Some concerns
The main issue is that outcome assessors were aware of intervention received. This may have influenced the assessment of the outcome. "All of these outcomes were the numbers of events as recorded in maternity records by clinical staff within the health facilities. Each facility within a district records birth events in a maternity record book. This book is collated monthly and summarised, presenting a sum total of each of the variables from the book (eg, number of births, number of women with pre-eclampsia, number of stillbirths (macerated and fresh), etc) and sent to a central point within the district for reporting to the Ministry of Health."	
Selection in the reported result	Low
The data produced followed the original analysis plan. "Descriptive statistics were generated for all variables, and maternal mortality ratios (per 100 000 live births) were calculated."	

PNM rates (per 1000 live births) and maternal mortality "The primary outcome, PNM rates and maternal mortality ratios were examined using an interrupted time series (ITS)."	
Overall	**Some concerns**

Gill et al 2011	
Randomisation Process	Low
Allocation was done by random. "Randomisation was done by generating 120 allocation slips (60 intervention and 60 control), which were placed in an opaque container. During a public ceremony, witnessed by all the birth attendants and study staff, the participants individually took a slip from the box and the group allocation was announced to the whole group. Using a public ceremony to carry out randomisation was consistent with local customs."	
Bias arising from the timing of identification and recruitment of individual participants in relation to timing of randomization.	Low
Participants were identified before randomisation. "We used an unblinded, cluster randomised and controlled study in which traditional birth attendants were randomly allocated to receive training." … "After randomisation, the control birth attendants returned to their villages and continued their existing standard of care; the intervention birth attendants remained to receive further training."	
Deviations from Intended Interventions	Some concerns
There was no blinding for the interventions, however this would unlikely introduce bias. "Fourthly, given the nature of the interventions in the context of an effectiveness trial, blinding the birth attendants' group allocation was clearly impossible. Since the birth attendants interacted in their communities, it is possible that some exchange of knowledge may have occurred from intervention to control birth attendants. Although we have no evidence that this actually occurred, we believe the effect of this would have been minimal for two reasons. Firstly, the intervention requires that a birth attendant not just be trained in the skills, but also have the equipment (masks, suction bulbs, receiving blankets, and amoxicillin tablets) for using those skills. Without these, a control birth attendant would not have been effective. Secondly, the effect of cross contamination of skills would render the control birth attendants more like the intervention ones. This would make it more difficult to measure a difference in birth outcomes between the two groups, and bias our results to the null. Therefore, the direction of this hypothetical bias would actually strengthen our conclusions by rendering them more conservative."	
Missing outcome data	Low
"Overall, 3497 of 3559 (98.3%) babies delivered in the study contributed valid data for the analysis." and …."In the sensitivity analysis, reanalysing the primary end point by treating the neonates who were lost to follow-up as "dead" rather than "missing" also had minimal impact on the primary end point (rate ratio 0.58, 95% confidence interval 0.41 to 0.84)."	
Measurement of the outcome	Some concerns
The measurement or ascertainment of the outcome did not differ between the two groups. The outcome assessors were aware however of the intervention received. "The birth attendants completed a standardised birth record for every delivery, capturing basic information about the mother's antenatal status, interventions provided during delivery, and the infant's vital status on the day of delivery. The birth attendants were instructed to inform their assigned data collector within 48 hours of a delivery. The data collector then retrieved the delivery report from the birth attendant, reviewed and verified the contents of the report with the birth attendant, and carried out up to two follow-up visits (at one and four weeks) with the mother and infant pair."	
Selection in the reported result	Low
Analysis was done according to a pre-specified analysis plan. No evidence of selection bias. "For the mortality end points, we carried out a modified intention to treat analysis, where participants who were lost during follow-up were treated as missing rather than as deaths. We also carried out a sensitivity analysis for our primary end point in which participants who were lost to follow-up were analysed under the assumption that they represented unrecorded deaths.	

Overall	**Some concerns**

Jokhio et al 2005	
Randomisation Process	Low
"With a simple cluster-randomization sampling scheme, and with a computer-generated procedure, Larkana's seven talukas were allocated to intervention or control groups." No significant difference in baseline characteristics to suggest bias. Multilevel modelling was used to adjust for cluster randomisation.	
Bias arising from the timing of identification and recruitment of individual participants in relation to timing of randomization.	Low
Participants were identified before randomisation, hence no potential for recruitment bias because randomisation happens after.	
Deviations from Intended Interventions	Low
The outcome assessors were not aware of the purpose or comparative nature of the study. "Although the traditional birth attendants and Lady Health Workers could not be blinded to the intervention, observer bias is unlikely to have affected the reporting of the primary outcomes of perinatal and maternal mortality. Lady Health Workers, who collected data on the primary outcomes in both groups, were not aware of the purpose or comparative nature of the study."	
Missing outcome data	Low
No information if outcomes are available for nearly all participants, but there is no evidence that result is biased by missing data. "In the sensitivity analysis, reanalysing the primary end point by treating the neonates who were lost to follow-up as "dead" rather than "missing" also had minimal impact on the primary end point (rate ratio 0.58, 95% confidence interval 0.41 to 0.84)."	
Measurement of the outcome	Some concerns
The measurement or ascertainment of the outcome did not differ between the two groups. The outcome assessors were aware however of the intervention received.	
Selection in the reported result	Low
No evidence of selection bias in reporting of favourable results.	
Overall	**Some concerns**

Kestler et al 2020	
Randomisation Process	Some concerns
Some aspects of the allocation sequence were not random. Baseline characteristics do not suggest an imbalance. "Randomization consisted of random allocation of the six subdistricts to one of the six study sequences with two restrictions: (1) the subdistrict allocated to the first sequence was pre-specified and not randomly allocated; (2) the subdistricts selected for subsequent sequences alternated between the two districts to create a balance of the roll out across the districts."	
Bias arising from the timing of identification and recruitment of individual participants in relation to timing of randomization.	Low
Low risk, as potential participants were identified prior to randomisation. "The 33 health centers were grouped into six subdistricts of 4–6 adjacent centers, which each received and implemented the intervention in a step-wise fashion. Randomization consisted of random allocation of the six subdistricts to one of the six study sequences with two restrictions."	
Deviations from Intended Interventions	Some concerns

"Owing to the nature of the intervention, neither patients nor healthcare practitioners were blind to the intervention."	
Missing outcome data	No information
No information if outcomes are available for nearly all participants, but there is no evidence that result is biased by missing data.	
Measurement of the outcome	Some concerns
"Data analysts were not masked to intervention exposure owing to the sequential roll out of the intervention. Data collection included the total number of health centre deliveries, and individual maternal and perinatal morbidity and mortality outcomes." Assessment could have been influenced by knowledge of the intervention, but there is no evidence that it did.	
Selection in the reported result	Low
Data was analysed with a pre-specified plan, no evidence of selection on basis of multiple eligible measurements.	
Overall	**Some concerns**

Kumar et al 2012	
Randomisation Process	Low
Allocation was random and baseline characteristics were equal between control and intervention groups. "The gram sabha (average population 3500) was chosen as the cluster unit, and 13 clusters were allocated to each study arm via stratified randomization, with standard-of-living index and religion as stratification variables."	
Bias arising from the timing of identification and recruitment of individual participants in relation to timing of randomization.	Low
The region and clusters were identified prior to randomisation. Therefore there is low risk of selection bias.	
Deviations from Intended Interventions	Some concerns
Participants were aware of the interventions, there was no blinding to interventions received. There were no significant further deviations from intended interventions.	
Missing outcome data	Some concerns
There is no information what proportion of data is missing and what impact this might have.	
Measurement of the outcome	
"The evaluation team consisted of independent data collectors, with 1 supervisor for every 6 data collectors. The demographic surveillance system captured pregnancy outcomes and vital events, including maternal death. Maternal death was defined as death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the duration and site of the pregnancy, from any cause related to or aggravated by the pregnancy or its management, but not from accidental or incidental causes. A detailed verbal and social autopsy instrument was administered to families of all deceased women."	
Selection in the reported result	Low
No evidence of selective reporting of data from multiple analysis. "Analysis was by intention to treat at cluster level. To account for clustering, point estimates for all endpoints were calculated as the mean of cluster event rates, giving an equal weight to each cluster."	
Overall	**Some concerns**

Kumar et al 2008	
Randomisation Process	Low

Allocation Sequence was random, was concealed and no difference in baseline characteristics. "Stratifi ed cluster randomisation was done at Johns Hopkins University using Stata 7.0 (StataCorp, College Station, TX, USA) to allocate the 39 cluster units randomly to the three study groups, yielding three allocation sequences of 13 clusters each."	
Bias arising from the timing of identification and recruitment of individual participants in relation to timing of randomization.	Low
The region and cluster were selected before randomisation, therefore low risk of selection bias.	
Deviations from Intended Interventions	Some concerns
Participants were aware of the interventions, there was no blinding to interventions received. "The study had two distinct and administratively independent components: the intervention (development phase and implementation phase), and evaluation. Because of the visible nature of the intervention, allocation was not masked; however, boundaries to limit communication between the two teams were closely monitored."	
Missing outcome data	Low
No information if outcomes are available for nearly all participants, but there is no evidence that result is biased by missing data. "All data forms underwent scrutiny for logical inconsistencies, skip patterns and missing values. The data were coded and double-entered into a relational database on Microsoft Access 2000. The data entry interface was designed to check for referential integrity, missing values and acceptability constraints. Errors identified at any level were referred back to the field for correction."	
Measurement of the outcome	Some concerns
The measurement or ascertainment of the outcome did not differ between the two groups. The outcome assessors were aware however of the intervention received. "Systems were put in place to ascertain pregnancy and birth outcomes in the study population by the independent evaluation team recruited and trained for this purpose. Tracking of all outcomes at 28 days after birth, namely miscarriages, stillbirths, livebirths, and neonatal deaths, in the entire study area, was done by the independent evaluation team."	
Selection in the reported result	Low
There does not appear to be bias in selective reporting of outcomes based on multiple analyses. "There was no prespecified plan for statistical analysis; however, we have used conservative analytical methods. The baseline covariates used for adjustment were identified before the adjusted analysis was done."	
Overall	**Some concerns**

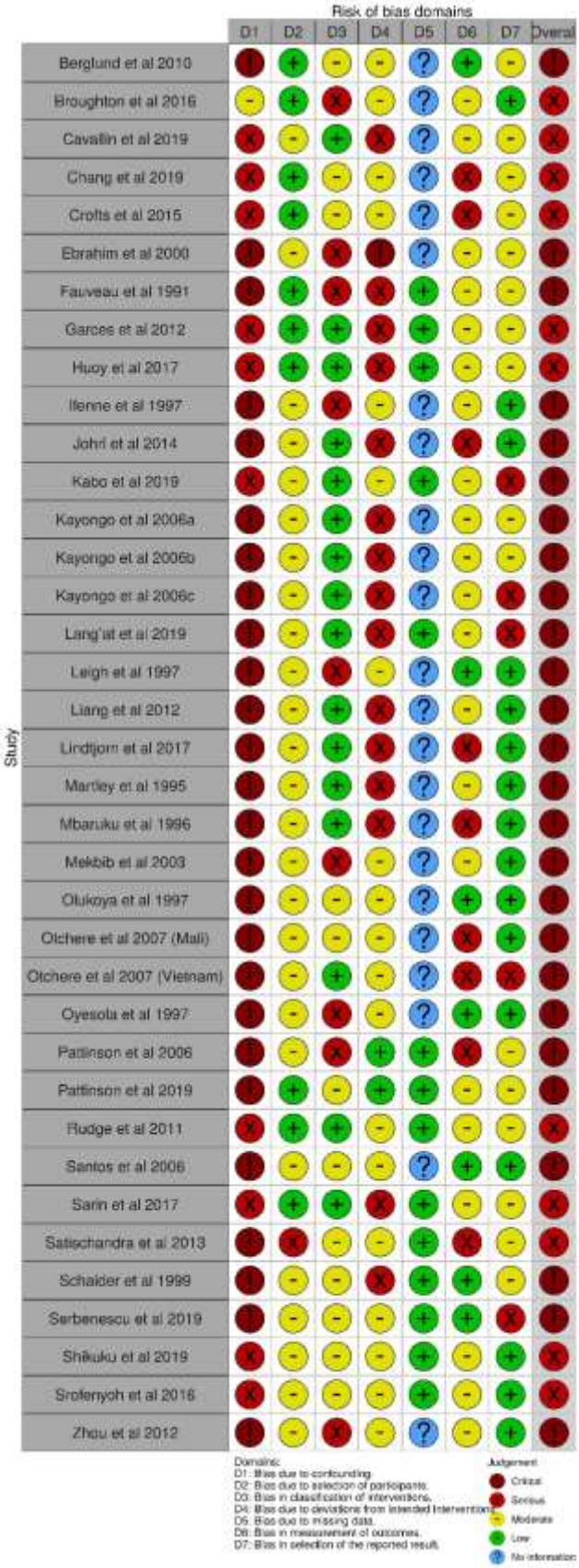
van den Broek et al 2019	
Randomisation Process	Low
Random Allocation sequence with concealment, baseline characteristics were equal between the intervention and control groups. "HCFs were clustered by district for randomisation, delivery of the intervention and the analysis. The sequence of implementing the intervention was determined using simple random sampling by an independent person drawing folded pieces of paper bearing the 11 district names from a hat, which was documented."	
Bias arising from the timing of identification and recruitment of individual participants in relation to timing of randomization.	Low
Cluster selection occurred before randomisation. "About 50% of all maternal deaths in South Africa occur in 12 of the 45 districts that do not have a medical school; these districts were selected for the trial."	
Deviations from Intended Interventions	Some concerns
Participants were likely aware of the interventions. There were no documented deviations from intended interventions which would have had a substantial impact on the result.	
Missing outcome data	Low

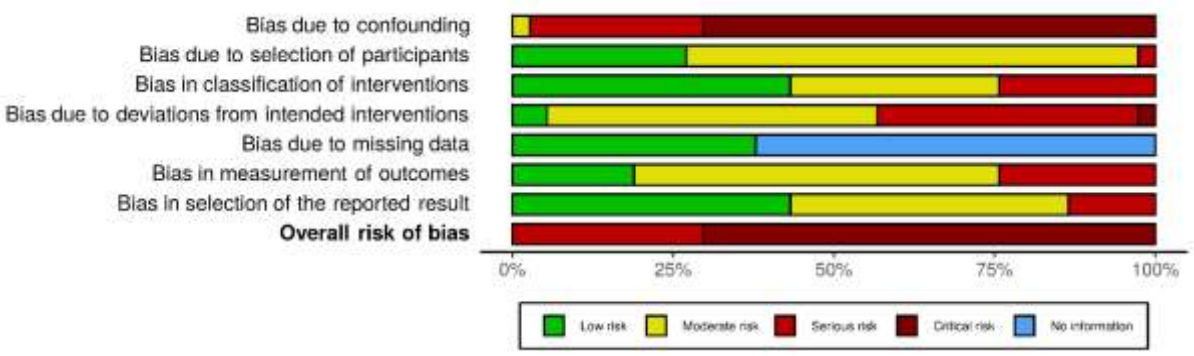
Data capture was almost complete. No significant missing data. "Most HCFs provided data every month. However, there were five facilities for which data were missing for a non-transition month on 21 occasions (0.7% of total): 9 occasions in two facilities preintervention (once for a facility in district 9 and 8 times for a facility in district 10) and 12 occasions in three facilities postintervention (4 and 6 times, respectively, for two facilities in district 2, 2 times for a facility in district 7). Reasons for this included HCF shut and/or missing birth registers at time of assessment."	
Measurement of the outcome	Some concerns
The assessors are aware of interventions received. Knowledge of the intervention status could have influenced outcome but there is no evidence that it did. "The primary outcome measures, at HCF level, identified in the ISRCTN registration were SBR (stillbirths per 1000 births), ENND rate (ENND per 1000 live births), institutional maternal mortality ratio (iMMR per 100 000 live births) and direct obstetric case fatality rate."	
Selection in the reported result	Low
Data was analysed with a pre-specified plan, no evidence of selection on basis of multiple eligible measurements. "The protocol was registered retrospectively at the time when it became possible to register step-wedge designed trials; maternal and newborn mortality were identified as societal outcomes to be assessed."	
Overall	**Some concerns**

Walker et al 2016	
Randomisation Process	Low
Study states is "randomized" but no mention of method of randomisation. No baseline imbalance to suggest bias.	
Timing of identification and recruitment of individual participants in relation to timing of randomization.	Low
Selection of clusters before randomisation occurred, therefore low risk of selection bias. "only facilities on a list of those with higher than average incidence of maternal death provided by the National Center for Gender Equity and Reproductive Health where considered for inclusion.	
Deviations from Intended Interventions	Some concerns
Participants were aware of the interventions. There is no blinding in the study.	
Missing outcome data	Low
"There were missing data for all clinics in the first-, fifth-, and ninth-month postintervention. The gaps in data prevent us from performing the initially planned analyses of all 12 months of follow-up data. The data, however, are missing equally for each site, and thus should not introduce additional bias, but rather lower the power to detect impacts."	
Measurement of the outcome	Some concerns
The outcome assessors were not blind to the intervention. No evidence that it had influenced outcomes. "Trained field workers visited each of the 24 hospitals before the intervention to collect baseline facility inventory and epidemiologic data and returned quarterly to collect primary outcome data." "We identified hospital-based neonatal mortality and morbidity cases from the nurse registries in the delivery rooms, operating rooms, and neonatal intensive care units (NICUs). Fieldworkers verified inconsistencies in the medical records or death certificate. When the information was not available from the hospital registries, data were collected from the epidemiology and statistics department."	
Selection in the reported result	High
Multiple time points were measured, and multiple analysis of data was undertaken. There is high risk for selective outcome reporting. "The matched design of the study was taken into account by including dummy variables of the matched pairs as covariates. Because of the matched design, the randomization and the DID analytic strategy are all controlling for potential confounding, we decided not to adjust for covariates in the analysis because these adjustments might be unnecessary and consume degrees of freedom (of particular concern due to the small sample size), which in turn would increase the imprecision of our estimates."	

Overall	**High**

Risk of Bias for Observational Studies- ROBINS I





Berglund et al 2010	
Bias due to confounding	Critical
In this study, confounding is inherently not controllable as the intervention spans across several regions. The effect of the intervention is measured before implementation using baseline statistics, and after intervention. There are many confounding factors which are not controllable in this instance.	
Bias in selection of participants	Low
In this study design, all participants who would have been eligible for the target trial were included in the study and for each participant, start of follow up and start of intervention coincided.	
Bias in classification of interventions	Moderate
Intervention status is well defined; and some aspects of the assignments of intervention status were determined retrospectively due to the nature of the study. This was not adjusted in the analysis. The proportion of participants for which this was the case was too low to induce important bias.	
Bias due to deviation from intended interventions	Moderate
Due to the nature of the study design, there were deviations from intended intervention, but their impact on the outcome is expected to be slight.	
Bias due to missing data	No information
No information on how missing data was handled.	
Bias in measurement of outcomes	Low
The methods of outcome assessment were comparable across intervention groups; "The variables were recorded into study protocols daily at the participating maternities by local staff, mostly midwives working in the delivery ward, according to written definitions for each variable. A monitoring coordinator appointed by the project checked and completed all protocols at each facility. The MIHP-team checked the reliability at site visits. Data were computerized by MIHP staff at the head office in Kiev. Data were analyzed in three-month periods during the follow-up period and compared with baseline."	
Bias in selection of the reported result	Moderate
The outcome measurements and analyses are consistent with an a priori plan; and are clearly defined and both internally and externally consistent; There is no indication of selection of the reported analysis from among multiple analyses; and there is no indication of selection of the cohort or subgroups for analysis and reporting on the basis of the results.	
Overall	**Critical**

Broughton et al 2016	
Bias due to confounding	Moderate
There is potential for confounding. Confounding domains that were controlled for were measured validly and reliably. Appropriate baseline and endline variables were measured and analysed between intervention and non-intervention groups. Authors used appropriate analysis method that controlled for all the important confounding	

domains. "Data were analyzed using difference-in-differences logistic regression controlling for potential confounders." …. "Change in neonatal mortality between intervention and non-intervention parishes in Cotopaxi provided by the INEC was analyzed using linear regression weighted by the counties' number of annual births."	
Bias in selection of participants	Low
Selection of study participants were not based on characteristics observed after the intervention. All participants who would have been eligible for the target trial were included in the study, and for each participant, start of follow up and start of intervention coincided.	
Bias in classification of interventions	Serious
Intervention status is not well defined; not clear how intervention vs control was established.	
Bias due to deviation from intended interventions	Moderate
Due to the nature of the study, there were deviations from usual practice, but their impact on the outcome is expected to be slight.	
Bias due to missing data	No information
The methods in which missing data is handled is not reported.	
Bias in measurement of outcomes	Moderate
The methods of outcome assessment were comparable across intervention groups; The outcome measure is only minimally influenced by knowledge of the intervention received by study participants. "Facility quality of care was assessed monthly through measurement of quality indicators calculated by facility QI teams using aggregate data extracted from clinical records' reviews. Each month QI teams sampled clinical records by choosing 30 randomly from a list of all records of women who had received antenatal, delivery, and postpartum care in the month."	
Bias in selection of the reported result	Low
The outcome measurements and analyses are clearly defined with an established a priori plan. "With a rural baseline sample of 259 women and end-line sample of 237 women, the rural sample had over 99% power to detect an increase of 50% in postpartum visits within 48 h of birth in the intervention group compared with a 30% increase in the control group, given their respective baseline levels of 52.5 and 70.0%, with a Type I error of 0.05"	
Overall	**Serious: The study has some important problems**

Cavallin et al 2019	
Bias due to confounding	Serious
At least one known important domain was not appropriately measured, or not controlled for.	
Bias in selection of participants	Moderate
Selection of study participants were not based on characteristics observed after the intervention. Due to the nature of the longitudinal study, the start of follow up and start of intervention do not coincide for all participants, and the proportion of participants for which this was the case was too low to induce important bias.	
Bias in classification of interventions	Low
Intervention status is well defined; and Intervention definition is based solely on information collected at the time of intervention.	
Bias due to deviation from intended interventions	Serious
The analysis was not appropriate to estimate the effect of starting and adhering to intervention, allowing for deviations (in terms of implementation, adherence and co-intervention) that were likely to impact on the outcome.	
Bias due to missing data	No information

How missing data was handled was not reported	
Bias in measurement of outcomes	Moderate
The methods of outcome assessment were comparable across intervention groups; and the outcome measure is only minimally influenced by knowledge of the intervention received by study participants; and any error in measuring the outcome is only minimally related to intervention status. "Quality assessment was performed in 2012 and 2016 by the same team using the same assessment tool, in order to ensure consistency and comparability. Quality was assessed using the World Health Organization's maternal and neonatal quality of hospital care assessment tool"	
Bias in selection of the reported result	Moderate
The outcome measurements are clearly defined and both internally and externally consistent; and there is no indication of selection of the reported analysis from among multiple analyses	
Overall	**Serious: the study has some important problems**

Chang et al 2019	
Bias due to confounding	Serious
Confounding expected, at least one or more domains were not adequately controlled for. Does not appear to be an analysis to adjust for confounders.	
Bias in selection of participants	Low
All participants who would have been eligible for the target trial were included in the study; and for each participant, start of follow up and start of intervention coincided.	
Bias in classification of interventions	Moderate
Intervention status is well defined; and Intervention definition is based solely on information collected at the time of intervention.	
Bias due to deviation from intended interventions	Moderate
Due to the nature of the interventions provided, there were deviations from usual practice that were unbalanced between the intervention groups and likely to have affected the outcome.	
Bias due to missing data	No information
No information on how missing data was handled.	
Bias in measurement of outcomes	Serious
The outcome measure was vulnerable to influence by knowledge of the intervention received by study participants and the outcome was assessed by assessors aware of the intervention received by study participants. "Hospital birth records and birth logs were used to collect data on patient demographics, as well as obstetric and neonatal outcomes. Medical and birth records were paper medical charts that were completed by physicians and nurses." The outcome measure was vulnerable to influence by knowledge of the intervention received by study participants and the outcome was assessed by assessors aware of the intervention received by study participants.	
Bias in selection of the reported result	Moderate
The outcome measurements are clearly defined and both internally and externally consistent; and there is no indication of selection of the reported analysis from among multiple analyses	
Overall	**Serious**

Crofts et al 2015	
Bias due to confounding	Serious

At least one or more confounding domains were not controlled for, we expect residual confounding.	
Bias in selection of participants	Low
All participants who would have been eligible for the target trial were included in the study; and for each participant, start of follow up and start of intervention coincided.	
Bias in classification of interventions	Moderate
Intervention status is well defined; and Intervention definition is based solely on information collected at the time of intervention.	
Bias due to deviation from intended interventions	Serious
There were deviations from usual practice that were unbalanced between the intervention groups and likely to have affected the outcome. This is due to the before and after nature of the study.	
Bias due to missing data	No information
No information on how missing data was handled.	
Bias in measurement of outcomes	Serious
The outcome measure was vulnerable to influence by knowledge of the intervention received by study participants and the outcome was assessed by assessors aware of the intervention received by study participants. There was no mention on how outcome data was collected.	
Bias in selection of the reported result	Moderate
The outcome measurements are clearly defined and both internally and externally consistent; and there is no indication of selection of the reported analysis from among multiple analyses.	
Overall	**Serious**

Ebrahim et al 2000	
Bias due to confounding	Critical
Confounding inherently not controllable. "A retrospective descriptive study was under-taken over a 3-year period" This was to assess the impact of free antenatal care in an entire region on maternal mortality. There are multiple confounding variables which are impossible to adjust for in this situation.	
Bias in selection of participants	Moderate
All participants who would have been eligible for the target trial were included in the study. There does not appear to be selection bias. Start of follow up and start of intervention do not coincide for all participants. The review authors are confident that the rate (hazard) ratio for the effect of intervention remains constant over time.	
Bias in classification of interventions	Moderate
Intervention status is well defined some aspects of the assignments of intervention status were determined retrospectively.	
Bias due to deviation from intended interventions	Critical
The analysis was not appropriate to estimate the effect of starting and adhering to intervention, allowing for deviations (in terms of implementation, adherence and co-intervention) that were likely to impact on the outcome.	
Bias due to missing data	No information
No information on missing data	
Bias in measurement of outcomes	
"The outcome measure is only minimally influenced by knowledge of the intervention received by study participants; and any error in measuring the outcome is only minimally related to intervention status. A	

retrospective descriptive study was under-taken over a 3-year period from 1 January 1994. All perinatal deaths, stillbirths of weight G1000 g and neonatal deaths up to and including the 6th day of life. were audited, to determine the perinatal mortality rate PMR. And avoidable factors for perinatal losses. Deaths were classified according to obstetric causes and avoidable factors were sought.	
Bias in selection of the reported result	Moderate
The outcome measurements and analyses are consistent with an a priori plan; or are clearly defined and both internally and externally consistent	
Overall	**Critical**

Fauveau et al 1991	
Bias due to confounding	Moderate
Confounding expected, all known important confounding domains appropriately measured and controlled for; and reliability and validity of measurement of important domains were sufficient, such that we do not expect serious residual confounding.	
Bias in selection of participants	Low
All participants who would have been eligible for the target trial were included in the study; and for each participant, start of follow up and start of intervention coincided.	
Bias in classification of interventions	Serious
Intervention status is well defined and Intervention definition is based solely on information collected at the time of intervention.	
Bias due to deviation from intended interventions	Serious
The analysis was not appropriate to estimate the effect of starting and adhering to intervention, allowing for deviations (in terms of implementation, adherence and co-intervention) that were likely to impact on the outcome.	
Bias due to missing data	No information
No information on missing data	
Bias in measurement of outcomes	Moderate
The methods of outcome assessment were comparable across intervention groups and the outcome measure is only minimally influenced by knowledge of the intervention received by study participants, any error in measuring the outcome is only minimally related to intervention status.	
Bias in selection of the reported result	Moderate
No evidence of selection bias of the reported result	
Overall	**Serious**

Garces et al 2012	
Bias due to confounding	Serious
Confounding expected, some confounding domains appropriately measured and controlled for. However there remains serious residual confounding. "Generalized estimating equation (GEE) extensions of logistic and proportional odds regression models that adjust for correlation of outcomes within cluster were used to determine differences in maternal and neonatal characteristics between the pre-ENC training and post-ENC training. Logistic models were used for binary data, proportional odds models with cumulative logit were used for ordered multinomial variables, and generalized logit multinomial models were used for nonordered multinomial variables."	

Bias in selection of participants	Low
All participants who would have been eligible for the target trial were included in the study and for each participant, start of follow up and start of intervention coincided.	
Bias in classification of interventions	Low
Intervention status is well defined; and intervention definition is based solely on information collected at the time of intervention.	
Bias due to deviation from intended interventions	Serious
The important co-interventions were not balanced across intervention groups, or there were deviations from the intended interventions and/or adherence) that were likely to impact on the outcome; the analysis was not appropriate to estimate the effect of starting and adhering to intervention, allowing for deviations (in terms of implementation, adherence and co-intervention) that were likely to impact on the outcome.	
Bias due to missing data	Low
Data were reasonably complete, missing data was mentioned, and it made up a 1% of total.	
Bias in measurement of outcomes	Moderate
The methods of outcome assessment were comparable across intervention groups; the outcome measure is only minimally influenced by knowledge of the intervention received by study participants. “Birth attendants collected all data on standardized data forms using numbered patient identifiers. Data forms were reviewed for accuracy by the community coordinators before submission to the local research office for data entry and transmission to the data coordinating centre."	
Bias in selection of the reported result	Moderate
No evidence of selection bias of the reported result	
Overall	**Serious**

Huoy et al 2017	
Bias due to confounding	Serious
Confounding expected, some confounding domains appropriately measured and controlled for. Although the reliability and validity of measurement of important domains were sufficient, residual confounding is to be expected. “Logistic regression models were used in time cohort analysis to adjust for confounding variables. All assumed predictors of death were included using a backward selection process with inclusion at significance level of five percent. The logistic model was evaluated by Receiver Operating Characteristics (ROC) analysis. A predictor is considered “fair” if the area under the ROC curve is 0.7-0.8 and “good” if larger than 0.8.15.”	
Bias in selection of participants	Low
All participants who would have been eligible for the target trial were included in the study and for each participant, start of follow up and start of intervention coincided. “The study population was defined by purposive sampling based on criteria of remoteness, poverty, and poorly developed medical infrastructure. Consequently, the intervention was carried out in a remote rural population of 200,000 inhabitants in 266 villages.”	
Bias in classification of interventions	Moderate
Intervention status is well defined; Start of follow up and start of intervention do not coincide for all participants; the proportion of participants for which this was the case was too low to induce important bias. “The DLS network had a vast outreach and it took two years to achieve adequate interaction between the three tiers of the system and to establish reliable systems for data gathering. For this reason, the cohort of 2005 and 2006 patients was used as baseline for the time controls.”	
Bias due to deviation from intended interventions	Serious

Due to the nature of the interventions involved, the important co-interventions were not balanced across intervention groups, or there were deviations from the intended interventions and/or adherence) that were likely to impact on the outcome; The analysis was not appropriate to estimate the effect of starting and adhering to intervention, allowing for deviations (in terms of implementation, adherence and co-intervention) that were likely to impact on the outcome.	
Bias due to missing data	Low
Data were reasonably complete. “The program coordinator collected the forms, validated entries, and collected missing information.”	
Bias in measurement of outcomes	Moderate
The methods of outcome assessment were comparable across intervention groups and the outcome measure is only minimally influenced by knowledge of the intervention received by study participants; any error in measuring the outcome is only minimally related to intervention status. "All deliveries were registered consecutively in case record forms: simple charts for TBAs and more comprehensive ones for HC staff. The program coordinator collected the forms, validated entries, and collected missing information."	
Bias in selection of the reported result	Moderate
The outcome measurements and analyses are consistent with an a priori plan; or are clearly defined and both internally and externally consistent; and There is no indication of selection of the reported analysis from among multiple analyses; and there is no indication of selection of the cohort or subgroups for a analysis and reporting on the basis of the results.	
Overall	**Serious**

Ifenne et al 1997	
Bias due to confounding	Critical
Bias inherently not controllable in this study.	
Bias in selection of participants	Moderate
Start of follow up and start of intervention do not coincide for all participants the authors used appropriate methods to adjust for the selection bias.	
Bias in classification of interventions	Serious
Intervention status is well defined; and some aspects of the assignments of intervention status were determined retrospectively.	
Bias due to deviation from intended interventions	Moderate
There were deviations from intended intervention, but their impact on the outcome is expected to be slight.	
Bias due to missing data	No information
No information on missing data	
Bias in measurement of outcomes	
The method was comparable across groups. "Data on utilisation and outcomes were collected from the ward register of daily admissions of women into the delivery suite and maternity and gynecological ward of the hospital. Case notes were studied and analysed manually, noting the age, parity, address, referral"	
Bias in selection of the reported result	Low
There is clear evidence (usually through examination of a pre-registered protocol or statistical analysis plan) that all reported results correspond to all intended outcomes, analyses and sub-cohorts.	
Overall	**Critical**

Johri et al 2014	
Bias due to confounding	Critical
Confounding inherently not controllable due to the large scale intervention which affects the district as a whole. There are other confounding factors which cannot be accounted for in this instance. "To assess whether eliminating user fees would affect child and maternal mortality, we triangulated evidence using multiple data sources and analytical techniques to assess the effect of the user-fee elimination programme on coverage of specific health interventions."	
Bias in selection of participants	Moderate
Selection into the study may have been related to intervention and outcome; The authors used appropriate methods to adjust for the selection bias;	
Bias in classification of interventions	
Aspects of the interventions were classified retrospectively "We used LiST default demography, proportional mortality and intervention effectiveness estimates. All other variables were classified into one of two categories."	
Bias due to deviation from intended interventions	Serious
The important co-interventions were not balanced across intervention groups, or there were deviations from the intended interventions (in terms of implementation and/or adherence) that were likely to impact on the outcome;	
Bias due to missing data	No information
No information	
Bias in measurement of outcomes	
The outcome measure was subjective (i.e. vulnerable to influence by knowledge of the intervention received by study participants); and the outcome was assessed by assessors aware of the intervention received by study participants. "Category 1 consisted of variables unaffected by user-fee elimination. We updated LiST parameters using data from household surveys,8,14–19 United Nations agencies' estimates,20,21 national administrative data22,23 and research reports.24 To ensure accurate estimation of mortality, category 1 indicators reflect changes in health-care coverage over the study period."	
Bias in selection of the reported result	Low
The outcome measurements and analyses are consistent with an a priori plan. "We developed multilevel Poisson models (district, primary health centre, monthly deliveries) to study the effect of the emergency obstetrical and neonatal care subsidy and user-fee elimination programme both individually and in combination on the likelihood of delivery in a primary health centre. We used sitewise random intercepts and slopes and estimated intervention effects as rate ratios.	
Overall	**Critical**

Kabo et al 2019	
Bias due to confounding	Serious
There is no mention of any adjusting for confounding variables in this study. Due to the before- and after study design, there are significant confounders which may affect the results.	
Bias in selection of participants	Moderate
All participants who would have been eligible for the target trial were included in the study; and for each participant, start of follow up and start of intervention coincided.	
Bias in classification of interventions	Low
Intervention status is well defined; and intervention definition is based solely on information collected at the time of intervention.	
Bias due to deviation from intended interventions	Moderate

There were deviations from intended intervention, but their impact on the outcome is expected to be slight.	
Bias due to missing data	No information
No information is reported about missing data or the potential for data to be missing.	
Bias in measurement of outcomes	Moderate
The methods of outcome assessment were comparable across intervention groups; and the outcome measure is only minimally influenced by knowledge of the intervention received by study participants. "Data collectors were required to carefully check all recorded responses and correct any possible errors. Study supervisors reviewed administered questionnaires on a daily basis and probed for and addressed data inconsistencies. The survey coordinator at the state level performed a second level review of the administered questionnaires. Data entry queries were run to identify any issue regarding inconsistent or missing information."	
Bias in selection of the reported result	Moderate
The outcome measurements and analyses are consistent with an a priori plan; or are clearly defined and both internally and externally consistent;	
Overall	**Serious**

Kayongo et al 2006a (Rwanda)	
Bias due to confounding	Critical
At least one known important domain was not appropriately measured, or not controlled for. There is no mention of controlling confounding variables in this study. Confounding is inherently not controllable. "The project was designed to work with three district hospitals — Gitwe, Rumera—Rukoma and Kabgayi in Gitarama Health Region. The target group consisted of 150,000 women of reproductive age who, based on the 2000 crude birth rate of 45 per 1000 population, would have an estimated 109,000 live births over 3 years."	
Bias in selection of participants	Moderate
All participants who would have been eligible for the target trial were included in the study; and for each participant, start of follow up and start of intervention coincided. "Following the baseline assessment of June 2000, full implementation of project interventions started in April 2001."	
Bias in classification of interventions	Low
Classification is on a population level, resulting in an intervention status that is well defined; and intervention definition is based solely on information collected at the time of intervention.	
Bias due to deviation from intended interventions	Serious
The important co-interventions were not balanced across intervention groups, or there were deviations from the intended interventions (in terms of implementation and/or adherence) that were likely to impact on the outcome; and the analysis was not appropriate to estimate the effect of starting and adhering to intervention, allowing for deviations (in terms of implementation, adherence and co-intervention) that were likely to impact on the outcome.	
Bias due to missing data	No information
No information is reported about missing data or the potential for data to be missing.	
Bias in measurement of outcomes	Moderate
The methods of outcome assessment were comparable across intervention groups and the outcome measure is only minimally influenced by knowledge of the intervention received by study participants. "Staff, including doctors and midwives, were trained and supported to ensure complete recording of case notes and filling out of registers. New registers were provided that contained columns for capturing key variables such as maternal complications and outcomes for each pregnancy. The project emphasized common agreement on definitions of obstetric complications, based on established standards and guidelines."	

Bias in selection of the reported result	Low
The outcome measurements and analyses are consistent with an a priori plan; or are clearly defined and both internally and externally consistent and there is no indication of selection of the reported analysis from among multiple analyses.	
Overall	**Serious**

Kayongo et al 2006b (Peru)	
Bias due to confounding	Critical
Due to the nature of the interventions and the population involved, there are several confounding variables not addressed, and furthermore, confounding is inherently not controllable. "The interventions include: improvements in infrastructure and facility setup; 1. data collection and information systems; 2. staff development and placement, quality improvement and supervision. In addition to these building blocks, the project addressed the referral and communication system and the mobilization of civil society."	
Bias in selection of participants	Moderate
All participants who would have been eligible for the target trial were included in the study; and for each participant, start of follow up and start of intervention coincided.	
Bias in classification of interventions	Low
Intervention status is well defined; and intervention definition is based solely on information collected at the time of intervention.	
Bias due to deviation from intended interventions	Serious
The important co-interventions were not balanced across intervention groups, or there were deviations from the intended interventions (in terms of implementation and/or adherence) that were likely to impact on the outcome; and the analysis was not appropriate to estimate the effect of starting and adhering to intervention, allowing for deviations (in terms of implementation, adherence and co-intervention) that were likely to impact on the outcome.	
Bias due to missing data	No information
No information is reported about missing data or the potential for data to be missing.	
Bias in measurement of outcomes	Moderate
The methods of outcome assessment were comparable across intervention groups and the outcome measure is only minimally influenced by knowledge of the intervention received by study participants. "The project team assisted the EmOC centers to standardize and streamline patient registers for the entry and tabulation of key maternal and newborn data. The goal was to get health personnel in the habit of monitoring the availability and use of EmOC and to make decisions for improving the quality of services. There are now only 3 registers for collecting information on emergency treatment, prenatal care, and delivery. These registries are now used throughout the region. To facilitate data analysis, information on obstetric complications was added to the registers and the analysis of maternal deaths was refined by separating indirectly from direct causes."	
Bias in selection of the reported result	Moderate
The outcome measurements and analyses are consistent with an a priori plan; or are clearly defined and both internally and externally consistent and there is no indication of selection of the reported analysis from among multiple analyses.	
Overall	**Serious**

Kayongo et al 2006c (Africa)	
Bias due to confounding	Critical

At least one known important domain was not appropriately measured, or not controlled for. Furthermore, due to the study design, bias is inherently not controllable.	
Bias in selection of participants	Moderate
All participants who would have been eligible for the target trial were included in the study; and for each participant, start of follow up and start of intervention coincided.	
Bias in classification of interventions	Low
Intervention status is well defined; and intervention definition is based solely on information collected at the time of intervention.	
Bias due to deviation from intended interventions	Serious
The important co-interventions were not balanced across intervention groups, or there were deviations from the intended interventions (in terms of implementation and/or adherence) that were likely to impact on the outcome; and the analysis was not appropriate to estimate the effect of starting and adhering to intervention, allowing for deviations (in terms of implementation, adherence and co-intervention) that were likely to impact on the outcome.	
Bias due to missing data	No information
No information is reported about missing data or the potential for data to be missing.	
Bias in measurement of outcomes	Moderate
The methods of outcome assessment were comparable across intervention groups and the outcome measure is only minimally influenced by knowledge of the intervention received by study participants. "CARE worked with hospital staff in each site to develop new or revised obstetric registers, ensuring that these tools accurately captured key information (obstetric admissions, numbers of deliveries, complications, maternal deaths, etc). In both Ethiopia and Tanzania, different information was captured in different registers all over the hospitals. The project created one register that consolidated essential information in one place, thereby improving the staff's ability to compile and review their data.	
Bias in selection of the reported result	Moderate
Outcomes are defined in different ways in the methods and results sections, or in different publications of the study;	
Overall	**Critical**

Lang'at et al 2019	
Bias due to confounding	Critical
Large scale population-based study requires adjustment of multiple confounding variables which was not done.	
Bias in selection of participants	Moderate
All participants who would have been eligible for the target trial were included in the study; and for each participant, start of follow up and start of intervention coincided.	
Bias in classification of interventions	Low
Intervention status is well defined; and intervention definition is based solely on information collected at the time of intervention.	
Bias due to deviation from intended interventions	Serious
The important co-interventions were not balanced across intervention groups, or there were deviations from the intended interventions (in terms of implementation and/or adherence) that were likely to impact on the outcome; and the analysis was not appropriate to estimate the effect of starting and adhering to intervention, allowing for deviations (in terms of implementation, adherence and co-intervention) that were likely to impact on the outcome.	

Bias due to missing data	Low
The analysis addressed missing data and is likely to have removed any risk of bias. “Owing to logistical and feasibility reasons, 127 public health institutions out of the total 267 in the 3 counties were purposively sampled. However, owing to data quality issues only 90 of these facilities with no missing data were included in the study. The other 37 health facilities were completely deleted from the analysis.”	
Bias in measurement of outcomes	Moderate
The methods of outcome assessment were comparable across intervention groups; and the outcome measure is only minimally influenced by knowledge of the intervention received by study participants; "The data were entered in a printed registry book at each health post by the health extension workers. Each month, nursing supervisors visited the health post, checking the registry for completeness, supervising the health extension worker and taking a copy of the registry book to the project office."	
Bias in selection of the reported result	Serious
There is a high risk of selective reporting from among multiple analyses.	
Overall	**Critical**

Leigh et al 1997	
Bias due to confounding	Critical
Bias inherently not controllable in this study.	
Bias in selection of participants	Moderate
Start of follow up and start of intervention do not coincide for all participants the authors used appropriate methods to adjust for the selection bias.	
Bias in classification of interventions	Serious
Intervention status is well defined; and some aspects of the assignments of intervention status were determined retrospectively.	
Bias due to deviation from intended interventions	Moderate
There were deviations from intended intervention, but their impact on the outcome is expected to be slight.	
Bias due to missing data	No information
No information on missing data.	
Bias in measurement of outcomes	Moderate
The methods of outcome assessment were comparable across intervention groups. Data on complications, admissions, deliveries and deaths were collected from the admission and delivery books. These hospital recordkeeping systems were upgraded in 1992 to collect more detailed information on women with complications. Thus, data from 1989 to 1992 may underestimate complications."	
Bias in selection of the reported result	Low
There is clear evidence (usually through examination of a pre-registered protocol or statistical analysis plan) that all reported results correspond to all intended outcomes, analyses and sub-cohorts.	
Overall	**Critical**

Liang et al 2012	
Bias due to confoundin	Critical

Large scale population-based study with multiple interventions suggests confounding is inherently not controllable.	
Bias in selection of participants	Moderate
All participants who would have been eligible for the target trial were included in the study; and for each participant, start of follow up and start of intervention coincided.	
Bias in classification of interventions	Low
Intervention status is well defined; and intervention definition is based solely on information collected at the time of intervention.	
Bias due to deviation from intended interventions	Serious
The important co-interventions were not balanced across intervention groups, or there were deviations from the intended interventions (in terms of implementation and/or adherence) that were likely to impact on the outcome; and the analysis was not appropriate to estimate the effect of starting and adhering to intervention, allowing for deviations (in terms of implementation, adherence and co-intervention) that were likely to impact on the outcome.	
Bias due to missing data	No information
No information is reported about missing data or the potential for data to be missing.	
Bias in measurement of outcomes	Moderate
The methods of outcome assessment were comparable across intervention groups; and the outcome measure is only minimally influenced by knowledge of the intervention received by study participants; “The baselines of maternal mortality in the three county groups were calculated based on data one year before the intervention program was implemented.” “MMR and cause-specific mortality were calculated by taking the live births as the denominator and the corresponding number of deaths as the numerator. Having been considered the change of MMR in each year during a period, Poisson regression assay was used to estimate the average annual reduction rate (AARR) of MMR and cause-specific mortality ratio.”	
Bias in selection of the reported result	Low
The outcome measurements and analyses are clearly defined and both internally and externally consistent. "Trends of Maternal Mortality Ratio and Hospital delivery Rate in the three priority county groups in China, 1999–2007."	
Overall	**Critical**

Lindtjorn et al 2017	
Bias due to confounding	Critical
At least one or more confounding domains were not controlled for, we expect residual confounding. An interrupted time series analysis of the impact of free maternal care requires adjustment of confounding variables. This is a large-scale population-based study which confounding is inherently not controllable. “this study evaluated the effects of several coordinated interventions to help improve effective coverage and reduce maternal deaths. Together with the Ministry of Health in Ethiopia, we designed a project to strengthen the health-care system.”	
Bias in selection of participants	Moderate
All participants who would have been eligible for the target trial were included in the study; and for each participant, start of follow up and start of intervention coincided.	
Bias in classification of interventions	Low
Intervention status is well defined; and intervention definition is based solely on information collected at the time of intervention.	

Bias due to deviation from intended interventions	Serious
The important co-interventions were not balanced across intervention groups, or there were deviations from the intended interventions (in terms of implementation and/or adherence) that were likely to impact on the outcome; and the analysis was not appropriate to estimate the effect of starting and adhering to intervention, allowing for deviations (in terms of implementation, adherence and co-intervention) that were likely to impact on the outcome.	
Bias due to missing data	No information
No information on missing data	
Bias in measurement of outcomes	Serious
The outcome measure was subjective (i.e. vulnerable to influence by knowledge of the intervention received by study participants); and the outcome was assessed by assessors aware of the intervention received by study participants;	
Bias in selection of the reported result	Moderate
The outcome measurements and analyses are consistent with an a priori plan; or are clearly defined and both internally and externally consistent; and there is no indication of selection of the reported analysis from among multiple analyses;	
Overall	**Critical**

Martley et al 1995	
Bias due to confounding	Critical
Confounders are impossible to control in this study	
Bias in selection of participants	Moderate
All participants who would have been eligible for the target trial were included in the study; and for each participant, start of follow up and start of intervention coincided.	
Bias in classification of interventions	Low
Intervention status is well defined; and intervention definition is based solely on information collected at the time of intervention.	
Bias due to deviation from intended interventions	Serious
The important co-interventions were not balanced across intervention groups, or there were deviations from the intended interventions (in terms of implementation and/or adherence) that were likely to impact on the outcome; and the analysis was not appropriate to estimate the effect of starting and adhering to intervention, allowing for deviations (in terms of implementation, adherence and co-intervention) that were likely to impact on the outcome.	
Bias due to missing data	No information
No information on missing data	
Bias in measurement of outcomes	Moderate
The methods of outcome assessment were comparable across intervention groups; and the outcome measure is only minimally influenced by knowledge of the intervention received by study participants. “In 1990, the maternal mortality ratio was seven per 1000 (10,553 deliveries); in 1991, the ratio was 9.9 per 1000 deliveries (10,301 deliveries total); this became 4.2 per 1000 deliveries in in 1990, the maternal mortality ratio was 7 per 1000, in 1991, was 9.9 per 1000 deliveries, this became 4.2 per 1000 deliveries in 1992 (the lowest in Korle Bu history).”	
Bias in selection of the reported result	Moderate
The outcome measurements and analyses are consistent with an a priori plan.	

Overall	**Critical**

Mbaruku et al 1996	
Bias due to confounding	Critical
Confounding inherently not controllable in this large scale multi-interventional design with multiple confounders.	
Bias in selection of participants	Moderate
All participants who would have been eligible for the target trial were included in the study; and for each participant, start of follow up and start of intervention coincided.	
Bias in classification of interventions	Low
Intervention status is well defined; and intervention definition is based solely on information collected at the time of intervention.	
Bias due to deviation from intended interventions	Serious
The important co-interventions were not balanced across intervention groups, or there were deviations from the intended interventions (in terms of implementation and/or adherence) that were likely to impact on the outcome; and the analysis was not appropriate to estimate the effect of starting and adhering to intervention, allowing for deviations (in terms of implementation, adherence and co-intervention) that were likely to impact on the outcome.	
Bias due to missing data	No information
No information on missing data	
Bias in measurement of outcomes	Serious
The methods of outcome assessment were comparable across intervention groups; and the outcome measure is may be influenced by knowledge of the intervention received by study participants. “A review of all case notes of maternal deaths, admission records, nurses' shift reports and operation theatre records was carried out.”	
Bias in selection of the reported result	Moderate
The outcome measurements and analyses are consistent with an a priori plan; or are clearly defined and both internally and externally consistent; and there is no indication of selection of the reported analysis from among multiple analyses;	
Overall	

Mekbib et al 2003	
Bias due to confounding	Critical
Bias inherently not controllable in this study.	
Bias in selection of participants	Moderate
Start of follow up and start of intervention do not coincide for all participants the authors used appropriate methods to adjust for the selection bias;	
Bias in classification of interventions	Serious
Intervention status is well defined; and some aspects of the assignments of intervention status were determined retrospectively	
Bias due to deviation from intended interventions	Moderate
There were deviations from intended intervention, but their impact on the outcome is expected to be slight	

Bias due to missing data	No information
No information on missing data	
Bias in measurement of outcomes	Moderate
The methods of outcome assessment were comparable across intervention groups. How this data was gathered was not clear.	
Bias in selection of the reported result	Moderate
The outcome measurements and analyses are consistent with an a priori plan; or are clearly defined and both internally and externally consistent and there is no indication of selection of the reported analysis from among multiple analyses.	
Overall	**Critical**

Olukoya et al 1997	
Bias due to confounding	Critical
Bias inherently not controllable in this study.	
Bias in selection of participants	Moderate
Start of follow up and start of intervention do not coincide for all participants the authors used appropriate methods to adjust for the selection bias;	
Bias in classification of interventions	Moderate
Intervention status is well defined; and some aspects of the assignments of intervention status were determined retrospectively	
Bias due to deviation from intended interventions	Moderate
There were deviations from intended intervention, but their impact on the outcome is expected to be slight	
Bias due to missing data	No information
Bias in measurement of outcomes	Low
The methods of outcome assessment were comparable across intervention groups; "Data for complications and deaths were collected using monthly data summaries from the registers of the maternity and gynaecology wards."	
Bias in selection of the reported result	Moderate
The outcome measurements and analyses are consistent with an a priori plan; or are clearly defined and both internally and externally consistent and there is no indication of selection of the reported analysis from among multiple analyses.	
Overall	**Critical**

Otchere et al 2007 (Mali)	
Bias due to confounding	Critical
Bias inherently not controllable in this study.	
Bias in selection of participants	Moderate
Start of follow up and start of intervention do not coincide for all participants the authors used appropriate methods to adjust for the selection bias;	

Bias in classification of interventions	Moderate
Intervention status is well defined; and some aspects of the assignments of intervention status were determined retrospectively	
Bias due to deviation from intended interventions	Moderate
There were deviations from intended intervention, but their impact on the outcome is expected to be slight	
Bias due to missing data	No information
No information on missing data.	
Bias in measurement of outcomes	Serious
The methods of outcome assessment were not comparable across intervention groups; "To facilitate our project monitoring and evaluation, we developed weekly and monthly summary forms that captured key variables and combined information from these with patient notes. The pulling of patient information onto one form improved midwives' ability to compile, understand and review the data and use them to improve the care they provided. We believe the forms we developed will serve as an example for the MOH when they decide to review the existing record keeping system. We also introduced the UN Process Indicators to hospital staff as a means of tracking and monitoring availability of obstetric services"	
Bias in selection of the reported result	Moderate
The outcome measurements and analyses are consistent with an a priori plan; or are clearly defined and both internally and externally consistent and there is no indication of selection of the reported analysis from among multiple analyses.	
Overall	**Critical**

Otchere et al 2007 (Vietnam)	
Bias due to confounding	Critical
Bias inherently not controllable in this study.	
Bias in selection of participant	Moderate
Start of follow up and start of intervention do not coincide for all participants the authors used appropriate methods to adjust for the selection bias.	
Bias in classification of interventions	Moderate
Intervention status is well defined; and some aspects of the assignments of intervention status were determined retrospectively.	
Bias due to deviation from intended interventions	Moderate
There were deviations from intended intervention due to the nature of the intervention, but their impact on the outcome is expected to be slight.	
Bias due to missing data	No information
No information on missing data.	
Bias in measurement of outcomes	Serious
The methods of outcome assessment were not comparable across intervention groups; "The project applied the 6 UN process indicators for monitoring the availability and use of obstetric services. In a review of patient information, it was found that information recorded was insufficient to meet the needs of the project. Therefore, in addition to using existing MOH recording formats, the project team developed monitoring tools that captured the following key variables to facilitate monitoring and evaluation of the project: cesarean delivery, maternal deaths from direct causes, number and type of obstetric complications, treatment given and treatment outcomes. A 3-day training workshop was organized in each province on managing health information. The training aimed to improve health workers' perception of data collection and reporting. To maintain quality and ease of data collection, a weekly, monthly, and quarterly system of collection and aggregation was adopted."	

Bias in selection of the reported result	Moderate
The outcome measurements and analyses are consistent with an a priori plan; or are clearly defined and both internally and externally consistent and there is no indication of selection of the reported analysis from among multiple analyses.	
Overall	**Critical**

Oyesola et al 1997	
Bias due to confounding	Critical
Bias inherently not controllable in this study.	
Bias in selection of participants	Moderate
Start of follow up and start of intervention do not coincide for all participants the authors used appropriate methods to adjust for the selection bias;	
Bias in classification of interventions	Serious
Intervention status is well defined; and some aspects of the assignments of intervention status were determined retrospectively	
Bias due to deviation from intended interventions	Moderate
There were deviations from intended intervention, but their impact on the outcome is expected to be slight	
Bias due to missing data	No information
No information on missing data.	
Bias in measurement of outcomes	Low
The methods of outcome assessment were comparable across intervention groups. "Data were collected from three main sources in the hospital: the maternity ward register; the surgical register; and a specially designed PMM questionnaire for women with complications."	
Bias in selection of the reported result	Low
The outcome measurements and analyses are consistent with an a priori plan; and are clearly defined and both internally and externally consistent; There is no indication of selection of the reported analysis from among multiple analyses; and there is no indication of selection of the cohort or subgroups for analysis and reporting on the basis of the results.	
Overall	**Critical**

Pattinson et al 2006	
Bias due to confounding	Serious
At least one known important domain was not appropriately measured, or not controlled for. There are controllable confounders in this study, as it is retrospective cohort study in a single institution.	
Bias in selection of participants	Moderate
All participants who would have been eligible for the target trial were included in the study; and for each participant, start of follow up and start of intervention coincided.	
Bias in classification of interventions	Serious
Major aspects of the assignments of intervention status were determined in a way that could have been affected by knowledge of the outcome.	

Bias due to deviation from intended interventions	Low
Any deviations from intended intervention reflected usual practice; The important co-interventions were balanced across intervention groups, and there were no deviations from the intended interventions (in terms of implementation or adherence) that were likely to impact on the outcome.	
Bias due to missing data	Low
Bias in measurement of outcomes	Serious
The outcome measure was subjective (i.e. vulnerable to influence by knowledge of the intervention received by study participants); and the outcome was assessed by assessors aware of the intervention received by study participants. "Data on women with SAMM and maternal deaths was collected every morning at the respective hospitals and a "near miss" form was completed for each woman with SAMM and the maternal death notification form used for all maternal deaths. The data were entered on the Maternal Morbidity and Mortality Audit System (MaMMAS) database."	
Bias in selection of the reported result	Moderate
The outcome measurements and analyses are consistent with an a priori plan; or are clearly defined and both internally and externally consistent; and there is no indication of selection of the reported analysis from among multiple analyses; "The outcome measures were the maternal mortality ratio (MMR), mortality index defined as the number of maternal deaths, divided by the sum of women with SAMM and maternal deaths and expressed as a percentage."	
Overall	**Serious**

Pattinson et al 2019	
Bias due to confounding	Critical
Confounding inherently not controllable in this study. It is a longitudinal observational before-and after study. "To determine whether there was a change in the number of maternal deaths and in the iMMR over time."	
Bias in selection of participants	Low
All participants who would have been eligible for the target trial were included in the study; and for each participant, start of follow up and start of intervention coincided.	
Bias in classification of interventions	Moderate
Intervention status is well defined; and some aspects of the assignments of intervention status were determined retrospectively.	
Bias due to deviation from intended interventions	Low
Any deviations from intended intervention reflected usual practice.	
Bias due to missing data	Low
Data were reasonably complete. "The National Committee on Confidential Enquiries into Maternal Deaths (NCCEMD) is responsible for the confidential enquiries into maternal deaths in SA and produces triennial reports entitled 'Saving Mothers'. The NCCEMD records all maternal deaths that occur in health institutions in SA but does not record the facility where the death occurred, only the health district and the level of care that the institution provides."	
Bias in measurement of outcomes	Moderate
"Before commencing the project, a baseline assessment of each district was carried out with special reference to the availability of basic and comprehensive emergency obstetric signal functions"	
Bias in selection of the reported result	Moderate

The outcome measurements and analyses are consistent with an a priori plan; or are clearly defined and both internally and externally consistent. There is no indication of selection of the reported analysis from among multiple analyses.	
Overall	**Critical**

Rudge et al 2011	
Bias due to confounding	Serious
At least one known important domain was not appropriately measured, or not controlled for. "Simple linear regression models were adjusted to estimate the referral system's annual effects on the total number of deliveries, C-section rates, and perinatal mortality rate in the two hospitals."	
Bias in selection of participants	Low
All participants who would have been eligible for the target trial were included in the study; and for each participant, start of follow up and start of intervention coincided.	
Bias in classification of interventions	Low
Intervention status is well defined; and Intervention definition is based solely on information collected at the time of intervention.	
Bias due to deviation from intended interventions	Moderate
Any deviations from intended intervention reflected usual practice; or any deviations from usual practice were unlikely to impact on the outcome.	
Bias due to missing data	Low
Proportions of and reasons for missing participants were similar across intervention groups.	
Bias in measurement of outcomes	Moderate
"Maternal and perinatal outcomes in both hospitals were analyzed according to referral status. Data were obtained using linked hospital delivery and birth logs, patient medical records and necropsy reports or death certificates." The methods of outcome assessment were comparable across intervention groups	
Bias in selection of the reported result	Moderate
The outcome measurements and analyses are consistent with an a priori plan; or are clearly defined and both internally and externally consistent and there is no indication of selection of the reported analysis from among multiple analyses.	
Overall	**Serious**

Santos et al 2006	
Bias due to confounding	Critical
Bias inherently not controllable in this study.	
Bias in selection of participants	Moderate
Start of follow up and start of intervention do not coincide for all participants the authors used appropriate methods to adjust for the selection bias.	
Bias in classification of interventions	Moderate
Intervention status is well defined; and some aspects of the assignments of intervention status were determined retrospectively due to the nature of the study.	
Bias due to deviation from intended interventions	Moderate

There were deviations from intended intervention, but their impact on the outcome is expected to be slight	
Bias due to missing data	No information
No information on missing data.	
Bias in measurement of outcomes	Low
The methods of outcome assessment were comparable across intervention groups; "A one page data collection form was designed for monthly summaries containing the number of deliveries, complications (by type), medical interventions performed (the 8 EmOC signal functions5), and the number of direct and indirect maternal deaths by cause. Participating facilities sent monthly reports first to the district headquarters and from there a district level report was sent to the statistical department of the Provincial Health Directorate in Beira."	
Bias in selection of the reported result	Low
There is clear evidence (usually through examination of a pre-registered protocol or statistical analysis plan) that all reported results correspond to all intended outcomes, analyses and sub-cohorts.	
Overall	

Sarin et al 2017	
Bias due to confounding	Serious
At least one known important domain was not appropriately measured, or not controlled for. “To assess chance and control for other effects, segmented regression analysis was used. Each segment of the series was allowed to exhibit both a level and a trend that followed an intervention. This statistical model estimates level and trend in the pre-intervention segment and changes in level and trend after the intervention.”	
Bias in selection of participants	Low
All participants who would have been eligible for the target trial were included in the study; and for each participant, start of follow up and start of intervention coincided.	
Bias in classification of interventions	Low
Intervention status is well defined; and intervention definition is based solely on information collected at the time of intervention. “we could not estimate the effect of external variables, such as the effect of other interventions to improve care. However, no drastic changes to the macro-level factors (policy and program) occurred in the 26-month period under reporting”	
Bias due to deviation from intended interventions	Moderate
There were deviations from usual practice that were unbalanced between the intervention groups and likely to have affected the outcome. This is due to the nature of the intervention; the intervention groups may deviate from usual practices more than other groups.	
Bias due to missing data	Low
Proportions of and reasons for missing participants were similar across intervention groups;	
Bias in measurement of outcomes	Moderate
"Data were self-collected by the teams of health workers and came from existing hospital records which included patient case files, ANC cards and delivery registers. These data are routinely collected as part of the ANC, delivery and post-partum procedures, and we did not collect additional data. Each month, project staff verified and recorded data in a predesigned Excel database. Data were then aggregated at district, state, and finally at aggregate level, with data verification at each step." The outcome measure is only minimally influenced by knowledge of the intervention received by study participants; and any error in measuring the outcome is only minimally related to intervention status.	
Bias in selection of the reported result	Moderate

The outcome measurements and analyses are consistent with an a priori plan; and are clearly defined and both internally and externally consistent; There is no indication of selection of the reported analysis from among multiple analyses; and there is no indication of selection of the cohort or subgroups for analysis and reporting on the basis of the results.	
Overall	**Serious**

Satischandra et al 2013	
Bias due to confounding	Critical
Confounding not controllable in this study.	
Bias in selection of participants	Serious
Selection into the study was related (but not very strongly) to intervention and outcome; and this could not be adjusted for in analyses;	
Bias in classification of interventions	Moderate
Intervention status is well defined; and some aspects of the assignments of intervention status were determined retrospectively.	
Bias due to deviation from intended interventions	Moderate
There were deviations from intended intervention, but their impact on the outcome is expected to be slight.	
Bias due to missing data	Low
Proportions of and reasons for missing participants were similar across intervention groups;	
Bias in measurement of outcomes	Serious
The outcome measure was subjective (i.e., vulnerable to influence by knowledge of the intervention received by study participants) and the outcome was assessed by assessors aware of the intervention received by study participants.	
Bias in selection of the reported result	Moderate
The outcome measurements and analyses are clearly defined and both internally and externally consistent; and there is no indication of selection of the reported analysis from among multiple analyses.	
Overall	

Schaider et al 1999	
Bias due to confounding	Critical
Bias not controllable in this study.	
Bias in selection of participants	Moderate
Start of follow up and start of intervention do not coincide for all participants; the authors used appropriate methods to adjust for the selection bias.	
Bias in classification of interventions	Moderate
Intervention status is well defined; and some aspects of the assignments of intervention status were determined retrospectively.	
Bias due to deviation from intended interventions	Serious
Due to the nature of the intervention there were deviations from usual practice that were unbalanced between the intervention groups and likely to have affected the outcome.	

Bias due to missing data	Moderate
"Complete data including maternal mortality data were available for 19,666 deliveries (83% of total)."	
Bias in measurement of outcomes	Low
Proportions of and reasons for missing participants were similar across intervention groups. "IMC, in collaboration with the Angolan Ministry of Health, designed a simple delivery registration form which was distributed to all TBAs by the TBA supervisor. After each delivery, the TBAs were required to complete a registration form. After each delivery, the TBAs were required to complete a registration form with the following information..."	
Bias in selection of the reported result	Moderate
The outcome measurements and analyses are clearly defined and both internally and externally consistent and there is no indication of selection of the reported analysis from among multiple analyses.	
Overall	**Critical**

Serbenescu et al 2019	
Bias due to confounding	Critical
Confounding is inherently not controllable in this study due to the large-scale interventions.	
Bias in selection of participants	Moderate
Start of follow up and start of intervention do not coincide for all participants; the authors used appropriate methods to adjust for the selection bias;	
Bias in classification of interventions	Moderate
There were deviations from intended intervention, but their impact on the outcome is expected to be slight.	
Bias due to deviation from intended interventions	Moderate
There were deviations from intended intervention, but their impact on the outcome is expected to be slight.	
Bias due to missing data	Low
Proportions of and reasons for missing participants were similar across intervention groups;	
Bias in measurement of outcomes	Low
The methods of outcome assessment were comparable across intervention groups; and the outcome measure was unlikely to be influenced by knowledge of the intervention received by study participants. "used multiple monitoring and evaluation processes with varied data sources (Table 4). Comparisons of maternal and perinatal outcomes were made between a baseline period (June 2011–May 2012) and Year 1 (June 2012–May 2013) after full implementation of SMGL interventions."	
Bias in selection of the reported result	Serious
There is suggestion of multiple analyses of data that is may not be representative of the entire population. "The results shown here are based on 4-district data analyses performed for each country"	
Overall	**Critical**

Shikuku et al 2019	
Bias due to confounding	Serious
At least one known important domain was not appropriately measured, or not controlled for. The presence of a control group means that some degree of confounding is potentially controllable in this instance. “This was a	

nonequivalent control group pretest – posttest design, a quasi-experimental design that involves an experimental treatment and two groups (study and control) of subjects, not randomly assigned, observed before and after its implementation."	
Bias in selection of participants	Moderate
Start of follow up and start of intervention do not coincide for all participants the authors used appropriate methods to adjust for the selection bias. There is evidence for appropriate selection of the control group.	
Bias in classification of interventions	Moderate
Intervention status is well defined; and some aspects of the assignments of intervention status were determined retrospectively.	
Bias due to deviation from intended interventions	Moderate
There were deviations from intended intervention, but their impact on the outcome is expected to be slight.	
Bias due to missing data	Low
Proportions of and reasons for missing participants were similar across intervention groups.	
Bias in measurement of outcomes	Moderate
The methods of outcome assessment were comparable across intervention groups; and the outcome measure is only minimally influenced by knowledge of the intervention received by study participant "Data was collected using the MOH tools available at the health facility level – MOH 333 (Maternity register that provides a daily activity of deliveries and their outcomes including obstetric and perinatal complications) and MOH 711 summary report."	
Bias in selection of the reported result	Low
There is clear evidence (usually through examination of a pre-registered protocol or statistical analysis plan) that all reported results correspond to all intended outcomes, analyses and sub-cohorts. "The findings for the indicators of interest from the two time periods were compared through a two-sample test of proportions, and MOH summary data and program reports were also reviewed to triangulate the information obtained from the DHIS2."	
Overall	**Serious**

Srofenyoh et al 2016	
Bias due to confounding	Serious
Confounding expected, some important confounding domains appropriately measured and controlled for. Although reliability and validity of measurement of important domains were sufficient, serious residual confounding exists. "To explore potential confounding between CQI activities and staffing, a third set of OLS regressions was performed using the CQI and staffing factors with significant correlation and which were predictive of outcome (i.e. in the same direction as the outcome trend). Every possible combination was analysed using OLS regression for the four outcomes: all deliveries, OH, HDoP, and CF1."	
Bias in selection of participants	Moderate
Start of follow up and start of intervention do not coincide for all participants the authors used appropriate methods to adjust for the selection bias.	
Bias in classification of interventions	Moderate
Intervention status is well defined; and some aspects of the assignments of intervention status were determined retrospectively due to the nature of the interventions.	
Bias due to deviation from intended interventions	Moderate
There were deviations from intended intervention, but their impact on the outcome is expected to be slight.	
Bias due to missing data	No information

No information on missing data	
Bias in measurement of outcomes	Moderate
The method was comparable across groups. "Maternal mortality ratio (MMR) data were obtained from the local Maternal and Child Mortality Report System"	
Bias in selection of the reported result	Low
The outcome measurements and analyses are consistent with an a priori plan; or are clearly defined and both internally and externally consistent and there is no indication of selection of the reported analysis from among multiple analyses.	
Overall	**Moderate**

Zhou et al 2012	
Bias due to confounding	Critical
This pre and post intervention study is inherently not able to control the confounding factors.	
Bias in selection of participants	Moderate
Start of follow up and start of intervention do not coincide for all participants the authors used appropriate methods to adjust for the selection bias.	
Bias in classification of interventions	Serious
Intervention status is well defined; and some aspects of the assignments of intervention status were determined retrospectively.	
Bias due to deviation from intended interventions	Moderate
Due to the nature of the intervention, there were deviations from intended intervention, but their impact on the outcome is expected to be slight.	
Bias due to missing data	No information
No information on missing data	
Bias in measurement of outcomes	Moderate
The method was comparable across groups. "Maternal mortality ratio (MMR) data were obtained from the local Maternal and Child Mortality Report System"	
Bias in selection of the reported result	Low
There is clear evidence (usually through examination of a pre-registered protocol or statistical analysis plan) that all reported results correspond to all intended outcomes, analyses and sub-cohorts.	
Overall	**Critical**