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Impact of Helping Babies Breathe (HBB), a basic neonatal resuscitation educational program for birth attendants in low-resource setting: a systematic review

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A B S T R A C T

Background: Reducing neonatal deaths and mortality due to birth asphyxia from preventable causes have been a continuing challenge in low-resource settings where the burden is high. The development of effective low cost interventions and their delivery are needed to bring down the number of deaths from birth asphyxia. Helping Babies Breathe (HBB), which is a neonatal resuscitation educational curriculum using "train the trainer" model aimed for birth attendants working in low-resource settings, are now being promoted as a strategy to improve the quality of care of the non-breathing newborn. However, its impact has not been fully evaluated.

Objectives: To assess the impact of HBB training of birth attendance working in low-resource settings on neonatal mortality and the learners' educational outcomes.

Design: Systematic review of HBB intervention. Registration reference: PROSPERO 2014: CRD42014007274.

http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42014007274

Data Sources: PubMed, Excerpta Medica Database (EMBASE), the Cumulative Index to Nursing and Allied Health Literature (CINAHL), Cochrane Library, Database of Abstracts of Reviews of Effects (DARE) as well as grey literature including neonatal resuscitation web-pages, conference proceedings and reference list of relevant articles without time and language restrictions.

Selection criteria: Randomized controlled trials, cluster randomized trials, quasi-experimental studies including quasi-randomized trials, controlled before-after studies, observational studies including interrupted time series that have reported objectively measured professional practice, patient outcomes, health-resource/service utilization of the Helping Babies Breathe

educational curriculum were included. Other studies reporting on basic or advanced resuscitation guideline educational programs were excluded.

Data collection and analysis: The review author (MP) independently extracted data, assessed the quality of studies and selected studies to be included. The supervisor (GA) was consulted to discuss the results and resolve any uncertainty. Additional information was requested from the author of one of the included studies. There were insufficient amount of data to perform pooled analyses, so a meta-analysis was not appropriate. The study results were therefore structurally synthesised and appraised. Standardized abstractions tables were made with the statistical software Review Manager (RevMan 5.2) and study quality of clinical outcomes were assessed by adapted GRADE methodology.

Results: Six observational before-after studies were included. A total of 102 083 newborn infants and 1027 birth attendants from various professions (both skilled and semi-skilled) fulfilled the inclusion criteria. Two studies evaluated the impact of HBB training versus standard care on neonatal mortality, and one of them assessed both neonatal outcome and educational outcomes. Four studies evaluated exclusively the impact of HBB on educational outcomes. All studies were conducted in low-resource settings. Evidence from these two observational studies show that facility-based HBB neonatal resuscitation may avert a substantial number of early (within 24 hours of birth) intrapartum related ("birth asphyxia") deaths and fresh stillbirths. There is also promising evidence that birth attendants trained in the HBB curriculum significantly improve their knowledge and preparedness for neonatal emergencies in low-resource settings compared to those with no additional training, but there seems to be insufficient evidence to prove that these newly acquired skills in neonatal resuscitation are transferred into clinical practice.

Authors Conclusions: The HBB in-service training appears to have the potential to reduce neonatal mortality in low resource settings. There is also some evidence of educational benefit for those who receive the training. Further studies are needed for evaluating the implementation strategies of HBB in-service training of birth attendants that ensure retention of their knowledge/skills and improve clinical performance both in a hospital and community context.

B A C K G R O U N D

The Millennium Development Goals (MDGs) are the world's time-bound and quantified targets designed to improve the social, economic, and health conditions for those people who are living in the world's poorest countries (Sachs, 2005). To be able to meet the MDGs by 2015, it is urgent that national data on the causes of child mortality are regularly updated to steer national and international research and programmatic priorities (Black et al., 2010). The world has made substantial progress in achieving many of the Millennium Development Goals, and a welcomed progress has been made for the MDG-4, which calls for a two-thirds reduction in under five mortality rates from 1990 levels (UN, 2013). According to the MDG Report 2013, the mortality rate for children worldwide under-five years of age dropped by 41% from 87 deaths per 1000 live births in 1990 to 51 deaths per 1000 live births in 2011. Unfortunately, little emphasis has been placed on the health of newborns, and the neonatal mortality (defined as death before one month of age) is now over-representing the global under-5 mortality rate, see Figure 1 (UNICEF, 2013). Child survival programmes have primarily focused on prevention of diarrhoea, pneumonia and malaria as well as vaccine preventable conditions which are leading causes of death after the first four weeks of life (Martines et al., 2005). Therefore, the first month of life is now recognized as a critical time

that requires focused interventions and efforts must be redoubled to be able to meet the global MDG-4 2015 target (UN, 2013).

The overwhelming majority of all neonatal deaths (99 %) take place in the poorest regions and countries of the world (Lawn et al., 2005) usually within hours after birth (Black, Morris & Bryce, 2003). This inequity in health care is an immeasurable injustice for those families living in the most underprivileged areas within these countries. In these high burden areas, also most of the world's 60 million home births occur, and in the poorest quintile of many low-resource countries, as many as 90% of mothers deliver babies at home without the presence of a skilled midwife (Gwatkin, Bhuiya & Victora, 2004).
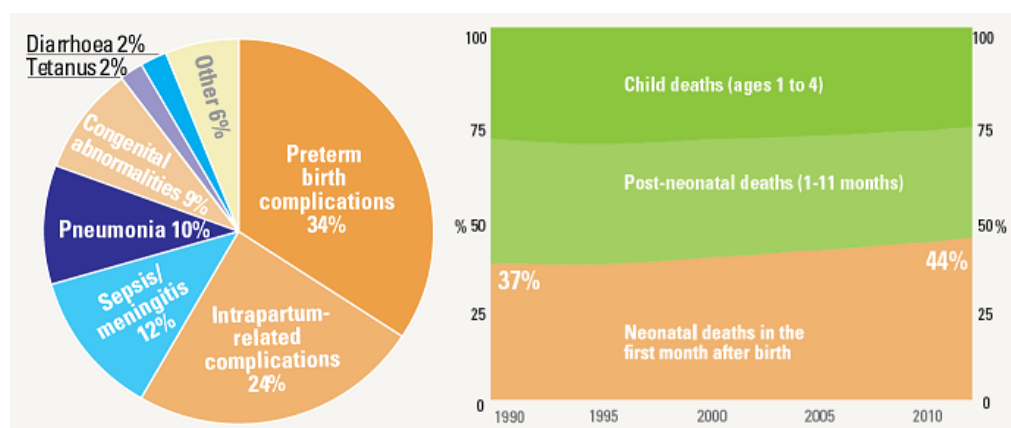

Figure 1. Most neonatal deaths are from preventable causes and neonatal deaths are a growing share of under-five deaths worldwide (Source: UNICEF analysis based on IGME, 2013, WHO and CHERG 2013) The cause distribution is calculated by applying the percentage breakdown by cause in 2010 provided by CHERG to the estimates of the number of under-five years of age deaths in 2012 provided by IGME. All the estimates are rounded, and therefore may not sum to 100%.).

The presumed main causes of neonatal deaths have remained unchanged over the last decade and are due to complications of infections (26%), intrapartum complications (24%) including intrapartum-related hypoxia, (previously termed "birth asphyxia") and preterm delivery (34%) with breathing problems during or after delivery, with low birth weight as a primary contributory cause of mortality and morbidity, as well as congenital abnormalities (9%) (UNICEF, 2013). However, the exact cause of neonatal deaths can be challenging to

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determine for health care workers. The neonates can often exhibit few specific symptomatic reactions to illnesses and their clinical manifestations of various diseases tend to overlap in neonates (Lunze, Bloom, Jamison, & Hamer, 2013). Also, many of these early neonatal deaths and stillbirths occur at home, unobserved and uncounted for in official health statistics (Lawn, Cousens, Darmstadt, Paul & Martines, 2004). The uncertainty that surrounds these estimates is also often due to an almost complete lack of quality vital registration system in high burden areas (Black et al., 2010; Lawn et al., 2011; Spector & Daga, 2008). According to Black et al. (2010) many analyses are based on retrospective household surveys and most cause-specific data rely on verbal autopsy without consistent definitions and algorithms, see Figure 2. From the reporting of neonatal mortality, it is unclear how many of these deaths that are related to poor newborn resuscitation. Some academics hypothesise that some recorded stillbirths may actually not be stillborn, but live births resulting in very early neonatal deaths. These newborns may be hypoxic due to difficulties during labour and birth, and they may be mistaken as stillbirths. In this cohort of stillbirths some would respond to resuscitative efforts from birth attendants skilled in neonatal resuscitation (Nelson, Simonsen, Henry, Wilder & Rose, 2011). In fact, among millions of infants documented as stillborn in low-resource settings, one could question how many of these would respond to the life-saving measure of neonatal resuscitation?
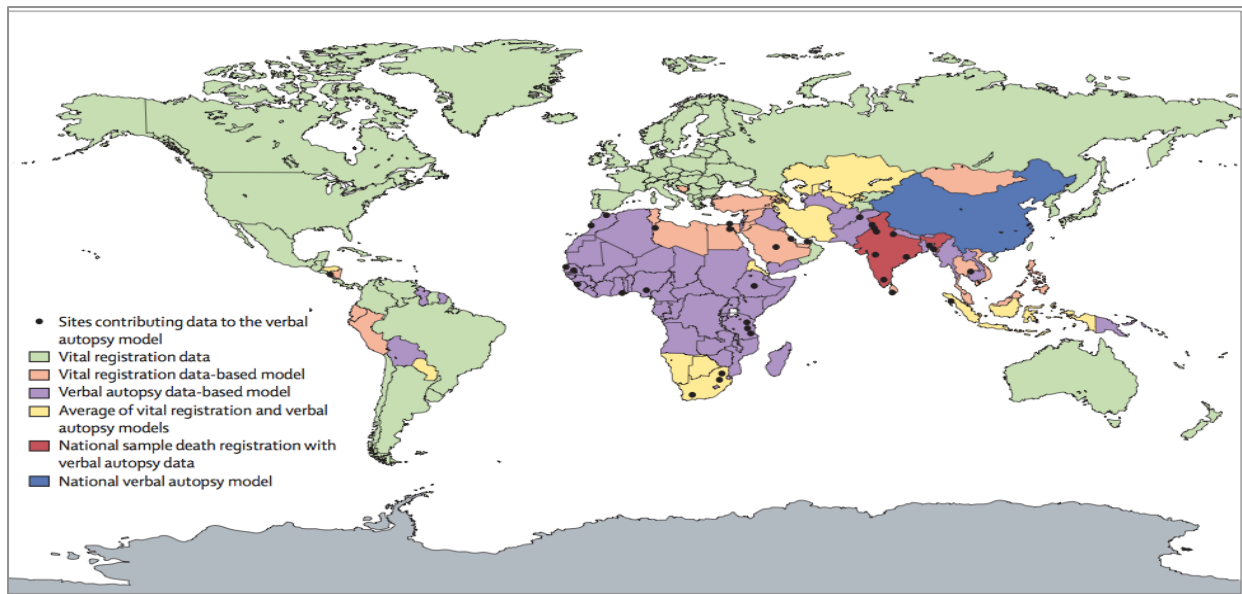
Figure 2. Methods used to estimate causes of neonatal mortality (0-28 days) in 2008 (Source: Black et al., 2010)

Especially the first hour after birth and the first day of life are critical for newborn survival. Approximately 50-70% of neonatal deaths may occur within the first day of life (Kruger, Niemi, Espeland, Naman & Malleyeck, 2012; Lozano et al., 2011; Nga, Hoa, Malqvist, Persson & Ewald, 2012). According to current estimates on neonatal mortality rates, from 2.9 to 3.6 million newborns die during the neonatal period (Black et al., 2010; Lozano et al., 2011; Oestergaard et al., 2011). A comparable number of infants are estimated to be stillborn (Lawn et al., 2005; Spector & Daga, 2008). Worldwide, an estimated 904000 neonatal deaths related to intrapartum hypoxic events ("birth asphyxia") in term infants and over one million intrapartum stillbirths occur each year (Lawn et al., 2009). Furthermore, more than one million preterm newborns die from complications of preterm delivery, such as respiratory distress syndrome, and many of these newborns also require assistance to breathe at birth (Lawn et al., 2009). Among the survivors of intrapartum-related neonatal deaths, one million children may develop cerebral palsy, serious learning difficulties or other forms of disability each year (WHO, 2005). The psychological and sociological burdens are impossible to measure.

Since prematurity and intrapartum hypoxic events are the leading cause of early deaths in many neonates, implementation of basic neonatal resuscitation and essential newborn care worldwide may have a substantial impact on newborn survival and save hundreds of thousands of newborn lives each year. When addressing neonatal health care, public health interventions need to extend from pregnancy, through the childbirth and the neonatal period and time after (Martines et al., 2005). Importantly, birth attendants should be trained in basic resuscitation and newborn care, particular those working in a community setting, since most babies are born at home (Wall et al., 2009).

According to Wall et al. (2009), approximately 10 million newborn babies need some degree of resuscitation such as tactile stimulation or airway clearing or positioning, see Figure 3. During the process of natural birth, the babies experience intermittent hypoxia as the respiratory exchange at the placenta is prevented for the duration of the contractions (Symonds, Arulkumaran & Symonds, 2013). At birth, the baby's lungs are filled with amniotic fluid; this fluid must be cleared and replaced with air within seconds after delivery. Almost all babies manage to breathe fine by themselves, the few that do not may require help to initiate breathing at delivery (O'Donnell, Davis & Colin, 2003). This transition from intrauterine to extra-uterine life depends on several factors, and problems may begin primarily in the mother, the placenta or the foetus, but present in the newborn baby as ineffective or absent breathing efforts immediately after birth. Approximately 6 million babies born annually need basic neonatal resuscitation with a face-mask resuscitator (Lee et al., 2011). Some non-breathing infants with primary apnoea will respond to simple stimulation alone, such as drying, warming and rubbing the back or feet. However, secondary apnoea might not respond with simple stimulation, as their bradycardia primarily results from hypoxemia and respiratory failure. It may be very difficult to distinguish between the two at the time of delivery, and face-mask ventilation is indicated if brief stimulation does not result in
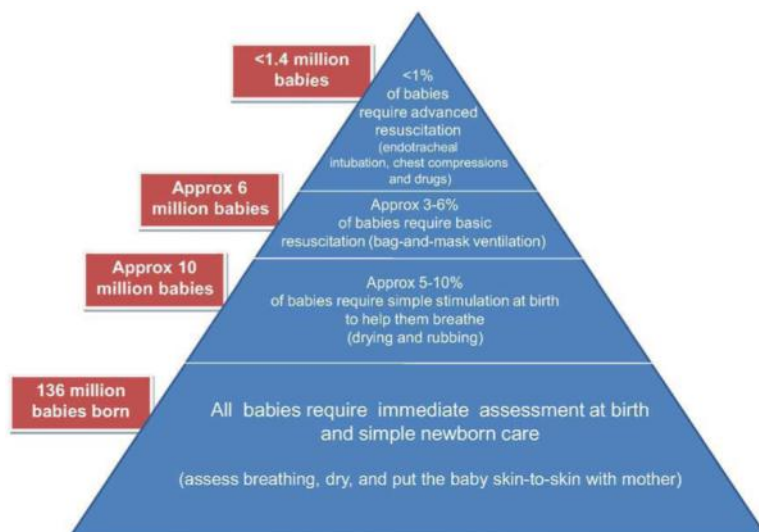
spontaneous breathing (Lee et al., 2011).

Figure 3. Estimates of global numbers of babies undergoing resuscitation at birth. Source: Wall et al., 2009; using estimates based on references data from (Palme et al., 1992; Deorari et al., 2001; Zhu et al., 1997; Kattewinkel Textbook of Neonatal Resuscitation, 2005; WHO Basic Newborn Resuscitation, 1997; Perlman et al., 1995).

In fact, all newborns that are resuscitated receive help to breathe, ranging from simple stimulation to assisted ventilation, and this is the most important part of neonatal resuscitation (Saugstad, 1998; Tan, Schulze, O'Donnell & Davis, 2005). More advanced neonatal resuscitation, including chest compression, endotracheal intubation and medications and supplementary oxygen are required in less than 1 % of births and most of these babies require on-going neonatal intensive care. Unfortunately, these advanced life-saving measures and technology are unavailable in many low-resource settings today (Wall et al., 2009). While systematic in-service training in resuscitation is very central in modern neonatology, the capacity to provide systematic training in neonatal resuscitation and guidelines on neonatal resuscitation is almost completely lacking in most low-resource countries (Lee et al., 2011). According to Rowe et al. (2005) there are multiple determinants for the poor performance in these settings. The obvious ones are lack of knowledge, skills and motivation. Other factors can be challenging working environments in the health facilities, such as lack of supplies and

medical equipment, poor supervision and leadership as well as lack of participation in planning and little peer support. However, some prior reviews have generated evidence that neonatal resuscitation is possible with basic equipment and skills in low-middle income settings that have potential to save newborn lives (Newton & English, 2006; Singhal & Bhutta, 2008; Singhal & Niermeyer, 2006; Wall et al., 2009). A recent systematic review on neonatal resuscitation training in health care facilities reports that training of birth attendants could avert 30% of intrapartum-related neonatal deaths (Lee et al., 2011). Currently the coverage of neonatal resuscitation is low in countries where the burden of neonatal deaths is high. Today, a variety of neonatal resuscitation courses are being promoted as a strategy to train health care workers to become better qualified taking care of seriously ill newborns or children in an emergency setting.

There is a number of algorithms and newborn resuscitation guidelines, most can be found online free of charge. Many of these are based more on expert consensus than on rigorous evidence, partly because of the issues surrounding whether a randomized controlled trial would be ethical on a subject that already has an established practice (Wall et al., 2009). Some of the courses used to teach neonatal resuscitation are the; Newborn Life Support (NLS), the Neonatal Resuscitation Program (NRP), WHO's Essential Newborn Care Course, and the Paediatric Life Support courses. According to a recent review (Opiyo & English, 2010), there seems to be inadequate evidence to confirm that in-service training in neonatal resuscitation improves birth attendants' skills and performance when caring for a critical ill baby or child, although there is some evidence of benefit.

Description of the intervention

In 2010, based upon the experience and results of an earlier neonatal resuscitation program and the Global Network for Women's and Children's Health Research, First Breath Study Group (Carlo et al., 2010), the Helping Babies Breathe (HBB) program was developed by the

American Academy of Paediatrics (AAP) to create an evidence-based program to reduce global neonatal mortality. The HBB is an initiative of the AAP as well as many collaborative partners, including the United States Agency for International Development (USAID), WHO, National Institute of Child Health and Development (NICHD), Saving Newborn Lives, International Liaison Committee on Resuscitation (ILCOR) and other public and private globally minded organisations (Steele, 2013).

This scientifically based program was primarily designed to equip birth attendants working in low-resource settings with skills for neonatal resuscitation and newborn care. The Global Implementation Task Force of the American Academy of Paediatrics developed this curriculum. It is based on the neonatal evidence evaluation of International Liaison Committee on Resuscitation (ILCOR). The content of HBB are in line with international health policy and guidelines through WHO technical expert review. This guideline recognises that in many low-resource countries only one birth attendant may be available, and must provide care to both mother and newborn. The main objective of the HBB programme is to train birth attendants in low-resource settings in the essential skills of basic newborn resuscitation, with the goal of having at least one skilled resuscitator present (with the equipment needed) at the birth of every baby (American Academy of Paediatrics, 2011). The Helping Babies Breathe educational program is culturally sensitive, pictorial and competency based guideline. The equipment is affordable, and is appropriate for clinical use, simulation training and continued practice. It can be locally taught to health care workers in diverse venues (clinics or educational institutions) and locations and no electricity or computers are needed. The educational kit includes an action plan, flip-over facilitator guide and a student workbook (Figure 4). A low-cost newborn simulator with ability to imitate an umbilical pulse, face-mask resuscitator and bulb suction that can be cleaned by boiling is included for hands-on training and to meet clinical needs (Little et al., 2011).

Figure 4. Helping Babies Breathe teaching materials and equipment (Photo credit: Laerdal Global Health.)

It is a hands-on course and focuses on simple techniques like keeping the baby warm, rubbing the baby dry, and if necessary, suctioning the baby's mouth and correct application of a positive air resuscitator for face-mask ventilation (FMV) within 60 seconds if needed, often referred to as the Golden Minute (Little et al., 2011). As consistent with recent evidence it is correct to use room air during face-mask ventilation. The guidelines for oxygen use during neonatal resuscitation have changed significantly based on evidence that a high concentration of oxygen immediately after birth is harmful to both term and preterm infants. The organs particular vulnerable are the eyes, lungs and brain (Harach, 2013). According to a systematic review and meta-analysis (Saugstad et al., 2008), there is a reduction in the risk of neonatal mortality and a trend towards a reduction in the risk of severe hypoxic ischaemic encephalopathy in newborns resuscitated with room air. Therefore, neonatal resuscitation of term infants should begin with air. If administration of supplementary oxygen is needed because hypoxia persists, it should be regulated by blending oxygen and air. If available, the concentration should be guided by pulse oxymetry monitor (Davis & Dawson, 2012).

Why it is important to do this review

According to the Helping Babies Breathe Status Report (April 2013), HBB has been introduced in 60 countries worldwide and in which 17 of them have national plans coordinated by governments. More than 130 000 health workers have been trained in the HBB curriculum. Also, more than 120 000 face-mask ventilators and 150 000 suction devices and 50 000 newborn-simulators have been supplied on a not-for-profit basis. Furthermore, another 4500 HBB training kits have been donated. Therefore, it is timely to review the progress of HBB educational program and its impact.

OBJECTIVE

The objective of this systematic review is to critically appraise, synthesize and present the up-to-date published evidence on the impact of HBB educational program for birth attendants working in low-resource countries and get a clearer understanding of its effects on learner behaviour, professional practice, patient care and newborn outcome.

The PICO process was applied (Population, Intervention, Comparison, and Outcome) to frame the research question. The healthcare staff/ birth attendants (both skilled and semi-skilled) taking care of newborn infants who are not breathing at birth are the "Population" of interest. "Intervention" is HBB educational program aimed at improving the basic newborn resuscitation skills and competency of the birth attendants working in low-resource settings. The "Comparison" was performed with the standard care provided by the birth attendants (both skilled and semi-skilled) who had not attended the HBB training. The "Outcomes" of interest were (i) overall neonatal mortality and (ii) birth attendants knowledge, skills and performance in basic newborn resuscitation.

METHODS

Criteria for considering studies for this review

Only original research published in peer-reviewed journals were included. The types of study designs considered were randomized controlled trials, cluster randomized trials, quasi-experimental studies including quasi-randomized trials, controlled before-after studies, observational studies as well as interrupted time series that have evaluated the effects of the Helping Babies Breathe educational program on at least one of the outcomes listed above. Only studies with HBB interventions that included training of birth attendants were

considered. Studies on other neonatal resuscitation guidelines or additional interventions were excluded.

Types for participants

Eligible participants include: all skilled healthcare professionals/birth attendants (doctors, physician's assistants, midwives, nurses) and semi-skilled (traditional birth attendant, lay midwives, community/village health workers) involved in caring for a newborn baby in a hospital/health care facility or community in low-resource countries (as classified according to the World Bank list of countries). Studies that had participants from middle and high-income countries were excluded.

Types of interventions

HBB in-service training of birth attendants was the intervention of interest. HBB training was defined as training in the HBB curriculum, other than the usual neonatal resuscitation training that healthcare professionals/birth attendants may or may not have received from their governmental or non-governmental organisation. The HBB curriculum included training in immediate and accurate assessment of the newborn status after birth (by one minute of age; often referred to as the Golden Minute) drying the baby and keeping warm (preventing hypothermia), cutting the umbilical cord, assessing respiratory drive and stimulation, clearing the airway, and assisting with positive pressure ventilation via face mask ventilation with room air if needed. The comparison group did not have HBB training and provided usual care to babies with birth asphyxia.

Types of outcome measures

Studies were included only if they reported at least one of the following primary and secondary outcomes that were objective and clinically relevant. Morbidities, such as hypoxic-

ischemic injury or neonatal apnoea as an outcome were not extracted, because they often are assessed subjectively and can be difficult to determine in a low-resource setting.

Primary outcomes

Neonatal mortality was defined as death in the first 28 days of life in newborn infants requiring basic neonatal resuscitation. Neonatal mortality is defined as the number of neonatal deaths from any cause among total live births: (i) Early (birth to 7 days of age) neonatal mortality and (ii) late (8 to 28 days of age) neonatal mortality per 1000 live births.

Secondary outcomes

Where reported, the following educational outcomes were considered; (i) birth attendants' knowledge and skills acquisition (written test or skill appraisal pre- and post-resuscitation training), (ii) birth attendant's practical performance in the delivery room (adherence to HBB guidelines and proper use of HBB equipment) demonstrated by direct observation by an evaluator or by other methods of documentation and (iii) birth-attendant's practical performance of neonatal resuscitation on simulator mannequin.

Search methods for identification of studies

Electronic searches

To identify potential studies for inclusion in this review, the following electronic bibliographic medical databases were searched with no language or time restriction up to 25th of March 2014. The databases searched included PubMed, Excerpta Medical Database (EMBASE), the Cumulative Index to Nursing and Allied Health Literature (CINAHL), Cochrane Library as well as the Database of Abstracts of Reviews of Effects (DARE) and Clinicaltrials.gov. No articles of potential interest were identified in non-English/Scandinavian languages. The search strategy terms included keywords: (neonatal OR

infant OR newborn) AND (resuscitation OR emergency care OR life support) AND (birth asphyxia OR hypoxia) AND (nurse OR midwifes OR physician OR doctors OR assistant OR traditional birth attendant OR village health worker) AND (in-service training OR education), AND (developing countries and low-resource setting) OR (Helping Babies Breathe). Snowball searching added no literature referenced in key papers. Efforts were also made to contact investigators and program managers for unpublished data. Appendix 1 shows the terms used in the PubMed search strategy. We modified this search strategy as appropriate for other databases.

Searching other resources / grey literature

Websites for neonatal resuscitation and simulated health care training were searched; (http://www.resus.org.uk, http://nrr.org/web2012/, http://www.helpingbabiesbreathe.org, http://www2.aap.org/nrp/, http://www.resus.org.au, http://www.laerdalglobalhealth.com/doc/2482/Helping-Babies-Breathe, http://www.who.int/maternal_child_adolescent/documents/basic_newborn_resuscitation/en/, http://www.heart.org/HEARTORG/, http://ssih.org/about-ssh, http://www.pas-meeting.org

Data collection and analysis

Selection of studies

Initially, the review author (MP) independently scrutinised the electronic searches and acquired full text manuscripts of the relevant studies based on the pre-determined review criteria outlined in the protocol. The supervisor (GA) was consulted with the results. We resolved any uncertainty or disagreement through discussion and did not require third person consultation.

Data extraction and management

The information was extracted (electronically) independently from each article using an adapted Effective Practice and Organization of Care (EPOC) Collection Template tool. The information extracted included; i) study population, setting and eligibility, ii) study design and methods, iii) interventions, iv) outcome measures and results, v) applicability and other information when needed (EPOC Resources for review authors, 2013). This paper focuses mainly on primary and secondary outcomes that were objective and clinically relevant as stated in the protocol registered at PROSPERO. When information regarding any of the data was unclear or not given, attempts were done to contact authors of the original studies with a request to provide further information. Only one investigator (Goudar et al., 2013) was e-mailed to provide further details on their adjusted NMR data, and their data was received shortly after.

Assessment of risk of bias in included studies

The review author (MP) assessed the risk of bias in each included study individually. The dimensions outlined in the Cochrane Handbook of Systematic Reviews of Interventions were used in the assessment. The following seven domains related to risk of bias were assessed in each trial; (i) random sequence generation (selection bias), (ii) allocation concealment (selection bias), (iii) blinding of participants and personnel (performance bias), (iv) blinding of outcome assessors, (v) incomplete outcome data, (vi) selective reporting (reporting bias) and (vii) other potential biases to validity (Higgins & Green, 2008). For each of the domains above (i - vii), the author assigned a judgement relating to the risk of bias by answering a pre-specified question for each of these sections. The judgement of "Low risk" indicated low risk of bias for all key domains, "High risk" indicated high risk of bias for one or more key domains, and "Unclear" indicates unclear risk of bias for one or more key domains. However, this tool developed by the Cochrane Collaboration was not developed with non-randomized

studies in mind, and the seven domains are not necessarily appropriate for non-randomized studies in all sections. The last domain (vii) is added to assess the risk of bias due to confounding which is often problematic in observational studies (Higgins & Green, 2008). The assessment was added to the tables; "*Characteristics of included studies*" (Appendix 2) and summarised in graphical summaries (Figure 5 and 6).

Overall risk of bias

It is recommended by the Cochrane Collaborations that systematic reviews should have at least two authors involved in processes of; i) electronic searches, ii) the selection of studies, iii) data extraction and iv) assessment of bias in the included studies to reduce the risk of bias in influencing the review (Higgins & Green, 2008). However, due to the nature of this thesis having only one review author, the risk of bias cannot be excluded in any of the steps mentioned above. But to minimise the risk of bias from influencing the results of this review, the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines was used as a framework for this review methodology (Moher et al., 2009). This guideline consists of a 27-item checklist (for review authors to check their review before submission) and a four-phase flow diagram. The flow diagram illustrates the total number of references retrieved, the total number of abstracts screened, the total full-text papers screened and the total papers included (Appendix 3 and 4).

Data synthesis

All identified studies included used the HBB training program as their primary intervention and its effect on the primary and secondary outcomes identified in this systematic review. They are all observational before-after studies but they have been executed differently (6 months to 2 years study period). Only two studies documented the impact of HBB training on newborn survival with clinical outcomes of NMR but they were defined differently (24 hours versus 28 days and fresh stillbirth versus stillbirth). Also the possibility of refresher training

varied, 1-day HBB training with the possibility of refresher training versus 1-day HBB training combined with "on-the-job" refresher training of all birth attendants during the whole study period. The four remaining studies focused on the impact of HBB training on educational outcomes and used various tools for practical evaluation (videotaped neonatal care versus observer assessment in simulated scenarios). The HBB training also varied in length (1-day versus 2-days training). Ideally, a meta-analysis of the included study outcomes should have been performed, but this was not possible due to the small number of included studies and the differences in their execution and outcome measures. Consequently, the results are presented in a structured synthesis.

Rating the quality of evidence on primary and secondary outcomes

The table, "*Characteristics of included/excluded/on-going studies*" and the figures "Risk of bias graph" and "Risk of bias summary" were adapted using Review Manager software (RevMan 5.2) which is a part of the Cochrane Information Management System (IMS). The primary outcomes were checked for accuracy, and presented in the Summary of Findings Table, adapted from "Worksheets for preparing Summary of Findings table using GRADE" (EPOC, 2013). The data are presented as per. 1000 live births; they are analysed using relative risk (RR) and Odds Ratio (OD). The 95% confidence interval (CI) was reported on all estimates in tables. A modified GRADE (Grades of Recommendation, Assessment, Development, and Evaluation) criteria were used to rate the quality of evidence for clinical outcomes, which reflects the confidence that the estimates of the effect are correct to support a particular decision or recommendation (Belshem et al., 2011). The GRADE guideline provides a transparent and structured process for presenting evidence, even though it cannot be presented in a meta-analysis. Quality of a body of evidence involved consideration of; i) study design, ii) limitation in their methods, iii) consistency, iv) precisions and v) directness/external validity. Additional considerations included the magnitude of the effect,

presence or absence of a dose-response gradient and direction of plausible biases (Guyatt et al., 2011).

R E S U L T S

Results of the search

In total 661 citations were identified (Appendix 3). From the electronic and supplementary grey literature searches, and after adjusting for duplicates, 634 remained, all written in English. Of these, 615 studies were discarded because after reviewing the abstracts it appeared that these papers clearly did not meet the inclusion criteria. The full text of the remaining of 19 citations was examined in more detail. Within these citations, one PhD thesis was included consisting of three individual studies. However, none of these studies met the inclusion criteria as described in our protocol and therefore excluded. Two on-going studies were identified and excluded as no data were yet available for use. Also, three conference abstracts were available online, though not included in this review as only full-text articles were eligible for inclusion. Thus, this systematic review consists of a total of 6 included studies.

Included studies and their context

The studies covered a period of 4 years, and all studies were carried out in low-resource settings in Tanzania (Ersdal et al., 2013), (Msemo et al., 2013); India (Goudar et al., 2013); Ethiopia (Hoban et al., 2013), Rwanda (Musafili et al., 2013); Pakistan and Kenya (Singhal et al., 2012). All included papers have been published in peer-reviewed journals. The total number of skilled and semi-skilled birth attendants included in the HBB training studies was 1027. Just a few of these health workers were trained as HBB facilitators and master trainers. Only two studies Singhal et al. (2012) and Ersdal et al. (2013) included semi-skilled health workers; lady health workers and lady health visitors in Pakistan, and ward attendants and student nurses in Tanzania. Participants were recruited from available birth attendants and represented several professional categories; doctors, medical officers, nurses, midwife,

auxiliary nurse midwife and anaesthetic and operation nurses. Most training took place in a hospital or health clinic facility.

Description of studies

See Appendix 2: *Characteristics of included studies; Characteristics of excluded studies; Characteristics of on-going studies*

Only two of the included studies, Goudar et al. (2013) and Msemo et al. (2013), evaluated the impact of HBB resuscitation training and newborn care of birth attendants on neonatal mortality (NMR) as their primary objective. They also assessed if this educational program would enhance the birth attendants knowledge and skills in emergency care of a non-breathing baby at the time of delivery. However, the two studies differ in their characteristics. Firstly, in the study by Goudar et al. (2013) primary clinical outcome was NMR (death within 28 days of birth) and stillbirth (SB) as well as the incidence of fresh SB. Other reported outcomes were educational such as; i) trainee knowledge, assessed by MCQ, ii) Face mask ventilation (FMV) skills, assessed by a 12 items checklist and iii) two Objective Structured Clinical Evaluation (OSCE) forms that test learners' responses to standardized case studies. OSCE-A evaluated the birth attendants' performance on thorough drying, assessment of crying, positioning the baby and clearing the airway. OSCE-B evaluated the birth attendants' performance on assessing the newborns breathing, appropriate mask selection and application, clearing the baby's airway and ventilation with corrective actions. In contrast, Msemo et al. (2013) reported their clinical outcome differently from the conventional NMR and used early NMR (24 hours) and fresh stillbirth as the primary outcome. Also, they only observed the use of HBB key competency skills, such as use of stimulation, suction and FMV skill by birth attendants before and after HBB training in the delivery room, not doing any formal testing. In total these two studies enrolled 102 083 newborn infants and most of these babies were

born in a hospital or health clinic facility, only a few (9 babies) in the study by Goudar et al. (2013) were born at home with a Traditional Birth Attendant (TBA). Both studies had the same pre-defined inclusion criteria for the newborns; women delivering at 28 weeks' gestation or more were eligible to participate. In Msemo et al. (2013), the time frame from baseline (2 months) and to the closing date for inclusion was 3,5 years. Goudar et al. (2013) only collected data for 6 months in each of the pre- and post-HBB periods and included 4187 births before HBB training and 5422 births after HBB training. Msemo et al. (2013) included a total of 8124 newborn in baseline data and 78500 newborns after the HBB intervention. Both studies collected data from rural and urban communities, primary health centres and hospital and used the "train-the-trainer model" and paired teaching and skills and practice exchange. Likewise, both studies based their in-service training on the HBB course material and baseline characteristics seemed similar in both groups.

In the study by Goudar et al. (2013), master trainers and trainers taught 599 birth attendants from rural communities, primary health centres and hospitals. Multiple HBB courses were conducted and the second set of courses permitted a single repetition for birth attendants desiring a refresher course and included birth attendants who had not received HBB training due to provider staff turnover. In contrast, Msemo et al. (2013) did not disclose how many birth attendants they trained, but they trained "all" their birth attendants for 1-day course, and provided "on-the job" refresher training during the whole study period. They placed a simulator in the delivery suite where every birth attendant needed to show the application of basic skills in resuscitation before starting a shift. They focused mainly on training midwives compare to Goudar et al. (2013) who mainly trained physicians. Furthermore, Goudar et al. (2013) collected de-identified clinical outcomes during admission at the clinic before discharge, checking the areas' vital events registry through 42 days after birth, and by

telephone interview of those not covered by the register. Msemo et al. (2013) placed a computer in every labour ward for data entry and transmission of data to a central repository in the Health Ministry in the capital.

The next four included studies by (Singhal et al., 2012; Ersdal et al., 2013; Musafili et al., 2013; Hoban et al., 2013) assessed only the educational impact (secondary outcomes) of HBB curriculum on birth attendants' knowledge, skills and performance in the delivery room or at simulated training. All used the "train-the -trainer" model where facilitators were selected, trained to deliver the standardised HBB educational program, and then made responsible for training birth attendants within their medical facility or community. Almost all studies, expect Msemo et al. (2013), used a similar or modified version of the OSCE assessment and MQC related to the HBB competencies to test their birth attendants skills and performance. The first study by Singhal et al. (2012) is often described as the pilot study of the HBB program. This study's main objective was to develop an educational program designed to train health care providers (31 facilitators and 102 learners) to carry out neonatal resuscitation in low-resource settings. Educational outcomes relevant to this review were the birth attendants' knowledge (MCQ), observation of face-mask ventilation skills and the OSCE-A and B before and after the intervention. Learning sessions were completed in one day. Data from each site was analysed independently.

The second study by Musafili et al. (2013) had a similar objective to Singhal et al. (2012), to evaluate the immediate effect of HBB training on neonatal resuscitation. They trained 118 birth attendants from three hospitals using MQC test and practical evaluation with OSCE A and B. But the researchers did not use the OSCE B for the pre-test as it was considered too difficult to pass without formal training in neonatal resuscitation. However, they also wanted to evaluate the long-term effect of HBB training and retested the birth attendants 3 months

after the training was completed. In this evaluation the OSCE B was included.

The third study by Ersdal et al. (2013) assessed the effect on professional neonatal resuscitation skills and management strategies among birth attendants using simulations scenarios seven months before and after completing the 1-day HBB training. They also wanted to document neonatal management in the delivery room during the 14 months study period. Sixteen research assistants were trained to observe the 39 birth attendants' performance related to the delivery and newborn care. Demographic data were noted and included in a "self-assessment form" about the level of confidence they felt in performing neonatal resuscitation and newborn care. Finally, they were asked to list eight key points of preparing for a delivery and newborn care. First two simulation scenarios "routine care" and "neonatal resuscitation" were performed and videotaped as baseline data. Then seven months later after the 1-day HBB training the participants were retested in the same simulated scenarios. The research team collected observational data continuously during the whole study period. Data on 2745 and 3116 newborns were included before and after training respectively. The Kirkpatrick model (Level 1- 4) of evaluation was used to assess the effect of stimulation based HBB training. Only 33% of the 39 learners could be retested due to organizational constraints, additional 14 birth attendants were therefore recruited (they had all previously completed HBB training) to be evaluated with the remaining 13 participants from the first pre scenario test group. In total, 27 participants were interviewed and videotaped post HBB training.

The fourth study by Hoban et al. (2013) selected and trained 111 birth attendants for a 2-days HBB training course. Before and after training, birth attendants completed a modified 10-question MCQ from the original 16-question HBB MCQ test. The participants were evaluated on basic post-training face-mask ventilation skills using a seven-item checklist from the HBB

manual. In the end, the participants completed a form with demographic data and they were asked to describe the HBB course feedback. Due to time constraints, the largest site (n=42 birth attendants) had only post-test result available. As a result, this site was therefore only included for face-mask ventilating testing and qualitative analyses, leaving remaining four sites, all rural with 69 birth attendants, for the analysis of knowledge transfer.

Risk of bias in included studies

The review included six observational before-after studies covering HBB in-service training of a wide variety of birth attendants and their professional care of newborns not breathing at the time of birth. There was some consistency in methodological approach, as all included studies employed a controlled before-after design. None of the included studies had a low risk of bias for all criteria, suggesting that there is some level of plausible bias in each of the studies included. Assessment of key criteria and its justification for risk level assignation is described in more detail in the "*Characteristics of included studies*" (Appendix 2) and summarised below. The figures provide graphical summaries of the review author's judgements about each methodological quality across studies presented as percentages (Figure 5) as well as judgement of methodological quality for each included study (Figure 6).
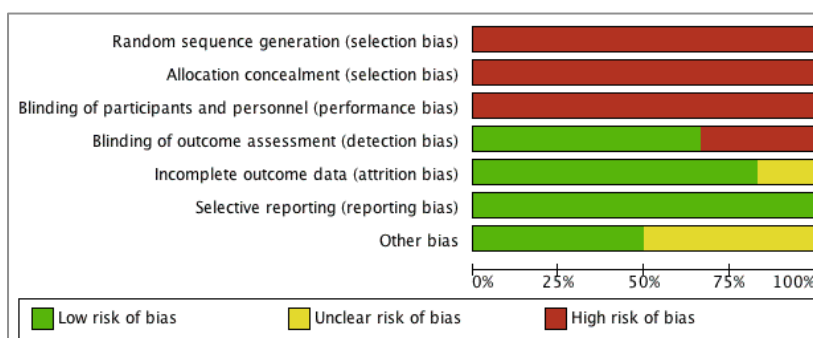

Figure 5. "Risk of bias graph": review author's judgements about methodological quality presented as percentages across all included studies

Figure 6. "Risk of bias summary": review authors judgements about methodological quality of each included study

Allocation

According to the EPOC Resources for review authors (2013), non-randomised studies should score "high risk" both in; sequence adequately generated, allocation concealment as well as blinding of participants and personnel, due to the nature of the non-randomised design of the study. Also the intervention of HBB neonatal resuscitation on newborn care or its training cannot be implemented masked.

Blinding of outcome assessment

Among these six included studies, the two main studies assessing the impact on neonatal mortality tried to reduce attrition bias by blinding outcome assessment. Msemo et al. (2013), did not state if their study data were anonymized or de-identified, but their data were entered into a central repository in the capital city. Goudar et al. (2013) stated that they de-identified

their clinical mortality outcomes into a data registry. The four remaining studies assessing educational outcome have trouble with masking due to the nature of the study design. Singhal et al. (2012), Hoban et al. (2013) and Ersdal et al. (2013) do not mention any blinding of outcomes, but they have an objective MCQ test and observational checklist to follow. Musafili et al. (2013) used the same observer to re-evaluate participants, but tried to minimise potential bias with codes so previous scores of the participants were unknown for to the observer.

Incomplete outcome data (attrition bias)

Overall, incomplete outcome data and, did not appear to be a problem in the study included, neither did loss of follow up or incorrect analysis.

Selective reporting

Reporting bias was judged to be low in all studies. In all studies outcomes listed in the "Methods" section were comparable to those reported in the "Results" section and all outcomes were included. However, it is worth mentioning that the studies by Goudar et al. (2013) and Msemo et al. (2013) are both published in *Paediatrics*, the official journal owned by the American Academy of Paediatrics, the developer of HBB educational programme.

Other biases

All included studies seem to try to describe confounding factors relevant to their study context, and attempt to control for confounding with a wide range of statistical methods as appropriate. All six studied performed a baseline survey and this seemed to be comparable to the study groups in all studies. The baseline imbalances were largest in the study by Msemo et al. (2013), related to the 2-months baseline versus 2 years study period. However, the study hospital's NMR was comparable to baseline data and had remained unchanged for many years according to the authors.

Language bias can be a potential threat in all studies, as none of the participants had English as their first language, though the researcher supported the participants with translation during training. Further, the researcher did not clearly state the pre-existing experience the birth attendants had in neonatal resuscitation, which can lead to bias. Also by mixing skilled and semi-skilled birth attendants might bias the results. Misclassification bias for stillbirths versus failed resuscitation was another potential source of bias in studies reporting on neonatal outcome. The magnitude of this bias is not clear. The validly of self-reporting of neonatal complications may also lead to bias. Almost all of the included studies were funded, or partly funded, given travel allowances or grants to the participating researchers or institutions by the developers of HBB curriculum; APP, Lærdal Foundation for Acute Medicine, Latter-Day Saints Charities and USAID. Musafili et al. (2013) were supported by the Swedish International Development Cooperation Agency (Sida). However, funding bias is judged to be of low risk to influence the results of the included studies.

Effects of interventions

Primary outcome: Neonatal Mortality Rate (NMR)

In Msemo et al. (2013) (see Table 1 Summary of Findings) the primary outcome of NMR, defined as early Neonatal Mortality (NMR 24 hours after birth) showed that HBB training of their participants resulted in a significant reduction in deaths from 13.4 to 7.1 per 1000 live-born deliveries (relative risk [RR] 0.53; 95% confidence interval [CI] 0.43-0.65; $p < 0.0001$. This equals a 47 % reduction in NMR. The reduction in NMR (24 hours) was significant for both normal and low birth weight as well as term and preterm infants. There was a significant decrease in Fresh Still Births (SB) after HBB intervention (19.0/1000 versus 14.5/1000 versus). This equals to a 24 % reduction in fresh stillbirths. Decreasing gestational age was associated with increased NMR (24 hours). The study by Goudar et al. (2013) (see Table 1

Summary of Findings) could not document that HBB training had a statistical significant impact on the NMR, which they defined as death after 28 days. NMR (28 days) was 1.8% before and 1.9% after HBB training [OR] 1.09, 95% [CI] 0.80-1.47, p = 0.59. The lack of differences in NMR (28 days) persisted also after adjustments for post HBB training, resuscitated, multiple gestation, mode of delivery and gestational age. However, the HBB training reduced the rate of SB without increasing NMR (28 days). SB declined from 3.0% to 2.3% [OR] 0.76, 95% [CI] 0.59-0.98 and the rate of fresh SB declined from 1,7% to 0.9% [OR] 0.54, 95% [CI] 0.37-0.78 after HBB training. This equals to a reduction of 48 %. Furthermore, the pre-discharge mortality was 0.1% in both periods. The unknown status at 28 days was 2 % greater after HBB training and statistically significant (p = 0.007).

Table 1. Summary of Findings on Neonatal Mortality Rate (NMR)

Msemo et al 2013 (n= 8124) (n=78500) / rates per 1000 liveborns.						
Outcomes	**Before HBB**	**After HBB**	**RR**	**95% CI**	**p-value**	**Certainty of the evidence (GRADE)***
NMR 24 h	13.4/1000	7.1/1000	0.53	0.43-0.65	p=<0.0001	⊕⊕⊕⊖
Fresh SB	19/1000	14/1000	0.76	0.64-0.90	p=0.001	⊕⊕⊕⊖
Goudar et al 2013 (n=4187) (n=5411) / rates per 1000 liveborns						
Outcomes	**Before HBB**	**After HBB**	**OR**	**95% CI**	**p-value**	**Certainty of the evidence (GRADE)***
NMR 28 d	18/1000	19/1000	1.09	0.80-1.47	p=0.59	⊕⊕⊕⊖
Fresh SB	17.2/1000	9.2/1000	0.54	0.37-0.78	p= ≤0.001	⊕⊕⊕⊖

* GRADE Working Group grades of evidence (EPOC 2013)
High quality: This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different is low. ⊕⊕⊕⊕
Moderate quality: This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different is moderate.⊕⊕⊕⊖
Low quality: This research provides some indication of the likely effect. However, the likelihood that it will be substantially different is high.⊕⊕⊖⊖
Very low quality: This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different is very high.⊕⊖⊖⊖

Secondary outcomes: Education

The study of Singhal et al. (2012) indicates significantly better theoretical knowledge and skills after HBB training, both for facilitators and learners. The percentage of facilitators who passed the MCQ was high both pre-course (75% in Kenya) and post-course (95% in Kenya and 82% in Pakistan). In Kenya, only 2 % learners passed pre-training MCQ, and 54% passed post-training (p = 0.05). For Pakistan no data are available on post-training MCQ passes. For face-mask ventilation skills, none of the learners in Kenya managed to pass the test pre-HBB training, and after HBB training only 15% passed. Similar findings are seen in Pakistan. The OSCE A and B was only tested after HBB training, and 60% passed OSCE A in Kenya, and 83% passed in Pakistan whereas 20.8% passed OSCE B in Kenya and 22.6% passed in Pakistan.

In the study of Musafili et al. (2013), the knowledge MCQ test score significantly improved after HBB course; $77 \pm 15\%$ versus $91 \pm 9\%$ (p < 0.001). The mean score obtained by learners on a post-course skill evaluation was $89 \pm 9\%$; 64% of the learners managed to pass the test. When they were retested 3 months later the knowledge remained at the same level. However, the scores on the practical evaluation of HBB were $89 \pm 9\%$ immediately after training and $83 \pm 16\%$ 3 months later. The percentage of passing grades were 64% after HBB training, but declined significantly to 43% (p < 0.001) 3 months later.

Ersdal et al. (2013) observed that 41% of the learners passed the "Routine care" scenario pre HBB training as compared to 74% post training, 7 months after the one-day course (p = 0.016). In the "Neonatal resuscitation" scenario 18% of the learners pre HBB training passed, compared to 74 % post training (p < 0.001). The number of birth attendants who managed to successfully apply the face-mask ventilation increased from 31% - 36% pre HBB training to

74% post training. However, improvement did not transfer into clinical practice in the delivery room. The number of newborn infants being suctioned and/or ventilated at the time of delivery did not change, and the use of stimulation actually decreased from 17.7% to 14.1%; p ≤ 0.0001), as well as mean time to start face-mask ventilation (76 ± 54s versus 89 ± 76s; p = 0.028) after HBB training. There were no correlations between frequency of attended deliveries, newborn care and resuscitations, theoretical knowledge and "pass/fail" performance. In the self-assessment forms, high self-confidence was related to reduced performance (p = 0.01). After HBB training the number of birth attendants who reported themselves as "always confident" decreased.

In the study by Goudar et al. (2013), birth attendants' knowledge and performance in neonatal resuscitation and newborn care systematically improved with HBB training. Learners with passing knowledge scores increased from 46.1% to 88.6% in the first HBB training, and from 69.3% to 90,4 % during the refresher sessions, both statistically significant (p ≤ 0.001). In the observed newborn care, neonatal resuscitation (defined as clearing the airway, specific stimulation to breath and/or face-mask ventilation) was done correctly by 28.9 % in the before HBB training group, but only 11.9 % did it in the after training period (p = 0.001). Further, in the pre HBB intervention period, 26.7 % had cleared the airway by suction compared with 10% in the post period (p = 0.001). It was also observed that 15.8 % of newborns in the before HBB training period and 9.1% in the after HBB training period received stimulation (p ≤ 0.001). Importantly, it was documented that 7.8 % of the newborns in the pre training period received timely "Golden Minute" face-mask ventilation, and only 22.3 % received it in the after training period.

Msemo et al. (2013) did not test their birth attendants' skills or performance, but they observed the impact of HBB training on the use of HBB key competencies in the delivery

room. There was no significant difference in the overall percentage of providers trained and the percentage that attended deliveries of infants who dies (p = 0.26). The use of stimulation increased before versus after HBB training from 47% to 88% (RR 1.87; 95% CI 1.82 - 190; p ≤ 0.0001), as did the use of suctioning from 15% to 22% (RR 1.40; 95% CI 1.33 - 1.46; p ≤ 0.0001). However, there was a sharp decline in face-mask ventilation before versus after HBB training from 8.2% to 5.2%.

In the study by Hoban et al. (2013), the neonatal resuscitation knowledge improved from 8.7/10 (SD 1.4) to 9.4/10 (SD 1.1; p = 0.003). During knowledge testing after HBB training, the birth attendants were 68% more likely to identify newborns that require resuscitation (p = 0.005), 75% more likely to correctly choose to begin face-mask ventilation in a non-breathing baby that is unresponsive to stimulation (p = 0.004) and 79% more likely to improve the mask seal when face-mask ventilation fails to produce adequate chest rise (p = 0.003). The significant pre-training (p = 0.003) knowledge differences between doctors and non-doctors disappeared (p = 0.212). Post-test scores increased as trainer and learner ratio decreased. The mean face-mask score was 5.7/7 (SD 1.6) with no obvious association between trainer and learner ratio and score. The two most frequently missed HBB steps (missed by more than one-third of the learners) required to improve ventilation if there is poor chest rise were; clearing oral secretions and squeezing the bag harder. Learners did well in forming a face-mask seal, ventilation at an appropriate rate and checking for chest rise, less than 10% of learners failed these items.

D I S C U S S I O N

To the best of our knowledge, this is the first systematic review that has evaluated the impact of the educational program of HBB for birth attendants working in low-resource settings and reported its impact on neonatal and educational outcome. Prior to this review, other reviewers

have provided evidence for the effectiveness of neonatal resuscitation and quality newborn care. Wall et al. (2009) reviewed the evidence for neonatal resuscitation guidelines content, training and competency needed. They also looked at the equipment and supplies necessary to have in place as well as cost and key program considerations specifically for low-resource settings. In addition, Lee et al. (2011) assessed the impact of immediate newborn assessment and stimulation as well as neonatal resuscitation (both advanced and basic guidelines) from high, middle and low-resource countries. Penfold, Willey & Schellenberg (2011) documented in their systematic review from sub-Saharan Africa that essential newborn care interventions such as hygienic birth, newborn resuscitation, breastfeeding and Kangaroo Mother Care for low-birth weight babies were associated with reduced risk of neonatal mortality. Also, training community birth attendants in resuscitation and administration of antibiotics as well as establishing women's groups could improve newborn survival. In a meta-analysis by Opiyo & English (2010) on in-service training for health care workers to improve newborn care in low-and middle-income countries, found limited evidence, but suggest that in-service training neonatal emergency care courses have potential benefit.

Although the worldwide acceptance of neonatal resuscitation being an important part of essential newborn care, there is limited evidence of its impact on neonatal outcome, mainly due to the ethical challenges of performing research on well-established life-saving health practices. No RCTs were found that could be included in this review. Performing RCTs on emergency obstetric care interventions are today regarded as highly unethical (WHO, 2011). It may also be difficult to implement a RCT due to logistical and economic reasons. In the context of HBB, random assignment of participants would restrict some birth attendant's basic education on life-saving competency and will be seen as unethical. In the absence of high-quality evidence, we must look for lower quality evidence to guide our decisions on the impact of HBB intervention and it seems that observational studies remain at the "top of the

hierarchy" of evidence available today. Nonetheless, observational studies remain susceptible to bias and confounding as this design restricts the ability to isolate the effect of the HBB intervention alone from other potential changes at the health facilities during the study period (Hannan, 2008). Therefore it is important to include information about how the included studies considered their potential confounders and methods used to control for confounding, as well as the confounding factors that have not been adjusted for (Higgins & Green, 2008). All the studies included in this systematic review had applicable types of participants, intervention and outcomes. A major strength seen in the included studies was the population-based design, the overall large sample size of included newborns as well as birth attendants living and working in areas with limited resources, the accurate clinic registries and the completeness of data collection, particularly on NMR data before discharge. The use of local trainers to train a broad spectrum of health care workers both skilled and semi-skilled was also positive, as it makes the HBB training easy to repeat.

The main limitation seen in this review was that the study designs were executed differently. It was therefore not possible to directly compare important clinical outcomes such as NMR, and perform a meta-analysis. Another limitation is that the NMR was reported only in two studies. Furthermore, none of the included studies had information on the cost of the HBB interventions. Cost-effectiveness research in health care is important to be able to combine interventions suitable for scaling up and to fit interventions to available health systems resources, particular in settings where resources are limited.

The principles of the GRADE system for evaluating the quality of evidence for outcomes reported were applied to this review. The GRADE system classifies the quality of evidence in one of four levels; high, moderate, low and very low. All six included studies included had a "high risk" of bias according to GRADE assessment tool in their random sequence generation, allocation concealment and blinding of performance and detection bias, largely due to the

nature of the intervention. But in the GRADE approach, quality means more than just judging the risk of bias when judging the body of evidence. Review authors generally tend to rate the quality of evidence from well-performed observational studies as low (Higgins and Green, 2008). However, if such studies yield large effects and there is no obvious bias explaining those effects, review authors may rate the quality of evidence as moderate or if the effect is large enough, even as high. The quality of evidence of an RCT and OS may be downgraded as a result of limitation in study design or implementation, poor precision of estimates (with wide confidence intervals), variability in the study results and indirectness of evidence or if publication bias is suspected (Guyatt et al., 2008).

Both Goudar et al. (2013) and Msemo et al. (2013) showed a statistically significant reduction in the fresh SB rates without a simultaneous increase in NMR. In addition, Msemo et al. (2013) documented a sustained significant reduction in NMR within 24 hours after implementation and two years thereafter. These mortality outcomes are at the top of the hierarchy of outcomes and critically important for decision making according to GRADE (Guyatt et al., 2008). There is also a large magnitude of the effect (RR <1), as well as good precision of estimates with "tight" confidence intervals. The findings are generalizable to low-income countries, publication bias is low and plausible biases seem few in this context of the early mortality rate. Accordingly, the quality of evidence of NMR outcomes was upgraded from "low" to "moderate". It is justifiable to suggest that newborn lives were saved after the implementation of HBB training of birth attendants in these two studies. Similar findings are seen in the systematic review by Lee et al. (2011). Their review consisted of 24 studies on neonatal resuscitation (both basic and advanced guidelines) reporting on mortality outcome. None of these studies used the HBB as a guideline for training their health care staff. They also documented that basic neonatal resuscitation had effect on intrapartum related term deaths ("birth asphyxia" in health facilities and the community). They also upgraded the

quality of evidence of this mortality outcome from low to moderate quality due to large magnitude of the effect, consistency across the studies and generalizability to low and middle income countries.

However, the study by Goudar et al. (2013) was not able to verify a statistically significant difference in their NMR (28 days). They argued that although the baseline NMR (1.8%) was high compared to high-income countries, it was too low to make a further reduction relatively difficult with the HBB intervention alone. Furthermore, many factors can potentially influence neonatal survival in the first four weeks of life, such as co-morbidity, the newborns' length of stay in the hospital, thermal protection, early breastfeeding, management of neonatal infection to mention a few. These potential confounders may influence the late neonatal mortality rate substantially, implying that NMR (28 days) needs further pre-post assessment to be able to verify if there is an impact of HBB on infant survival in the first month. For that reason, the early NMR (24 hours), may provide more valid assessment of the impact of neonatal resuscitation on newborn survival after birth asphyxia in the first day of life.

When looking at the birth attendant's performance on newborn care contrasting findings were observed. Firstly, Msemo et al. (2013) showed that HBB training was associated with a significantly increased number of children stimulated and suctioned in their data set. There was also a significant decrease in use of face-mask ventilation. As explained by the authors, these multifactorial findings are in line with what they found in experimental observations (Ersdal et al., 2012), i.e. most non-breathing babies are in primary apnoea with a heart rate and would initiate spontaneous breathing in response to drying and stimulation if done in a timely manner (60 seconds). Msemo et al. (2013) suggests that this is the most plausible explanation for the significant decline in NMR (24 h) and fresh SB rates. However, Goudar et al. (2013) report the exact opposite. After HBB training birth attendants actually performed

less stimulation and suctioning, and increased the use of face-mask ventilation. They argue that a plausible reason for this finding is that "thorough drying" which also provides cutaneous stimulation, as it is the first step in the HBB action plan before "stimulation" and may induce breathing. This could therefore explain the decline in fresh SB, and why researchers found that fewer infants required resuscitation in the post-training period, including additional stimulation and clearing of the airway. They suggest that future studies should report; "thorough drying" to clarify this issue. The large difference in sample size between these two studies, and that the observers/or researchers might have "defined" stimulation differently can yield these conflicting results.

Can improvements in neonatal resuscitation skill after HBB training result in decreased stillbirths without increasing NMR? Goudar et al. (2013) suggest that before HBB training, live born babies without obvious signs of life might have been misidentified as fresh SB. Similar findings are reported by other authors too (Daga 1992; Cowles 2007; cited in Spector & Daga, 2008). Some of these infants might be in a prolonged state of secondary apnoea as a result of complications during labour, and they may be unresponsive to face-mask ventilation and neonatal resuscitation. Enhancing the monitoring of the foetus during labour, or having appropriate referral system in place for high-risk pregnancies could prevent some of these deaths.

Moreover, the included studies did report positive educational outcomes following successful HBB training. Birth attendants' knowledge and performance systematically improved immediately after being trained, although this improvement did not transfer to clinical practice and many learners had difficulties retaining practical skills after attending the short course of HBB training, particularly the face-mask ventilation. However, the quality of evidence of measured educational outcomes; i) knowledge attainment, ii) HBB neonatal resuscitation performance in simulated scenarios and iii) HBB neonatal resuscitation

performed in the delivery room, were all judged to be "low" according to GRADE. Although they had similar baseline, few participants were lost to follow-up, and the generalizability was good, the magnitude of the effect reported was weak. Also the educational outcomes were low on the "hierarchy" compared to mortality outcomes. Furthermore, the studies were all quite small in sample size and the issues of confounding were judged to be of "high risk" or "unclear risk".

The five studies that reported on educational outcomes collected their data through MCQ tests, observational checklist as well as direct observation, and video recording of the performance in the simulated scenarios. In the study by Singhal et al. (2012), theoretical knowledge significantly increased immediately after the course. However, no significant improvement of face-mask ventilation skills was seen, neither in facilitators' nor in learners' group. Many also had difficulties with the OSCE assessment. The authors suggest that these findings might be due to the inexperience and unfamiliarity with face-mask ventilation, insufficient time to practice and lack of prior exposure to OSCE format. In the study by Musafili et al. (2013), the birth attendants significantly improved their knowledge and retained it for at least 3 months, however, their HBB practical skills in simulated scenarios dropped to unsatisfactory levels. Moreover, Hoban et al. (2013) who did a 2-days course, showed that knowledge in neonatal resuscitation improved significantly. Also the pre-training knowledge differences between professions disappeared after training, meaning that both skilled and semi-skilled birth attendants had profited from HBB training. But their study also indicated that participant's skills in face-mask ventilation testing varied widely, although the vast majority passed the basic steps of ventilation with face-mask resuscitator. Goudar et al. (2013) found that birth attendants' knowledge increased after training, but the rate of correct application of face-mask ventilation within the Golden Minute was low, only 22.3% after the training period. Ersdal et al. (2013) had similar findings. Birth attendants performed better in

simulated situations 7 months after the HBB training, but this improvement did not transfer into clinical practice. Another unexpected finding was that learners' self-assessment with high self-confidence actually performed worse when retested. After training, this degree of self-confidence decreased significantly. This can be seen as a benefit of simulation based training according to the authors. However, their findings should be carefully considered, as these findings might have been influenced by high staff turnover as well as the number of deliveries had been increasing, without corresponding increases in staff. Also, their study was small in sample size and birth attendants were unfamiliar with simulation based testing.

As seen from the above discussion, the majority of birth attendants faced difficulties on clinical performance on ventilation, even after HBB training. This is of great concern as it is one of the key competencies required for neonatal resuscitation. However, these findings are also echoed in other studies (Enweronu-Laryea et al., 2009; Harvey et al., 2007). Neonatal resuscitation of a wet, non-breathing baby remains among the greatest challenge to birth attendants, particular in a low-resource settings, where many work alone in a hectic environment, and many might not have had sufficient opportunity to manage these critically ill children. Intuitively one would suggest that simulation-based training with HBB curriculum might offer direct positive impact on the performance on newborn resuscitation. Indeed, several studies have demonstrated the value of simulation-based clinical training in neonatal resuscitation, both in high-income and low-resource settings (Kaczorowski et al., 1998; Carlo et al., 2009; Jabir et al., 1009; Bookman et al., 2010; Rovamo et al., 2011). At the same time, there is a broader concern for the maintaining of skills (Kaczorowski et al., 1998; Carlo et al., 2009; Bookman et al., 2010). One-day HBB training may improve long term performance in simulated setting, but it is insufficient to translate those skills into clinical practice (Ersdal et al., 2013). The provision of refresher trainings and perhaps a focus on time management strategies as well as an emphasis on routine assessment of provider knowledge,

competency and skill maintenance are likely to be of importance (Lee et al., 2011). In fact, the HBB guideline will not help a single newborn unless they are translated into clinical practice. To improve performance and maintenance of knowledge and skills are the provision of retraining sessions or refresher courses scheduled at regular intervals recommended by some authors (Skidmore & Urguhart, 2001; Hamilton 2005). Additional point to make is whether the facilitators were sufficient qualified to "train-the-trainers". Findings of Singhal et al. (2012), imply that the facilitators needed to be better equipped to instruct learners.

Lastly, there are at least two large on-going trials whose results when available could be included in an update of this review that might give us more up-to date evidence on the impact of HBB on both neonatal and educational outcomes. Also, the results published in one of the excluded conference papers by (Mduma et al., 2013), disclose findings suggesting that implementing low-dose high frequency HBB training in the delivery room significantly improved performance and decreased neonatal mortality. What is more is that both on-going studies (KC et al., 2012) and (Bang et al., 2014) will include a qualitative part which documents health seeking behaviour from the mother/families that might give valuable new perspectives. The role of qualitative evidence is emerging in systematic reviews (Hannes et al., 2013). In one of these on-going studies (Bang et al., 2014), the HBB is included besides WHO Essential Newborn Care (ENC) training, which might be valuable as the HBB curriculum is designed to be part of a comprehensive neonatal care commitment of ENC consisting of universal precautions, routine neonatal care, resuscitation, keeping the baby warm, early and exclusive breastfeeding if possible, kangaroo care and small infant management as well as danger signs and recognition of illness.

AUTHORS'CONCLUSIONS

The HBB in-service training appears to have the potential to reduce neonatal mortality in low resource settings, and here is also some evidence of educational benefit for those who receive the training.

Implication for practice

Basic newborn care and neonatal resuscitation continues to remain a rarity in many low-resource countries, especially for the world's 60 million home births, which is in sharp contrast to the careful attention paid to the neonates born in high-income countries. The progress in scaling up quality care is slow and inequality is high, especially for skilled clinical interventions such as neonatal resuscitation. Situations may vary between and within countries, and there is no single solution for saving lives of newborn babies.

This systematic review offers encouraging evidence on the value of HBB training of birth attendants' in reducing the incidence of hypoxia-related early neonatal mortality in low resource settings. The training might help birth attendants to identify some of those severely depressed newborns as viable newborns rather than as stillbirths and give them simple neonatal resuscitation measures. These actions may change the lives of many parents and their newborn babies living in these high burden areas with a fragile health care system. Given the rapid rise in health care costs it has become crucial to focus on developing cost-effective and affordable ways to implement additional training for health care workers. Although single day courses may seem cost-effective at first glance, if the learners lack the necessary time needed to attain the new knowledge and practical skills, such as face-mask ventilation, the benefit of the course would be clearly limited. However, due to the complete lack of economic evaluation of the HBB training in the included studies, it is impossible to draw any conclusions on the cost-effectiveness of HBB neonatal resuscitation education in these

settings. We need to find ways to identify and reach the most vulnerable and to adopt equity focused approach to the implementation of policies regarding essential newborn care in the high burden areas of the world. There needs to be a commitment to provide refresher and periodic training, as well as monitoring practices to ensure high quality newborn care in their health facilities.

Implication for further research

Global health interventions require robust evaluation. Although most neonatal deaths occur in low-resource settings, most of the research addressing neonatal resuscitating has been done in high-income countries. There is a clear need for research to determine how best to incorporate neonatal resuscitation training into sustainable programs and provide this at a wider scale. Indeed, one important research question is what kind of refresher training and supervision systems that are needed for birth attendants to retain their skills. This is especially important in the community settings where supervision systems are weak, where most semi-skilled birth attendants are working and most birth take place. Furthermore, studies are also needed on the cost-effectiveness analysis of neonatal resuscitation programs, as documenting the potential cost of implementation and continuation of training would be of importance.

Also, the role of video recording for in-service training is unclear. A possible solution to deal with some of the ethical issues regarding the need for high quality RCTs of effectiveness of neonatal resuscitation courses could be to perform a RCT using simulated training and assessment. Further, there is also a need to consider the quality of care provided to newborns beyond consideration of survival alone. Many questions remain unanswered: How should a newborn that has been resuscitated be cared for, such as thermal management of the asphyxiated infant and management of convulsions? The growth and cognitive development of newborns after being resuscitated is also an important area of research. How do they

develop and function later in life? What is the burden of resuscitation to the parents and the society?

We know that neonatal survival is dependent on a whole range of interventions that cannot easily be separated. Additional research into non-facility determinants of health service quality such as health policy, supply distribution, community acceptability and equity of care may also prove to be beneficial. The findings from this review point towards the need to continue to strengthen the body of evidence, including both quantitative and qualitative methods, to ensure they can provide comprehensive insights into the effects of neonatal resuscitation training of birth attendants in this context.

ACKNOWLEDGEMENTS

Last, but not least, I would like to thanks my wonderful friends and family, particular my husband Vidar, for all the love and support they have given me during this time. Thank you all.

A P P E N D I X E S

Appendix 1. Search strategy in electronic databases 25.03.2014

PubMed

Search	Add to builder	Query	Items found	Time
#11	Add	Search (Helping Babies Breathe) OR ((((developing country OR low-resource setting))) AND (((((inservice training OR education)) AND (nurse OR midwife OR physician OR traditional birth attendant OR village health worker))) AND ((((newborn OR infant OR neonatal))) AND (resuscitation OR emergency care OR life support OR birth asphyxia OR hypoxia))))	125	08:28:13
#10	Add	Search (Helping Babies Breathe) AND ((((developing country OR low-resource setting))) AND (((((inservice training OR education)) AND (nurse OR midwife OR physician OR traditional birth attendant OR village health worker))) AND ((((newborn OR infant OR neonatal))) AND (resuscitation OR emergency care OR life support OR birth asphyxia OR hypoxia))))	3	08:23:24
#9	Add	Search Helping Babies Breathe	13	08:23:11
#8	Add	Search (((developing country OR low-resource setting))) AND (((((inservice training OR education)) AND (nurse OR midwife OR physician OR traditional birth attendant OR village health worker))) AND ((((newborn OR infant OR neonatal))) AND (resuscitation OR emergency care OR life support OR birth asphyxia OR hypoxia)))	115	08:22:52
#7	Add	Search (developing country OR low-resource setting)	103225	08:22:40
#6	Add	Search ((((inservice training OR education)) AND (nurse OR midwife OR physician OR traditional birth attendant OR village health worker))) AND ((((newborn OR infant OR neonatal))) AND (resuscitation OR emergency care OR life support OR birth asphyxia OR hypoxia))	1094	08:22:13
#5	Add	Search ((inservice training OR education)) AND (nurse OR midwife OR physician OR traditional birth attendant OR village health worker)	179088	08:21:28
#4	Add	Search (((newborn OR infant OR neonatal))) AND (resuscitation OR emergency care OR life support OR birth asphyxia OR hypoxia)	82010	08:20:19
#3	Add	Search resuscitation OR emergency care OR life support OR birth asphyxia OR hypoxia	787935	08:19:52
#1	Add	Search (newborn OR infant OR neonatal)	1128587	08:18:39

CINAHL

	Search ID#	Search Terms	Search Options	Actions
☐	S9	S7 OR S8	Search modes - Boolean/Phrase	View Results (176) View Details Edit
☐	S8	TX helping babies breathe	Search modes - Boolean/Phrase	View Results (5) View Details Edit
☐	S7	S3 AND S6	Search modes - Boolean/Phrase	View Results (172) View Details Edit
☐	S6	S4 AND S5	Search modes - Boolean/Phrase	View Results (83,877) View Details Edit
☐	S5	TX (nurse OR traditional birth attendant OR village health worker) OR TX midwives OR TX physician	Search modes - Boolean/Phrase	View Results (355,924) View Details Edit
☐	S4	TX in-service training OR TX education	Search modes - Boolean/Phrase	View Results (423,661) View Details Edit
☐	S3	S1 AND S2	Search modes - Boolean/Phrase	View Results (3,368) View Details Edit
☐	S2	TX (resuscitation OR emercency care OR life support) OR TX birth asphyxia OR TX hypoxia	Search modes - Boolean/Phrase	View Results (23,031) View Details Edit
☐	S1	TX newborn OR infant OR neonatal	Search modes - Boolean/Phrase	View Results (149,318) View Details Edit

EMBASE

	# ▲	Searches	Results	Search Type	Actions
☐	1	(newborn or infant or neonatal).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	980699	Advanced	Display / Delete / More ≫
☐	2	(resuscitation or emergency care or life support or birth asphyxia or hypoxia).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	236768	Advanced	Display / Delete / Save / More ≫
☐	3	1 and 2	29449	Advanced	Display / More ≫
☐	4	(in-service training or education).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	831973	Advanced	Display / Delete / More ≫
☐	5	(nurse or midwife or Physician or Physician or traditional brith attendant or village health worker).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	525621	Advanced	Display / Delete / Save / More ≫
☐	6	4 and 5	115501	Advanced	Display / More ≫
☐	7	3 and 6	224	Advanced	Display / More ≫
☐	8	helping babies breathe.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	15	Advanced	Display / Delete / More ≫
☐	9	7 or 8	237	Advanced	Display / More ≫

The Cochrane Library

		#			Results
⊖	⊕	#1	newborn or Infant or neonatal:ti,ab,kw (Word variations have been searched)	Ⓢ	38027
⊖ Edit	⊕	#2	resuscitation or emergency care or life support		39011
⊖ Edit	⊕	#3	birth asphyxia or hypoxia		2526
⊖ Edit	⊕	#4	#3 or #2		40977
⊖ Edit	⊕	#5	#4 and #1		3766
⊖ Edit	⊕	#6	in-service training or education		34099
⊖ Edit	⊕	#7	Nurse or midwife or physician or traditional birth attendant or village health worker		43894
⊖ Edit	⊕	#8	#6 and #7		9005
⊖ Edit	⊕	#9	#5 and #8		269
⊖ Edit	⊕	#10	developing country or low-resource setting		7960
⊖ Edit	⊕	#11	#9 and #10		132
⊖ Edit	⊕	#12	"helping babies breathe"		1
⊖	⊕	#13	#11 or #12		133

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Appendix 2 Characteristics of included and excluded studies

Characteristics of included studies [Ersdal et al., 2013]	
Methods	Observational study. Before (September 2009), HBB training 1-day (April 2010) and after (November 2010) study. Tanzania. Rural environment. Two simulation scenarios "routine care" and "neonatal resuscitation" were performed by 39 participant before -09 and 27 participants after -10 the HBB training. Two independent raters scored the videotaped scenarios. Observational data on neonatal management before (2745) and after (3116) the HBB training was collected in the delivery room by observing all births at the hospital. No power calculation
Participants	Healthcare professionals, skilled; midwife, anaesthetic nurse, operating nurse or student nurse and semi-skilled, ward-assistance. No significant differences between the 2 cohort
Interventions	HBB training, 1-day training course. Simulation observation in "neonatal care" and "neonatal resuscitation" in baseline, and 7 months after the 1-day HBB course.
Outcomes	Performance of " routine care" simulation and "neonatal resuscitation" simulation before and after HBB training and observed performance of stimulation, suction and face-mask ventilation of newborns in the delivery-room in the study period
Notes	Ethical approval is ok. Bias of the study design, Before and after study, confounding factors, such as high staff turnover, increased deliveries, without increasing staff- declining quality of performance under stress. The main author received financial support from Lærdal Foundation for Acute Medicine.
Risk of bias	

Item	Author's judgement	Description
Random sequence generation (selection bias)	High risk	Not applicable/non-random approach.
Allocation concealment (selection bias)	High risk	Not applicable/non-random approach
Blinding of participants and personnel (detection bias)?	High risk	Not applicable/non-random approach
Blinding of outcome assessment (attrition bias)	Low risk	Two "independent "observer scored the videotaped scenarios
Incomplete outcome data (attrition bias)	Unclear risk	Small sample size. Only 13 of the "true "participants were re-tested, but included new participants which had been trained in HBB
Selective reporting (reporting bias)	Low risk	Study appears to be free from selective reporting
Other bias	Unclear risk	Difficult to control the confounding factors, such as high staff turnover, increased deliveries, without increasing staff- declining quality of performance under difficult working condition?. The main author received financial support from Lærdal Foundation for Acute Medicine.

Characteristics of included studies [Goudar et al., 2013]		
Methods	Observational study. Before and after study. India. Power analysis done. A priori hypothesis regarding birth outcomes effect or sample size determinations were posed. 2-day workshops for regional trainers, who subsequently educated 599 birth attendants in HBB from rural primary health centres, district and urban hospitals. A total of 4187 birth before and 5411 births after HBB training was analysed	
Participants	Newborns and health care staff working in the delivering room. Note: 90% of the birth attendants who did FMV in both pre and post training periods were doctors, not nurses and midwives who generally work in the delivery room	
Interventions	Helping Babies Breathe in-service training	
Outcomes	Two types of Clinical outcomes: NMR (death within 28 days) SB. Three types of Educational Outcomes; trainee knowledge MQ test, Bag and Mask skills assessed by a checklist, OSCE assessment A and B	
Notes	Bias of the study design, Before and after study. OK power calculation. Ethics approval.	

Risk of bias

Item	Author's judgement	Description
Random sequence generation (selection bias)	High risk	Not applicable/non-random approach.
Allocation concealment (selection bias)	High risk	Not applicable/non-random approach
Blinding of participants and personnel (detection bias)?	High risk	Not applicable/non-random approach
Blinding of outcome assessment (attrition bias)	Low risk	De-identified clinical outcomes. Educational outcomes such as MCQ test unclear. Other educational outcomes difficult to blind.
Incomplete outcome data (attrition bias)	Low risk	Most data included for, particular for the most important outcomes- such as early NMR and SNB. But for Late NMR (28d days) during the post HBB period, some participants lost to follow-up due to increased use of study facilities by women not included in the Belgaum registry, as the MoH introduced a cash-incentive scheme to augment hospital delivery.
Selective reporting (reporting bias)	Low risk	Study appears to be free from selective reporting
Other bias	Unclear risk	Funded by; AAP, Lærdal Foundation for Acute Medicine, Latter-Day Saints Charities. Other confounders regarding to late NMR, such as breastfeeding, treatment of infections, keeping the baby warm to mention a few, is not considered.

Characteristics of included studies [Hoban et al., 2013]		
Methods	Observational study. Before and after study. Ethiopia. 5 sites for post. test result. Only 4 sites included for knowledge transfer. Remote areas	
Participants	Trainers: physicians and public health staff with HBB training from the Ethiopian MoH, AAP and NGO partners from Africa, the USA and Europa. Skilled and semi-skilled? healthcare personnel,42% nurses or midwives, 35% Physicians and 18% public health officers 5 % unknown. 69 participants in knowledge transfer. 111 total for BMV testing and qualitative analyses.	
Interventions	HBB training, 2 days training of lectures and skill practices	
Outcomes	Two types of Educational Outcomes; trainee knowledge MQ test, FMV skills assessed by a checklist. + training feedback.	

Notes	Bias of the study design, Before and after study. Ethics approval. No power calculation.	

Risk of bias

Item	Author's judgement	Description
Random sequence generation (selection bias)	High risk	Not applicable/non-random approach.
Allocation concealment (selection bias)	High risk	Not applicable/non-random approach. Selected by the MoH according to local needs.
Blinding of participants and personnel (detection bias)?	High risk	Not applicable/non-random approach
Blinding of outcome assessment (attrition bias)	High risk	Nothing mention in the paper about the blinding of outcome data or the assessor blind to the result of test.
Incomplete outcome data (attrition bias)	Low risk	Almost all outcome accounted for, very few lost to follow-up; 1-3 persons
Selective reporting (reporting bias)	Low risk	Study appears to be free from selective reporting
Other bias	Low risk	Unfunded project by the authors based on results of a funded training course. The funding sponsors of HBB Ethiopia did not contribute to the study design, analysis or interpretation of data. Lærdal Foundation funded one author with travel expenses to Ethiopia. Language Bias. Limited by translation of key messages.

Characteristics of included studies [Msemo et al., 2013]	
Methods	Observational study. Before and after study. Implemented at 8 hospitals in Tanzania. Trained 40 Master instructors, who then delivered the program to regional instructors who then again trained health providers in the smaller facility within each of the 8 districts. Unsure number of total birth attendants, but 8124 babies before and 78500 after. 86624 total of newborns.
Participants	Newborns and health care staff working in the delivering room. Major emphasis on grass-roots birth attendants/ midwives who practice in rural facilities, rather than on hospital based doctors.
Interventions	Helping Babies Breathe in-service training for 1-day. Strategies of refresher courses and require all birth attendants to demonstrate resuscitation skills with a simulator before starting a shift.
Outcomes	Two types of Clinical outcomes: Early NMR (within 24 hours) and Fresh SB. No educational outcome
Notes	Bias of the study design, Before and after study. Objectives: would HBB training enhance the skills of birth attendants including application of face-mask ventilation?. Ok power calculation. Ethics approval (does not report the conventional 28 day NMR, perhaps because of the difficulties involved with obtaining reliable follow-up in this population

Risk of bias

Item	Author's judgement	Description
Random sequence generation (selection bias)	High risk	Not applicable/non-random approach.
Allocation concealment (selection bias)	High risk	Not applicable/non-random approach
Blinding of participants and personnel (detection bias)?	High risk	Not applicable/non-random approach

Blinding of outcome assessment (attrition bias)	Low risk	Data is entered into a central repository in the MoH in Dar es Salaam
Incomplete outcome data (attrition bias)	Low risk	All data included for.
Selective reporting (reporting bias)	Low risk	Study appears to be free from selective reporting
Other bias	Low risk	Large difference in baseline data. However the data is representative and remained unchanged for many years according to the authors. Funded by the industry of HBB; the AAP and the Lærdal Foundation for Acute Medicine

Characteristics of included studies [Musafili et al., 2013]	
Methods	Observational Study. Before and after study. Rwanda. Aim: evaluated the immediate and long term effect of HBB training
Participants	Healthcare personnel: All skilled, nurses, midwives, nurse anaesthetists, doctors
Interventions	HBB training- 8 classroom hours and given in 1-day.
Outcomes	Educational outcomes of Knowledge (MCQ test) and practical skills (OSCE B)
Notes	Bias of the study design, Before and after study. No power calculation. Ethics approval.

Risk of bias

Item	Author's judgement	Description
Random sequence generation (selection bias)	High risk	Not applicable/non-random approach.
Allocation concealment (selection bias)	High risk	Not applicable/non-random approach
Blinding of participants and personnel (detection bias)?	High risk	Not applicable/non-random approach
Blinding of outcome assessment (attrition bias)	Low risk	Same observer re-evaluated participants after the course 3 months later (influenced by earlier results) To minimize this potential bias, all questionnaires were coded and none of the examiners was aware of previous scores for the same participants.
Incomplete outcome data (attrition bias)	Low risk	All outcomes accounted for. However, did not use OSCE B for the pre test (make sense, too difficult without formal training
Selective reporting (reporting bias)	Low risk	Study appears to be free from selective reporting
Other bias	Low risk	Two facilitators had colleagues among the trainees; the risk of subjectivity during the evaluation was minimized by the precise nature of the question. Incapacity to verify sources of knowledge or skills the participant may have acquired post training, and the health care workers who changed workplaces within the hospital between training and follow-up. Language bias: translation of HBB curriculum to French or Kinyarwanda would have been eliminated language bias, but they did support verbal translation if needed. Same trainers were also examiners conducted course from beginning to end- this may have averted any observational bias that could have stemmed from changing examiners. Funded by the (Sida)

Characteristics of included studies [Singhal et al., 2012]	
Methods	Pilot Study organised by multiple stakeholders and a Delphi panel of expert in global health and neonatal resuscitation. Observational study. Before and after. Kenya and Pakistan. Aim: evaluate the immediate effect of HBB training on knowledge and skills and data on facilitator and learner perceptions. Included were 31 facilitators, and a total of 102 learners.
Participants	Healthcare personnel: Kenya: All skilled, paediatricians, obstetricians, medical officers, nurses, midwives. Pakistan: Skilled and Semi-skilled: paediatrician, medical officers, nurses, lady health workers and lady health visitors.
Interventions	HBB training of health care staff. 1-day course (7 hours total, 6 h instructional and 1 hour post-testing for learners.
Outcomes	Educational outcomes: 1) Analysed facilitator and learner perceptions, 2) examined skill performance, and assessed the 3) quality of instruments used for learner evaluation as part of the formative evaluation of the HBB educational program. MCQ test, Bag and mask skill performance, OSCE A and B
Notes	Bias of the study design, Before and after study. Data for each site were analysed independently. None power calculation available in text. Ethics approval in all sites.

Risk of bias

Item	Author's judgement	Description
Random sequence generation (selection bias)	High risk	Not applicable/non-random approach
Allocation concealment (selection bias)	High risk	Not applicable/non-random approach
Blinding of participants and personnel (detection bias)?	High risk	Not applicable/non-random approach
Blinding of outcome assessment (attrition bias)	High risk	Nothing mention in the paper about the blinding of outcome data or the assessor blind to the result of pre-test.
Incomplete outcome data (attrition bias)	Low risk	All outcome accounted for, none- to very few lost to follow-up
Selective reporting (reporting bias)	Low risk	Study appears to be free from selective reporting
Other bias	Unclear risk	Small difference at site; in Kenya, the investigators trained 4 master trainers. In Pakistan, the investigators did not train master trainers. They themselves trained the facilitators. Funded by HBB industry: Lærdal Foundation for Acute Medicine, Latter-day Saint Charities, and USAID. AAP provided grant to div Universities. Language bias. Confliction with previous training or practice. Unfamiliar with testing format.

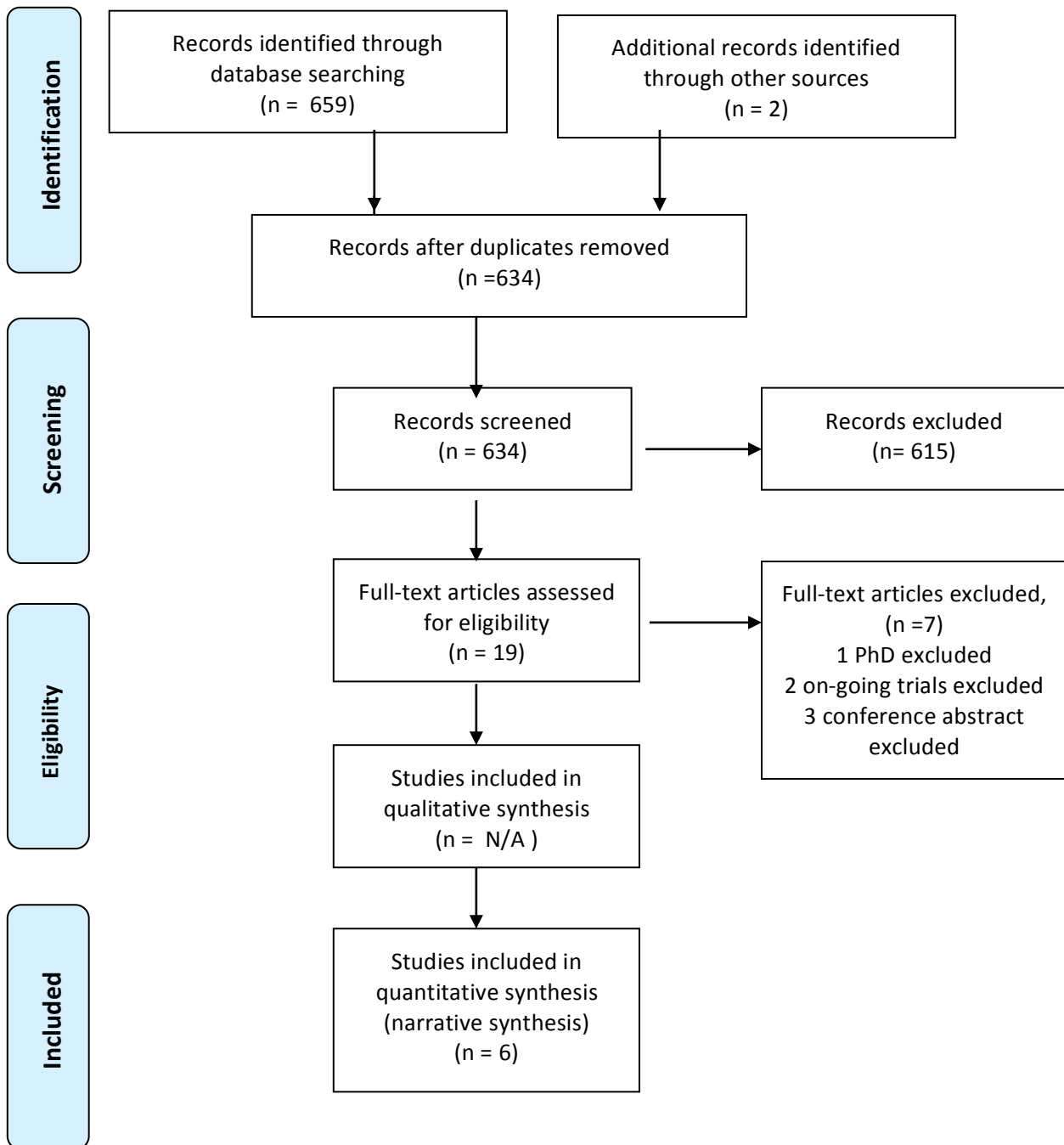| **Characteristics of excluded studies** |
|---|
| [Bookman et al., 2010] trained midwives in Ghana in a modified version from American Academy of Paediatrics Neonatal Resuscitation Program (NRP) to assess the short and long-terms educational effects of in service training was excluded as the training were out of the scope of HBB, as it included chest compressions, thought, no medications. |
| [Gill et al., 2011] Zambia. Prospective, cluster randomised and controlled effectiveness study in Zambia trained traditional birth attendants on a modified version of the American Academy of Paediatrics and American Heart Association, quite similar to the HBB curriculum was excluded due to delivering two interventions, (basic neonatal resuscitation and oral antibiotics to suspected neonates with sepsis with referral). |
| [Hole et al., 2012] Malawi. Before and after study of trainee's attitude, and skills. An observational longitudinal study of secondary data assessing neonatal mortality. Not HBB guideline. Based upon NRP guideline and included chest compressions |
| [Ersdal 2012] PhD thesis. "Appropriate intervention to reduce perinatal mortality and morbidity in low-resourced settings"

 This PhD consist of three studies about "birth asphyxia"; i) (Ersdal, Mduma, Svensen, Sundby, Perlman 2012; ii) Ersdal, Mduma, Svensen, Perlman, 2012; iii) Ersdal, Mduma, Svensen, Perlman 2012). However, none of these studies satisfied our inclusion criteria. Though, one of the thesis supplementary Appendix had preliminary data from the study of (Msemo et al., 2013), this study is included in our review with its full dataset, also identified in the electronic search. |
| [Kim et al., 2013] Assessing the capacity for newborn resuscitation and factors associated with providers' knowledge and skills: a cross-sectional study in Afghanistan.

 This study assessed the capacity for health care workers to perform newborn resuscitation at facilities offering comprehensive emergency obstetric and newborn care. This study was excluded, as the neonatal resuscitation guideline is not outlined. Also, is a "group" intervention, not a single intervention of HBB. The neonatal resuscitation guideline seems very similar to HBB, but not stated. |
| **Characteristics of on-going studies** |
| [KC et al., 2012 On-going study]. Nepal. Implementing a simplified neonatal resuscitation protocol- Helping Babies Breathe at birth (HBB)- at a tertiary level hospital in Nepal for an increased perinatal survival.

 Before-After intervention study; evaluate changes in intrapartum-related mortality and knowledge, attitudes and practices of birth attendants. Baseline data collection period: 9630 deliveries, showed that 41% of the breathing babies received some form of resuscitation (such as stimulation, suction, oxygen). However, none of the non-breathing babies received face-mask ventilation within 1 minute (Golden Minute). In the first two months of intervention, 33% of infants requiring face-mask ventilation received it within the Golden Minute. |
| [Bang et al., 2014 On-going study]. India and Kenya. Global Network for Women's and Children's Health research. Does implementation of Helping Babies Breathe (HBB) save lives?

 Including approximately 30 000 newborns .The objective of the study is to find out the impact of HBB training, alongside the Essential Newborn Care curricula. Does this training have an impact on perinatal mortality (fresh stillbirths and early neonatal deaths), among births of ≥1500g. Secondary goal: retention of resuscitation knowledge and skills, number of resuscitation, health seeking behaviour, facility deliveries as well as very early newborn death (24 hours) |
| [Ersdal et al., 2013 conference abstract]. Helping Babies Breathe (HBB) Training Is Associated with Reduced Early Neonatal Mortality (ENM); This Positive Benefit Is Reduced Due to Late Deaths (LD) .

 In their study HBB implementation was associated with a progressive decrease in ENM with time. Late deaths were common due to birth asphyxia and related complications in term and preterm infants and other morbidities. Premature babies were particular vulnerable, perhaps precipitated by hypothermia. They suggest that overall mortality was comparable between control groups. They further suggest that in order to continue the success of HBB, targeted strategies i.e. TEMP control and basic monitoring devices to detect cardio-respiratory instability may decrease late neonatal mortality rate in all infants but especially in the vulnerable premature infants. |

[Mduma et al., 2013 conference abstract]. Low-Dose High Frequency (LDHF) Helping Babies Breathe (HBB) Training Reduces Early Neonatal Mortality (ENM) within 24 Hours in a Rural African Hospital.

The objective was to document whether implementation of LDHF HBB frequent re-training simulation sessions would enhance performance of basic neonatal resuscitation in the delivery room, and thereby, reducing the incidence of ENM (within 24 hours) and the number of Fresh Stillbirths (FSB). These data reveal that LDHF simulator training and local mentoring has changed clinical practice among birth attendants in the clinic and enhanced neonatal resuscitation in the delivery room. The statistical significant decrease in ENM is likely to reflect the increase use of immediate stimulation of newborns with induction of breathing amount babies in primary apnoea.

[Haworth and Crehan, 2013. conferences abstract]. Multidisciplinary newborn resuscitation training in Ethiopia and the RCPCH VSO Fellowship Scheme.

In total number of 124 health care staff was trained in neonatal resuscitation with teaching materials adapted from Ethiopian WHO guidelines, NLS guidelines from ALSG and HBB. Pre and post course tests, and health care workers evaluative feedback forms measured the course success.

Appendix 3 PRISMA Flow Diagram

Identification	Records identified through database searching (n = 659)	Additional records identified through other sources (n = 2)
	Records after duplicates removed (n =634)	
Screening	Records screened (n = 634)	Records excluded (n= 615)
Eligibility	Full-text articles assessed for eligibility (n = 19)	Full-text articles excluded, (n =7) 1 PhD excluded 2 on-going trials excluded 3 conference abstract excluded
	Studies included in qualitative synthesis (n = N/A)	
Included	Studies included in quantitative synthesis (narrative synthesis) (n = 6)	

Appendix 4 PRISMA Checklist

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

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

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