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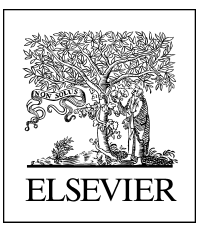

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Intrapartum-Related Deaths: Evidence for Action

Organizing Guest Editors:

Joy E. Lawn
Gary L. Darmstadt

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EDITORIAL

Reducing intrapartum stillbirths and intrapartum-related neonatal deaths

Acute intrapartum emergencies and poor fetal oxygenation commonly contribute to stillbirth and neonatal deaths, as well as to long-term neurologic disabilities including mental impairment and cerebral palsy [1–5]. Much of modern obstetric care in high- and many middle-income countries has been directed at reducing both antepartum and intrapartum fetal oxygen deprivation. These efforts have included the identification of women at risk, such as those women with pre-eclampsia, sickle cell disease and diabetes, and those with compromised fetuses at risk in the absence of maternal complications, such as those with growth restriction or oligohydramnios. Identification of these conditions in the antepartum period is usually followed by various types of prenatal screening to detect those fetuses at even higher risk for poor oxygenation. The use of ultrasound for monitoring amniotic fluid levels and fetal growth, electronic fetal heart rate monitoring, fetal movement counting, and Doppler blood flow measurements have all contributed to better identification of at-risk pregnancies [6–8]. At least as important is skilled care during labor, including fetal heart rate monitoring to identify those fetuses in jeopardy. Rapid instrumental birth or cesarean delivery results in substantial mortality reductions during labor and in the early neonatal period [9]. Thus, by and large, high-income countries have successfully reduced intrapartum fetal organ damage and the associated adverse pregnancy outcomes, including intrapartum stillbirth and intrapartum-related neonatal mortality [5].

In low- and middle-income countries, especially those without a well-functioning healthcare system, intrapartum fetal organ damage due to poor oxygenation remains a very substantial problem [5,10–13]. In these areas, because of chronic nutritional deprivation, increased exposure to environmental pollutants, and the presence of many poorly or untreated medical conditions, the risk of fetal damage during labor is substantially increased compared with that seen in high-income countries. As chronically malnourished women tend to have small pelvises, they are at increased risk of suffering long and obstructed labors, which also substantially increases the risk of the fetus or neonate suffering an intrapartum injury. Lack of access to appropriate obstetric care, especially during labor, compounds the risk of adverse fetal outcomes such as death or disability.

In this issue, an international team of over 30 distinguished investigators led by Drs Joy Lawn (Saving Newborn Lives/Save the Children), Gary Darmstadt (Gates Foundation), and Anne CC Lee (Johns Hopkins University) have presented an overview of intrapartum-related complications and their sequelae, and have undertaken a thorough evaluation of interventions that might potentially reduce their numbers [14–20]. This work—presented as a series of 7 papers in this Supplement to the *International Journal of Gynecology and Obstetrics*—originally began as an expert meeting on "birth asphyxia" held in Cape Town in 2002 and has been substantially updated and expanded. The work was funded by the Bill & Melinda Gates Foundation through the Saving Newborn Lives program of Save the Children because of the desire of both organizations to define more clearly the evidence base for programs and interventions to reduce intrapartum stillbirths and intrapartum-related neonatal deaths. The authors of these papers have provided a huge service to those interested in improving pregnancy outcomes in low- and middle-income countries (Fig. 1).

Interestingly, a major point in the first paper is a request for a change in terminology [14]. The authors argue that "asphyxia" is an imprecise term that is defined differently by many of its users, which does not help us much in either defining a suitable prevention strategy or choosing the appropriate timing for any proposed intervention. Instead, the authors propose the use of terms that describe the timing of the insult and the specific adverse outcome. We agree with this proposal and have therefore titled this commentary "Reducing intrapartum stillbirths and intrapartum-related neonatal deaths," and for the most part have tried to avoid the word "asphyxia."

While initially aimed at reducing intrapartum-related adverse outcomes, a careful reading of these papers provides a roadmap to reducing nearly all adverse pregnancy outcomes in low- and middle-income countries, since interventions aimed at reducing this complication should also have a substantial impact on other adverse perinatal and indeed maternal outcomes as well. We agree with the authors that the consequences of intrapartum fetal organ damage due to poor oxygenation are often difficult to distinguish from those associated with other perinatal conditions, including infection and trauma. However, differentiating the specific outcomes associated with each condition may not be that important. In fact, these conditions often co-occur, and when they present

Fig. 1. Prenatal care in rural Ethiopia. Photo reprinted with permission granted by Save the Children/Ethiopia 2008.

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together, substantially increase the likelihood of fetal/neonatal death or disability. In addition, intrapartum fetal organ damage due to poor oxygenation is the final common pathway for many stillbirths and early neonatal deaths, whether the precipitating event is hemorrhage associated with placental abruption or previa, obstructed labor, an umbilical cord complication, or pre-eclampsia/eclampsia. Interventions directed at poor fetal oxygenation, especially those involving system building, training, transportation and audits are likely to affect multiple conditions and outcomes. While not specifically evaluated in trials, the package known collectively as Emergency Obstetric Care, which focuses on timely cesarean delivery, along with other interventions to reduce maternal death and morbidity, should have an important impact on reducing intrapartum fetal organ damage due to poor oxygenation, and stillbirth and neonatal mortality as well.

Much of this series has focused on improving the functioning of the healthcare system. The reviews examining components of the healthcare system, with a careful examination of the different types of health providers working in various types of facilities and their training needs, are an especially thoughtful contribution [20]. Their focus on how to maximize the contribution of each type of provider is especially useful. The value of training the lay community and traditional birth attendants to recognize problems, stabilize women in jeopardy, and transfer them appropriately has been doubted by many. In this series, the authors put this issue into the proper context and provide evidence for benefit of identifying roles for community cadres and linking them to the healthcare system [18]. We have been especially impressed with the potential of community mobilization around issues related to birth planning and childbirth to improve various perinatal outcomes, particularly through increasing the proportion of women coming for facility birth [21]. We appreciate the authors' efforts in providing the evidence base for various community mobilization efforts to improve the system of pregnancy-related care. As the authors state, there is encouraging evidence that mobilizing communities to address pregnancy-related care is an important step in reducing the large burden associated with intrapartum complications [17].

The authors also discuss the use of emergency response teams and emergency drills [15]. Since an important contribution to the adverse outcomes associated with intrapartum asphyxia in low-income countries has been conceptualized as a series of delays—delay in recognizing the problem placing the pregnancy at risk, delay in arranging transportation to a medical facility, and delay in providing appropriate care at the facility—the emphasis throughout the papers on strategies to reduce these delays is important [22]. The thoughtful exploration of different methods for enhancing the availability of transportation to a facility for women in jeopardy was of particular importance in conceptualizing the creation of a medical care system for community-based deliveries.

The third delay, quality of care at facilities, is addressed in the paper reviewing the evidence for the content of neonatal resuscitation, provider training and competency, and equipment and supplies specifically for resource-constrained settings [16]. The authors estimate that basic neonatal resuscitation may avert 30% of intrapartum-related neonatal deaths in facility settings and emphasize that better use of resuscitation in those settings is more easily attainable than for community deliveries; they also provide a useful discussion on methods to improve resuscitation in facility settings. Since few newborns require resuscitation with an endotracheal tube and drugs, and in many cases these babies may not survive without ongoing ventilation, advanced neonatal resuscitation is not recommended as a priority in settings without neonatal intensive care. Currently, 60 million births per year occur outside facilities and the vast majority does not have access to resuscitation. Evidence presented here suggests that neonatal resuscitation may be performed by a range of health workers who already attend deliveries, with significant reductions of intrapartum-related stillbirths and neonatal deaths [23].

In the paper by Pattinson et al. [19], the authors show us that simply conceptualizing or creating an obstetric/neonatal care system is not enough. They make a very strong case that continuous evaluation of adverse outcomes directed toward finding correctable causes of death is an important component of any system of care directed at improving pregnancy outcomes. They emphasize that the effect of perinatal audit depends on the ability to close the audit loop. Without effectively implementing the solutions to the problems identified, audit alone will not improve the quality of care [24].

The major take-home message from this series is that there are 2 million or so intrapartum-related perinatal deaths in low-income countries [14]. The use of certain specific interventions has the potential to substantially reduce this burden as well as to improve a number of other adverse perinatal outcomes. However, we also know that attempts to introduce a single intervention are likely to produce only minimal benefits that are often not sustainable. Conversely, as presented in this series, a thoughtful evaluation of the current obstetric care system and the creation of an integrated system, including the capacity to identify obstetric complications, the ability to stabilize and transfer those women who are in jeopardy, and enhancing the ability of the health facilities to provide emergency obstetric and newborn care, will go a long way to improving perinatal outcomes in many low- and middle-income countries. This series outlines the potential for health systems in any setting to substantially reduce stillbirth and neonatal deaths, as well as maternal mortality, by prioritizing care at the time of birth.

Conflict of interest

The authors have no conflicts of interest to declare.

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Robert L. Goldenberg
Department of Obstetrics and Gynecology, Drexel University, Philadelphia, PA, USA
Corresponding author. Department of Obstetrics/Gynecology, Drexel University College of Medicine, 245 N. 15th Street, 17th Floor, Room 17113, Philadelphia, PA 19102, USA. Tel.: +1 215 762 2014; fax: +1 2157 62 2310.
E-mail address: rgoldenb@drexelmed.edu (R.L. Goldenberg).

Elizabeth M. McClure
Department of Epidemiology, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

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INTRAPARTUM-RELATED DEATHS: EVIDENCE FOR ACTION 1

Two million intrapartum-related stillbirths and neonatal deaths: Where, why, and what can be done?

Joy E. Lawn [a,*], Anne CC Lee [b], Mary Kinney [a], Lynn Sibley [c], Wally A. Carlo [d], Vinod K. Paul [e], Robert Pattinson [f], Gary L. Darmstadt [b,g]

[a] Saving Newborn Lives/Save the Children-USA
[b] Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA
[c] Nell Hodgson Woodruff School of Nursing and Rollins School of Public Health, Emory University, Atlanta, GA, USA
[d] University of Alabama at Birmingham, AL, USA
[e] Department of Pediatrics, All India Institute of Medical Sciences, New Delhi, India
[f] MRC Maternal and Infant Health Care Strategies Research Unit, University of Pretoria, Pretoria, South Africa
[g] Integrated Health Solutions Development, Global Health Program, Bill & Melinda Gates Foundation

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ABSTRACT

Background: Intrapartum-related neonatal deaths ("birth asphyxia") are a leading cause of child mortality globally, outnumbering deaths from malaria. Reduction is crucial to meeting the fourth Millennium Development Goal (MDG), and is intimately linked to intrapartum stillbirths as well as maternal health and MDG 5, yet there is a lack of consensus on what works, especially in weak health systems. *Objective:* To clarify terminology for intrapartum-related outcomes; to describe the intrapartum-related global burden; to present current coverage and trends for care at birth; and to outline aims and methods for this comprehensive 7-paper supplement reviewing strategies to reduce intrapartum-related deaths. *Results:* Birth is a critical time for the mother and fetus with an estimated 1.02 million intrapartum stillbirths, 904 000 intrapartum-related neonatal deaths, and around 42% of the 535 900 maternal deaths each year. Most of the burden (99%) occurs in low- and middle-income countries. Intrapartum-related neonatal mortality rates are 25-fold higher in the lowest income countries and intrapartum stillbirth rates are up to 50-fold higher. Maternal risk factors and delays in accessing care are critical contributors. The rural poor are at particular risk, and also have the lowest coverage of skilled care at birth. Almost 30 000 abstracts were searched and the evidence is evaluated and reported in the 6 subsequent papers. *Conclusion:* Each year the deaths of 2 million babies are linked to complications during birth and the burden is inequitably carried by the poor. Evidence-based strategies are urgently needed to reduce the burden of intrapartum-related deaths particularly in low- and middle-income settings where 60 million women give birth at home.
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1. Introduction

The fourth Millennium Development Goal (MDG) target for child survival is to reduce under-5 child mortality by two-thirds by 2015, with a global target of 32 per 1000 live births [1]. Given that the global neonatal mortality rate (deaths in the first 28 days of life) is 30 per 1000, the burden of deaths in the neonatal period alone approximates the entire MDG 4 target. While postneonatal mortality is being reduced [2], there has been limited progress in reducing the neonatal mortality rate. Hence, neonatal deaths account for an increasing proportion of under-5 mortality—now 42% of under-5 deaths compared with 37% of under-5 deaths in 2000 [1]. In low-income countries over the last decade there has been no measurable reduction in early neonatal mortality (deaths in the first week of life), yet high-income countries continue to make progress, and the gap between the rich and the poor continues to widen (Fig. 1). Therefore, reducing the global total of 3.82 million neonatal deaths [2], and particularly the 3 million who die in the first week of life (the early neonatal period), is crucial to meeting MDG 4. The solutions to reduce neonatal deaths, and especially early neonatal deaths, are intimately linked to maternal health and to provision of effective maternal and neonatal health services. Thus, addressing current global gaps for care at birth is critical to achieving both MDG 4 and MDG 5, for maternal mortality reduction.

Each year, an estimated 904 000 intrapartum-related neonatal deaths (previously termed "birth asphyxia") occur, accounting for approximately one-third of the early neonatal deaths [3,4]. Closely linked are an estimated 1.02 million intrapartum or "fresh" stillbirths; however, stillbirths are not currently recorded in MDG or Global Burden of Disease metrics [5]. While intrapartum-related neonatal deaths account for 9% of all under-5 child mortality, a proportion comparable to malaria, they are

* Corresponding author. Saving Newborn Lives/Save the Children USA, 11 South Way, Cape Town 7405, South Africa.
E-mail address: joylawn@yahoo.co.uk (J.E. Lawn).

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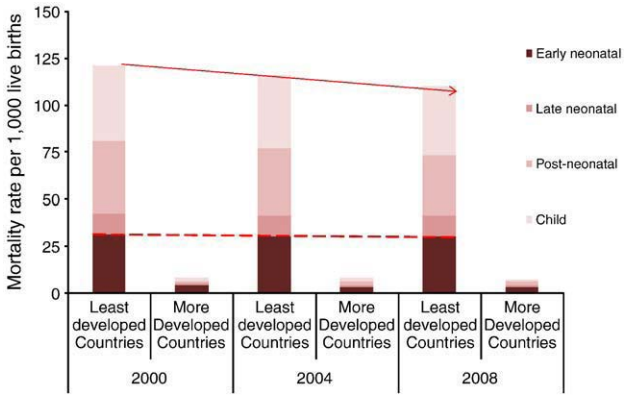

Fig. 1. Time trends in early, late, and postneonatal mortality 2000–2008, highlighting the lack of progress in reducing first-week deaths in low/middle-income countries and the increasing disparity with rich countries. Sources for data: UNICEF databases for child mortality (www.childinfo.org) [89]; WHO estimates for neonatal mortality [2].

not addressed in global health policy and programming. Despite availability of some data, this invisibility is mostly related to a lack of clarity in what we currently know works and vision for what could work in different health systems settings. Information is needed to guide programs, particularly in low-income countries where the majority of deaths due to intrapartum-related injury occur [6]. While there are accepted solutions feasible for scaling-up interventions within weak health systems and at community level for neonatal infections and preterm birth [7,8], the reduction of intrapartum-related neonatal deaths is more challenging. Success is dependent on immediate attention at the time of labor and birth, which in turn requires functional linkages between the community and facility and strengthening of health systems [3,6,9,10].

Progress has been made toward enumerating the global mortality burden of intrapartum-related hypoxic injury [1,3]. However, these clearer definitions of the burden must be linked to interventions and strategies that work. While there have been recent systematic reviews, most notably an extensive series related to the evidence for reducing stillbirths [11], there is a dearth of literature on what works for intrapartum-related deaths and especially what works at scale in low-resource settings.

1.1. Objectives

This paper is the first in a series entitled "Intrapartum-related deaths: Evidence for action." The goal of this series is to call the Maternal, Newborn, and Child Health (MNCH) communities to collective action, laying out the evidence and actions required to strengthen healthcare delivery systems and increase community mobilization to reduce the largely preventable and inexcusable 2 million deaths each year that are related to lack of care at birth.

The objectives of the series are as follows:

1. To summarize data regarding intrapartum-related outcomes for mother and fetus/neonate including:
   - Neonatal mortality outcomes notably intrapartum-related neonatal deaths, early neonatal mortality rate (ENMR), and neonatal mortality rate (NMR).
   - Impairment following intrapartum-related injury such as neonatal encephalopathy.
   - Linked outcomes, including the stillbirth rate (SBR) particularly intrapartum stillbirths, the perinatal mortality rate (PMR), and maternal mortality ratio (MMR).
2. To undertake new analyses to define the variation in terms of burden, coverage gaps/trends, and health system capacity in order to set data-based priorities to more systematically address the global burden of intrapartum-related deaths in varying health system settings.
3. To systematically review the evidence regarding interventions and strategies that avert intrapartum-related adverse outcomes, including:
   - Care at the time of childbirth, and ways to increase care provision, for example through task shifting (Paper 2) [12].
   - Neonatal resuscitation and post-resuscitation management (Paper 3) [10].
   - Improving linkages between community and facility (Paper 4) [13].
   - Community-based interventions (Paper 5) [14].
   - Perinatal audit (Paper 6) [15].
4. To synthesize policy implications for maternal, neonatal, and child health programs and to consider available evidence and experience with regard to various delivery strategies. We underscore differing priorities by varying health system capacity, and provide case studies with a focus on reducing delays, reaching under-served populations, and experience with large-scale programs [16].

In this first paper of the series, we summarize the global epidemiology of intrapartum-related stillbirths and neonatal deaths, including issues surrounding confusion of terminology, to guide programmatic action. We undertake a new analysis to define the variation of burden and identify trends and coverage gaps according to 5 categories of neonatal mortality, which are markers of health system performance for care at birth. In subsequent papers, we build on this analysis to set data-based priorities to more systematically prioritize actions to address the global burden of intrapartum-related deaths based on these 5 NMR categories.

2. The burden of intrapartum-related outcomes

2.1. Challenges to estimation

2.1.1. Lack of consistent definitions and terminology

The terms and definitions used to describe a baby in poor condition at birth have evolved over time, driven both by a greater understanding of pathophysiology and clinical manifestations, but also by increasing litigation in high-income countries. The word "asphyxia" is based on a Greek word meaning "pulseless" and is applied to a syndrome that combines hypoxia (low levels of oxygen) and metabolic acidosis [17]. "Birth asphyxia" is an imprecise term, that was broadly defined by the World Health Organization (WHO) in 1997 as the clinical description of a newborn who "fails to initiate or maintain regular breathing at birth" [18]; this term applies to an important clinical condition—the need for resuscitation—but is not predictive of outcome nor does it imply a particular causation (e.g. intrapartum hypoxia) since the baby may be not breathing for other reasons, for example prematurity. While many clinical markers have been used to indicate possible intrapartum injury, such as Apgar scores, fetal acidosis or fetal distress, these lack specificity and have low positive predictive value for long-term outcomes [19].

Over the last decades, there has been a paradigm shift in the terminology used to describe what has previously been called "birth asphyxia" or "perinatal asphyxia" [3,20–22]. Epidemiologic measurement of intrapartum injury has transitioned from process-based (e.g. obstructed labor, breech presentation) or symptom-based (fetal distress, Apgar scores) indicators to outcome-based measures of mortality and acute morbidity, usually defined through multi-indicator approaches. For example, intrapartum stillbirths weighing over 1000 g, or neonatal encephalopathy, is a syndromic diagnosis of a baby with impaired consciousness and other neurobehavioral symptoms (Table 1). These outcomes have improved correlation with etiology and with long-term prognosis [3].

Three consensus statements addressing the terminology and diagnosis of "birth asphyxia" have been released since 1996 [19,20,22]. All 3 statements have recommended that terms such as "birth asphyxia," "perinatal asphyxia," "fetal distress," "hypoxic-ischemic encephalopathy," or "post-asphyxial encephalopathy" should not be used unless

Table 1
Terms and definitions: Shifting from "birth asphyxia" to intrapartum stillbirths and intrapartum-related neonatal deaths.

MORTALITY OUTCOMES
• **Early neonatal death:** Death in the first 7 days of life.
• **Fetal death:** A baby born with no signs of life after 22 weeks of gestation (equivalent to 500 g). Late fetal death is a baby born dead after 28 weeks of gestation (equivalent to 1000 g) [94].
• **Stillbirth:** This will be taken as equivalent to late fetal death, that is a baby who is born with no signs of life after 28 weeks of gestation (equivalent to 1000 g) [11].
• **Intrapartum-related stillbirth:** A stillborn baby (shows no signs of life at delivery and weighs more than 500 g or is greater than 22 weeks of gestation) with intact skin and no signs of disintegration in utero. The death is assumed to have occurred in the 12 hours before delivery and was most likely due to an intrapartum hypoxic event. Babies with severe congenital abnormalities are not included (based on Wigglesworth's classification) [3].
• **Intrapartum-related neonatal deaths (previously called "birth asphyxia" deaths):** Neonatal deaths of term babies with neonatal encephalopathy (see below) or who cannot be resuscitated (or for whom resuscitation is not available). Where possible, other causes should be excluded such as lethal congenital malformations and preterm birth complications (less than 34 completed weeks of gestation or birth weight <2000 g). Also includes a smaller group of babies who die from birth injury without hypoxic brain injury; for example, organ rupture [3,21,23].
MORBIDITY OUTCOMES
• **Neonatal encephalopathy (NE):** "A disturbance of neurological function in the earliest days of life in the term infant manifested by difficulty initiating and maintaining respiration, depression of tone and reflexes, abnormal level of consciousness and often by seizures" [95,96], which may follow an intrapartum hypoxic insult or be due to another cause. Neonatal encephalopathy is usually separated into 3 grades (mild, moderate, severe) by clinical findings during the first week of life. Virtually all babies with mild NE who are normal at the end of the first week of life will be free of long-term neurological damage. The majority of infants with severe NE will die or manifest severe neurological impairment.
• **Hypoxic ischemic encephalopthy (HIE):** A syndrome of abnormal neurological behavior in the neonate, which is frequently associated with multi-system dysfunction and follows severe injury before or during delivery. There are several systems for categorizing HIE (most commonly into mild, moderate, severe). Most authorities now prefer the term Neonatal Encephalopathy and then specifying if the encephalopathy is associated with intrapartum injury.
• **Disability:** Any restriction or lack (resulting from an impairment) of ability to perform an activity in the manner or within the range considered normal for a human being (International Classification of Functioning, Disability and Health).
• **Cerebral palsy:** A non-progressive disorder of motor function, which may originate during pregnancy, delivery or in the postnatal period.
NEED FOR RESUSCITATION
• **"Non-breathing baby:"** Infant with perinatal respiratory depression after birth that may be due to any of a multitude of causes, including but not restricted to intrapartum hypoxia, respiratory distress syndrome-preterm birth, infection, general anesthesia during labor, meconium, intracranial disease, and neuromuscular disease. Some clinicians use the term depressed baby or "perinatal depression."

Source: References [70,75].

evidence of acute intrapartum causation is available [19,20,22]. In view of this, we use inverted commas for these traditional terms. The consensus statements suggested the term "neonatal deaths associated with acute intrapartum events." There has been slow uptake of this term, partly because it is long and not user-friendly. Since the late 1990s, the Scottish and UK Confidential Enquiry have transitioned from use of the term "birth asphyxia" to use either "death from intrapartum causes" [23] or "intrapartum-related neonatal death." However, there are still a range of terms in use, such as "delivery-related perinatal death" [24]. The terminology used in international health estimates and policy has not changed as yet.

In Table 1 we outline the terminology used in this series and the reasoning for this choice. The term "intrapartum stillbirth" is widely used and defines late fetal death during labor, clinically presenting as "fresh stillbirth." This is a time of death not a cause-of-death, but is commonly assumed to be predominantly associated with intrapartum hypoxic-ischemic injury [25]. For neonatal deaths, previously called "birth asphyxia" or "asphyxia-related neonatal deaths," we use the term "intrapartum-related neonatal death," which refers to liveborn babies who die in the first 28 days of life from neonatal encephalopathy or who die prior to onset of neonatal encephalopathy and have evidence of intrapartum injury (Table 1) [3,4,19,20,22]. The choice of "intrapartum-*related*" is deliberate since the intrapartum association may not necessarily be causal, or may indeed be acute-on-chronic insult for a growth-restricted fetus [26].

We use the descriptive term, "non-breathing baby," to refer to the infant with perinatal respiratory depression at birth that may be due to a variety of causes other than intrapartum hypoxia and acidosis. These conditions, which warrant neonatal resuscitation, include but are not restricted to, intrapartum insults, preterm birth, infection, general anesthesia during labor, meconium aspiration, intracranial disease, and neuromuscular disease.

2.1.2. Lack of comparable cause-specific data

Data regarding intrapartum-related hypoxic events (including intrapartum-related neonatal deaths and intrapartum stillbirths) are lacking in the regions where the burden is the greatest [3,27]. Reliable coverage with vital registration systems is available for less than 3% of all neonatal deaths and is not generalizable to typical low- and middle-income country settings [1]. Verbal autopsy methods (questionnaires used with family members after the death) are the only option for cause-of-death data for the majority of neonatal deaths and stillbirths [28]. There have been advances in case definitions and algorithms for use in verbal autopsy, but full consensus and consistent use is still lacking, particularly for hierarchical attribution if the baby died with signs suggestive of several possible causes-of-death [29–36].

2.1.3. Lack of reliable data on numbers and rates of neonatal deaths

Neonatal deaths that occur in the first hours after birth or in small babies are less likely than other neonatal deaths to be reported [37–39]. Furthermore, the liveborn baby who does not breathe at birth may be misclassified as a stillbirth for several reasons. In the home setting, when the infant is not examined by a professional health worker, the presence of a heart beat may not be assessed to determine whether the non-crying, non-breathing, non-moving infant was liveborn. Interestingly, in a before-and-after comparison of implementation of essential newborn care and neonatal resuscitation training in Zambia, stillbirth rates declined from 23 to 16 stillbirths per 1000 live births (RR 0.63; 95% CI, 0.44–0.88). The authors speculated that the apparent decrease in stillbirths may have resulted from effective resuscitation of liveborn babies who would have been previously misclassified as stillborn [40]. Additionally, recording an infant as stillborn may avoid a sense of blame for the family or birth attendant, or circumvent the need to fill out a death certificate [1].

2.2. The size of the problem

2.2.1. Intrapartum-related neonatal deaths

During the 1990s, estimates of the burden of "birth asphyxia" varied considerably from 400 000 to 1.6 million per year due in large part to the lack of data from low-income countries and varying case definitions and methods of estimation [41–43]. In 2005, the first set of systematic estimates were published for 194 countries using vital registration data, where available, and for countries without national data, using single-cause logistic regression modeling based on study datasets mainly from verbal autopsy data. This exercise resulted in a global estimate of 904 000 intrapartum-related neonatal deaths (range, 0.65–1.17 million) for the year 2000 [3]. In a subsequent exercise with the Child Health Epidemiology Reference Group, the proportionate distribution for 7 cause-of-death in the neonatal period was estimated for 193 countries, using new analysis of vital registration data for the 45 countries with available data. A multi-

cause regression model based on 56 input datasets was applied to estimate numbers for cause-of-death for those countries without representative data [4]. This multi-cause method is now the standard approach for estimation of neonatal cause-of-death used for United Nations estimates [44] as well as for the Global Burden of Disease [45]. Although these methods for estimating the national burden of intrapartum-related neonatal deaths differed, notably as single and multi-cause approaches, the global results from both methods were very similar: 904 000 (range, 650 000–1.17 million) [3] and 910 000 (range, 600 000–1.08 million) [4].

Although there is wide uncertainty around this data, it is clear that the number of deaths is huge. Intrapartum-related deaths are 1 of the top 5 causes of child deaths and account for more deaths each year than malaria or conditions prevented by immunizations, yet receive much less attention and funding [46].

The variation in cause-specific mortality rate according to category of NMR is shown in Fig. 2. In the lowest category (Categories 1), rates of intrapartum-related neonatal deaths are less than 0.5 per 1000 live births, whereas in the highest category (NMR>45), rates of intrapartum-related neonatal deaths are nearly 24-fold higher, at 11.8 per 1000 live births (Fig. 2).

2.2.2. Intrapartum-related impairment

The WHO World Health Report 2005 estimated that as many as an annual 1 million survivors of "birth asphyxia" may develop cerebral palsy, learning difficulties or other disabilities [44], although the methods to generate these estimates are not detailed. The Global Burden of Disease assessment concluded that "birth asphyxia" was responsible for 42 million disability-adjusted life years (DALYs), which is double that due to diabetes and almost three-quarters of the burden due to HIV/AIDS (58 million DALYs) [47].

However, these estimates are uncertain as there is a paucity of data from low- and middle-income countries and a complete lack of data on intrapartum-related impairment from community-based settings, where the majority of the burden occurs. Data on the global burden of intrapartum-related impairment are scarce and further limited by inconsistent definitional categories for impairment [48].

A systematic review and estimation exercise is being conducted by the Child Health Epidemiology Reference Group for the Global Burden of Disease Project to estimate the global incidence of neonatal encephalopathy. In brief, PubMed, Popline, Cochrane, EMRO, EMBASE, LILACS, and AIM databases were searched, all titles were reviewed, and articles were pulled that had potential data on incidence, case fatality or chronic disability. The searches and modeling are described elsewhere [49]. Here we report the preliminary findings of the reported neonatal encephalopathy incidence, neonatal case fatality, and disability by median and range for each NMR category.

Of the infants who survive the first few hours, the development of neonatal encephalopathy is strongly predictive of long-term neurodevelopmental disability [50–52], with the highest rates of death or disability associated with severe stage 3 neonatal encephalopathy (near 100%) and lower rates of adverse outcomes in mild stage 1 neonatal encephalopathy (32%) [52]. Table 2 shows the median incidence of neonatal encephalopathy by NMR category. In very low mortality settings (NMR<5), the median incidence of neonatal encephalopathy is 1.9 per 1000 live births (range, 0.7–6.0) compared with 26.5 per 1000 live births in the highest mortality settings (based on single study), a 14-fold disparity. The median neonatal case fatality for neonatal encephalopathy in very low mortality settings is 21% (range, 17%–37%) versus 31% (range, 20%–33%) in the high mortality settings (NMR 31–45), although there is a complete lack of data from very high mortality settings (>45%) and no data from community settings, where the majority of intrapartum-related events are concentrated. Across all NMR categories, approximately 25%–29% of neonatal encephalopathy survivors may have a long-term moderate or severe impairment. Systematic estimates for neonatal encephalopathy and related impairment will be completed and published in 2010.

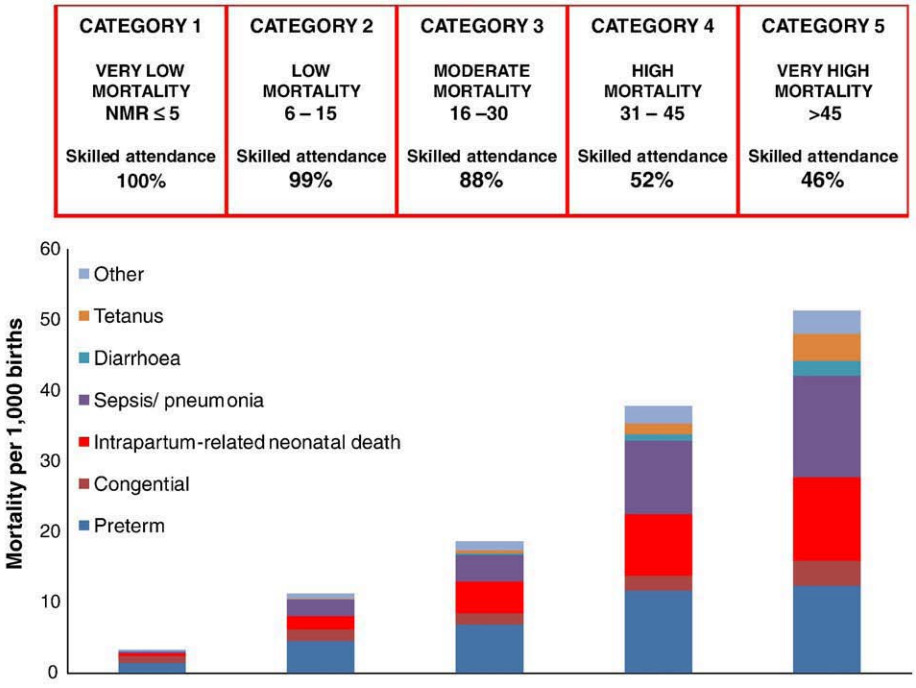

Fig. 2. Variation of cause-specific mortality across 193 countries organized according to five categories of neonatal mortality, as a marker of health system capacity. Sources: New analysis of 193 countries grouped by level of NMR into 5 categories adapted from Lancet Neonatal Series [1] 2005 and updated for 2009 using neonatal mortality [2] and revised neonatal cause-specific estimates for Countdown [72] 2008 based on methods from Lawn et al. [4] 2006. The skilled birth attendance is based on median, and the range is reported in Table 2.

Table 2
The variation in risk for maternal mortality and intrapartum-related outcomes for 193 countries organized according to five categories of neonatal mortality, as a marker of health system performance.

	CATEGORY 1 VERY LOW MORTALITY NMR ≤ 5	CATEGORY 2 LOW MORTALITY NMR 6–15	CATEGORY 3 MODERATE MORTALITY NMR 16–30	CATEGORY 4 HIGH MORTALITY NMR 31–45	CATEGORY 5 VERY HIGH MORTALITY NMR ≥ 45
Births	12 707 000	18 705 000	33 577 000	49 901 000	20 727 000
# of countries	*49*	*51*	*35*	*40*	*18*
Neonatal deaths	**42 000**	**212 000**	**627 000**	**1 891 000**	**1 065 000**
Skilled birth attendance (median %) (interquartile range)	100 (99–100)	99 (93–100)	88 (74–98)	52 (38–70)	46 (37–57)
Maternal mortality ratio (per 100,000)	12	112	168	570	920
Intrapartum stillbirth rate (per 1000)	1.2	3.8	6.1	10.1	11.4
Intrapartum-related NMR (per 1000)	0.5	1.9	4.5	8.7	11.8
Incidence of neonatal encephalopathy: Median (range)	1.9 (0.7–6.0)	6.7 (4.7–8.7)	9.8 (3.6–10.2)	13.4 (5.5–22.2)	26.5 (26.5)
Neonatal encephalopathy: neonatal case fatality Median (range)	21% (17–37)	12% (12%)	19% (10–28%)	31% (20–33%)	No data
Proportion of survivors with moderate-severe impairment: Median (range)	29% (6–54%)	27% (13–40%)	30% (21–40%)	25% (21–29%)	No data

Country groupings by category of NMR level are adapted from Lancet Neonatal Series 2005 [1]. Updated for 2009 births and mortality rates. Sources: MMR data from Hill et al. 2007 [58], IP stillbirth data from Lawn et al. 2005 [3], Neonatal mortality data WHO (UNICEF 2009 [2]). Intrapartum-related neonatal deaths ("birth asphyxia") for Countdown 2008 [72] based on methods from Lawn et al. 2006 [4].

2.3. Where?

2.3.1. Which countries?

As with early neonatal deaths, almost all intrapartum stillbirths (>99%) and intrapartum-related neonatal deaths occur in low- and middle-income countries. In high-income countries the rates and numbers of neonatal deaths are much lower, and the proportion attributed to be intrapartum-related is around 12% (Fig. 2). Hence, fewer than 50 000 intrapartum-related neonatal deaths occur in high-income countries. South Asia and Africa—with large numbers of births and deaths, and higher cause-specific intrapartum-related rates—together account for 73% of all intrapartum-related neonatal deaths worldwide (Fig. 3). These world maps, created by Worldmapper (Fig. 3) [53], adjust the scale of each country in proportion to the measure indicated, dramatically portraying the heavy burden in these regions. The 10 countries with the highest numbers of intrapartum-related neonatal deaths (Fig. 3a) and intrapartum stillbirths (Fig. 3b) are mainly those with the largest numbers of births (India, China, Democratic Republic of Congo, Pakistan, Nigeria, Bangladesh, Ethiopia, Indonesia, Afghanistan, and Tanzania). These 10 countries alone account for more than 65% of all intrapartum-related neonatal deaths.

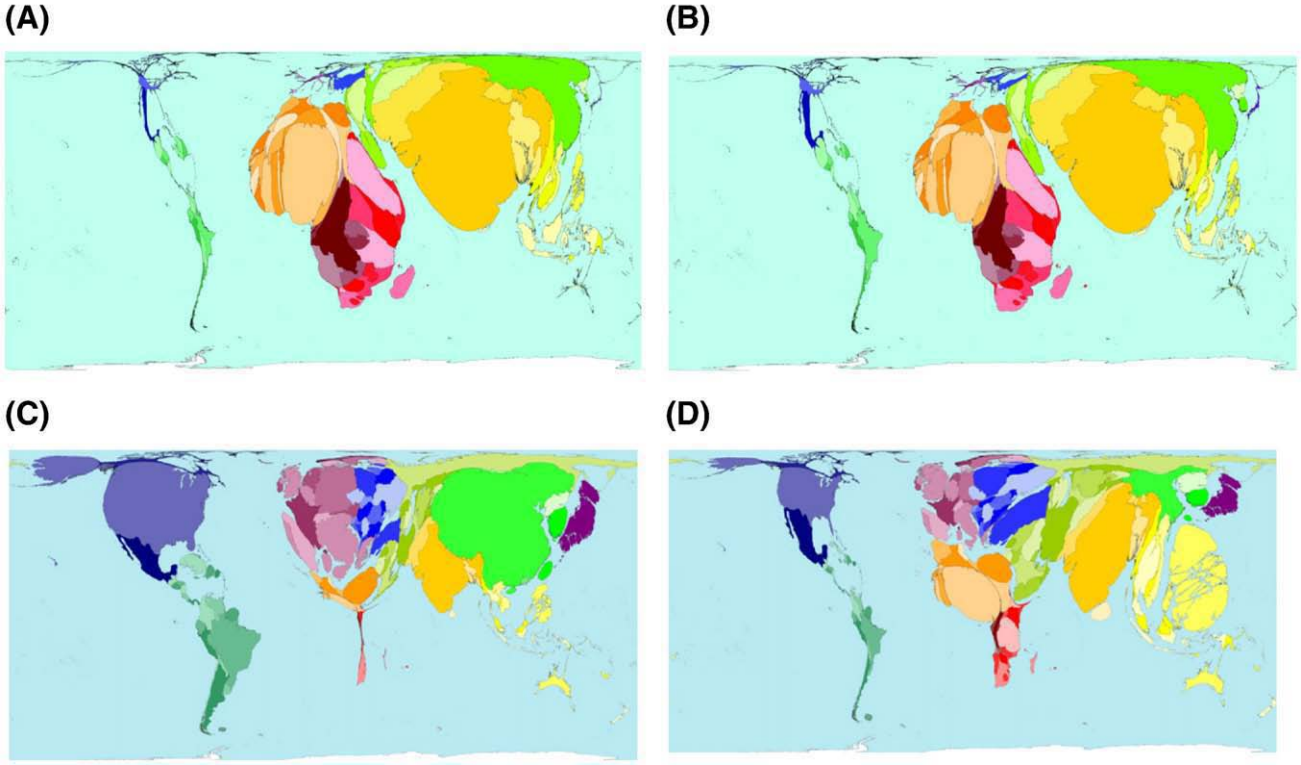

Fig. 3. Global density of intrapartum-related neonatal deaths, intrapartum stillbirths, physicians, and midwives. (A) Intrapartum-related neonatal deaths. (B) Intrapartum stillbirths. (C) Physician workforce. (D) Midwives working. Source: http://www.worldmapper.org/display.php?selected=215. http://www.worldmapper.org/display.php?selected=219. http://www.worldmapper.org/display.php?selected=260. © Copyright 2006 SASI Group (University of Sheffield) and Mark Newman (University of Michigan). Used with permission [53].

The countries with the highest rates of intrapartum stillbirth are primarily in West Africa, for example Cote d'Ivoire (14 per 1000) and Nigeria (11 per 1000), and South Asian countries with challenging geographical barriers and low access to skilled health care, such as Nepal (14 per 1000) and Pakistan (14 per 1000); however, these rates may underestimate the magnitude of the problem because of under-reporting, as discussed earlier.

2.3.2. Variation within countries: Inequities and gender

Disparities in intrapartum-related mortality rates are also evident within countries because the highest burden occurs among those with inequitable access to obstetric and immediate postnatal care. Neonatal mortality is much higher for the poorest of the poor. For example, in Nigeria the NMR is 23 per 1000 births for the highest income quintile, but 59 for newborns in the poorest quintile families. If all the babies in Nigeria had the same risk of neonatal mortality as the richest, then there would be 127 000 fewer newborn deaths in Nigeria each year [54]. The rural poor have the greatest geographic and financial challenges in accessing care, particularly emergency obstetric care (EmOC). Cesarean delivery rates in rural Sub-Saharan Africa are less than 1% [12].

Controlling for other factors, baby girls have a lower mortality rate than baby boys [55]. In societies where care is equal for boys and girls, the ratio of neonatal mortality for boys to girls is usually at least 1.2 or higher [1]. Analysis of Demographic Health Survey (DHS) data for African countries does not show a loss of this advantage for female babies, although DHS may not be sensitive enough to detect this difference. A number of studies from South Asia have reported reduced care seeking for girls, and even female infanticide [56].

2.4. When? Timing of stillbirths, maternal, and neonatal deaths

2.4.1. Timing of intrapartum-related neonatal outcomes

The vast majority of intrapartum-related neonatal deaths occur early: 78%–90% in the first 48 hours and almost all within the first week of life (97%–98%) [32,33,35,38]. Fig. 4 shows the timing of these deaths in a community setting in rural Nepal. Neonatal encephalopathy symptoms such as reduced consciousness and convulsions typically will manifest within the first 24 hours of life [57]; babies who die from neonatal encephalopathy do so primarily in the neonatal period, and mainly in the first days of life, even in countries with neonatal intensive care [51].

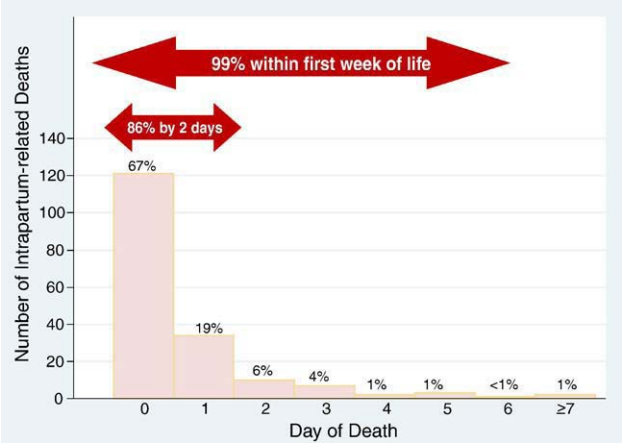

Fig. 4. Timing of intrapartum-related deaths in a community setting in rural Sarlahi, Nepal. Source: New analysis from dataset for Nepal Newborn Washing Study, Sarlahi Nepal [33,90–92]. Dataset from a cohort of 23 662 live births in the community-based study site in Sarlahi Nepal, where approximately 90% of births occurred at home and more than 80% without a skilled birth attendant. A total of 759 newborns died in the neonatal period (NMR 32), of which there were 180 intrapartum-related neonatal deaths of babies >34 weeks of gestational age. Almost all intrapartum-related neonatal deaths occurred in the early neonatal period: 67% in the first day of life, 86% in the first 2 days, and 99% within the first week of life.

2.4.2. Linked outcomes of intrapartum stillbirths and maternal deaths

Whilst around 23% of neonatal deaths globally are estimated to be intrapartum-related, the proportion of stillbirths and maternal deaths that are intrapartum-related is even higher: 32% and 42%, respectively (Fig. 5).

The first systematic estimates for intrapartum stillbirths were reported for 2000. National estimates for 192 countries based on 73 population-based study datasets from 56 countries yielded approximately 1.02 million annual intrapartum stillbirths (95% CI, 0.66–1.48). The disparity in intrapartum stillbirth rates is approximately 10-fold from the poorest to richest regions (Table 2); at country-level the disparity increases to over 50-fold, with rates of intrapartum stillbirth ranging from 0.3 to 15.5 per 1000 births [3].

There were an estimated 535 900 maternal deaths worldwide in 2005 [58]. The maternal mortality ratio (MMR) is high in the same countries where NMR, intrapartum-related neonatal deaths, and intrapartum stillbirth rates are high. For example, in the countries in Category 5 (NMR >45 per 1000), the MMR is 8-fold higher than for the countries with the lowest mortality (920 vs 12 per 100 000 births) (Table 2). Multiple regression analysis of global estimate data also reported a very close correlation between SBR and MMR [59].

Globally, an estimated 42% of maternal deaths are intrapartum-related, defined as during birth or the first day after birth (Fig. 5) [60]. Most of the direct obstetric causes of maternal deaths are intrapartum related including obstetric hemorrhage, puerperal sepsis, some hypertension complications, and anesthetic related. In South Africa, 39% of direct maternal deaths and 42% of perinatal deaths are directly intrapartum related—the largest causal group for either maternal deaths or perinatal deaths (Personal communication RC Pattinson, data from Saving Mothers Confidential Enquiries into maternal deaths in South Africa and Saving Babies 2006–2007: Sixth Perinatal Care survey of South Africa).

For mothers who die of an intrapartum cause, it is rare for the baby to survive. Maternal morbidity and "near miss" maternal deaths are also closely linked to adverse fetal and neonatal outcomes. Among women with obstetric fistula, a high proportion has experienced an intrapartum stillbirth or an intrapartum-related neonatal death, although systematic reporting for the perinatal outcomes is often lacking [11]. Likewise women with near miss often do not have a surviving baby, although few report on this outcome [61]. In South Africa, for 1002 maternal deaths and "near miss" maternal deaths (1997–2006), 325 babies were undelivered at the time of the mother's death. Among the 677 remaining pregnancies, the SBR was 182 per 1000 total births which is 10-fold higher than the SBR for uncomplicated pregnancies (Personal communication, RC Pattinson). There is a need to improve classification systems that better crosslink maternal and perinatal outcomes.

Therefore, the time of greatest risk of mortality and morbidity for both the mother and baby is at birth. Analysis of the average daily mortality rate for mothers and babies demonstrates a substantial rise in mortality for the mother at the initiation of labor and delivery, peaking at 0.8 per 1000 births at the time of birth, a 10-fold higher risk than for the rest of the postnatal period. The concurrent risk for intrapartum stillbirths is around 10 per 1000 births and for neonatal death on the first day of life it is around 11 per 1000 births. The convergence of increased mortality risk lasts into the first 2 postnatal weeks of life, although for both the neonate and the mother [60], it is most acute at birth and in the first 48 hours of postnatal life [62]. This underscores the urgent need to coordinate childbirth and early postnatal interventions for both the mother and baby [63].

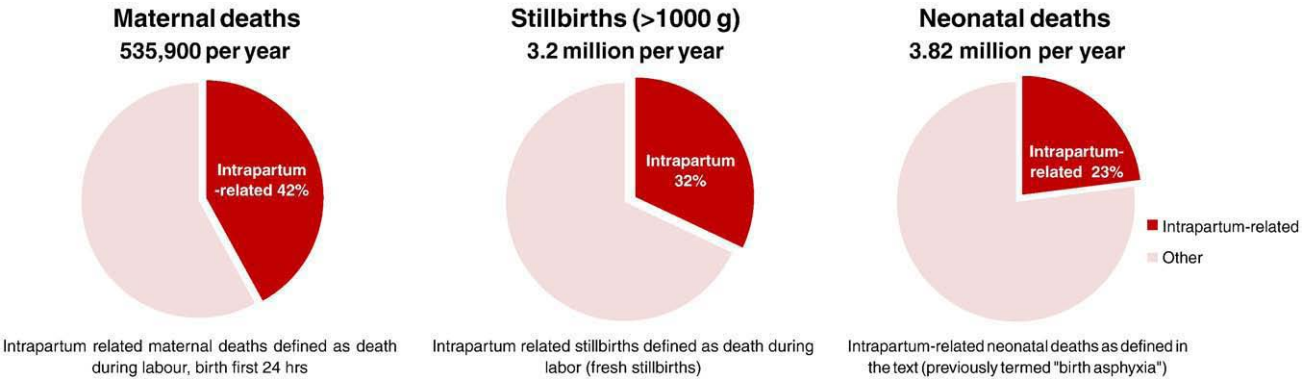

Fig. 5. Proportion of maternal deaths, stillbirths, and neonatal deaths that are intrapartum-related. Sources: Maternal deaths: WHO/UNICEF/UNFPA estimates, Hill et al. 2007 [58]. Timing of maternal deaths based on Li et al. 1996 [60]. Stillbirths: Stanton et al. 2006 [5]. Intrapartum stillbirth rate Lawn et al. 2005 [3]. Neonatal deaths: WHO (UNICEF 2009 [2]). Intrapartum-related neonatal deaths based on CHERG/WHO estimates [4] updated for 2009 using neonatal mortality [2] and revised neonatal cause-specific estimates for Countdown 2008 [72] based on methods from Lawn et al. 2006 [4].

2.5. Why?

2.5.1. Which cause, where, and why?

The successful transition of the newborn baby from life in utero to life at birth is based on a complex balance between the health of the mother, the course of the pregnancy, and the process of delivery and immediate postnatal care. During normal labor, the fetus will experience hypoxia but is able to tolerate this remarkably well. Problems occur if there is severe or sustained lack of oxygen to the fetus, which may occur before, during or after labor. Studies in industrialized settings give varying estimates for the proportion of neonatal encephalopathy in term infants that occurs during the intrapartum period, ranging from very low in some studies (~30%) [64,65] to much higher (~80%) in other more recent studies using magnetic resonance imaging [66]. For example, one large study in the UK found that 197 of 245 term babies with neonatal encephalopathy had evidence on cerebral magnetic resonance imaging that was diagnostic of an acute intrapartum insult [66]. Prenatal conditions may contribute to anywhere from 5-70% of cases of neonatal encephalopathy [64–66], and postnatal injury accounts for an estimated 10% of cases [67,68]. However, even in high-income countries, many questions remain unanswered.

The use of causal web analysis to take into account coexisting prenatal and intrapartum factors has been an important advance in understanding [26,69]. Studies assessing the timing of insult are not available from low-income country settings, but it is likely that intrapartum causes account for a larger proportion, given the higher incidence of serious complications in labor and reduced availability of skilled care during birth [70].

2.5.2. Maternal risk factors and complications

The inextricable connection between the health of the mother and fetus is demonstrated by the strong associations between maternal risk factors and morbidity and perinatal death (Table 3). While certain prepregnancy factors (such as maternal stunting or poor obstetric history) are consistently associated with elevated risk of perinatal mortality (risk range 1–5), prenatal conditions such as anemia or hypertensive disease, appear to be stronger risk factors (risk range 2–14). However, by far the most predictive factors for perinatal mortality are intrapartum complications (risk range 2–85), such as malpresentation or obstructed labor, that may increase the risk for perinatal death by a factor of 85. Identifying and intervening for these maternal conditions may have a significant impact on the health of the fetus and newborn, as well as the mother. The role of prenatal risk factor and complication screening in averting intrapartum-related deaths is discussed further in the fourth paper in this series [13]. The

Table 3
Adjusted odds ratio for risk factors for all-cause neonatal/perinatal deaths reported from population-based studies.

Time period	Risk factor	Adjusted odds ratio*	Approximate range
Before pregnancy	Maternal age		Approximate range 1 to 5
	<18 years	1.1–2	
	>35 years	1.3–2 (NS in 2 studies)	
	Maternal size		
	Height <150 cm	1.3–5	
	Pre-pregnancy wt <47 kg	1.1–2	
	Parity		
	Primigravida	1.3–2.2	
	Parity >6	1.4–1.5	
	Poor obstetric history (Previous perinatal death or instrumental delivery)	1.6–4	
During pregnancy (antenatal)	Multiple pregnancy	2.0–7	Approximate range 2 to 14
	Maternal anemia		
	(PCV<0.34)	NS in 4 studies	
	(PCV<0.21)	2–4	
	Maternal jaundice/cholestasis	2–8	
	Hypertensive disorders		
	Pre-eclampsia	2–4	
	Eclampsia	3–14	
	Diabetes	2–11	
	Syphilis (perinatal death)	1.7–6	
	Maternal malaria (blood test positive)	2–4	
	HIV	1.1–3	
	HIV and malaria	5	
	Post-term (>42 weeks gestation)	1.5	
	Preterm birth (<37 weeks gestation)	2–4	
During labor and childbirth (intrapartum)	Obstructed labor/dystocia	7–85	Approximate range 2 to 85
	Prolonged second stage	3–5	
	Meconium staining of liquor	12	
	Malpresentation		
	Breech	6–15	
	Other	8–34	
	Bleeding per vagina after 8th month	3–6	
	Maternal fever during labor (>38 °C)	10–11	
	Rupture of membranes >24 h	1.8–7	

Abbreviation: PCV, packed cell volume; NS, not significant.
* Odds ratios included are statistically significant and from population-based studies adjusting for major confounders (parity and socioeconomic status) and significantly associated with intrapartum stillbirth and/or neonatal death or perinatal death. Table adapted from Lawn et al. 2005 [1]. Figures rounded to the nearest whole number unless less than 2. References [97–110].

management of intrapartum-related complications is addressed in the second paper in the series [12].

2.5.3. The cultural curtain cloaking pregnancy and birth

For the 60 million women giving birth at home each year, physical distance is often a barrier. In many cases, there are also cultural norms that keep pregnancy hidden and preclude care seeking outside the home at the time of birth or in the postnatal period [11]. Should complications occur, which may be understood as having a non-biomedical cause, traditional remedies are often used, such as heated copper coins on the baby's back (Panel 1). While there are many gaps in service supply, understanding and addressing the socio-cultural context as well are critical to accelerating coverage of effective care.

2.6. Why? Health system gaps in coverage of care

2.6.1. The inverse care law

Table 2 demonstrates the inverse relationship between access to skilled care at birth and intrapartum-related neonatal mortality and intrapartum stillbirth rates across different mortality levels. In the lowest NMR categories, which have nearly universal skilled birth attendance, the rate of intrapartum-related NMR is as low at 0.45 per 1000 live births and the intrapartum stillbirth rate is 1.22 per 1000 births. Whereas in the highest NMR categories (Group 5), the median percentage of skilled birth attendance is less than 50%, and the rate of intrapartum-related NMR is 11.8 per 1000 and the intrapartum stillbirth rate is 11.4 per 1000. This is an ecologic association and cannot be taken as causal; however, skilled birth attendance and facility birth may be good markers of health system access and capacity [71]. Recent analysis, also ecologic, suggests that MMR and SBR are inversely related to access to cesarean delivery [59]. The countries with NMR over 30 per 1000 together account for 77% of the intrapartum-related mortality and yet the majority of births and deaths are at home. The data as well as care are lacking, and the health system and health information solutions must be based on this reality [16]. The inverse care law is vividly illustrated in Fig. 3, with global maps depicting the gross inequities in care coverage and intrapartum deaths.

The Worldmapper [53] figures show clearly that the highest density of intrapartum-related neonatal deaths and intrapartum stillbirths are concentrated in Sub-Saharan Africa and South Asia. Yet these are also the areas suffering from the most desperate shortage of physician workforce, with near absence of physicians (Figure 3c) and a dearth of midwives (Figure 3d). There is also inequitable distribution of health professionals within the countries. For instance, the doctor population ratio in urban areas in India is 1.3 per 1000 population, whereas it is just 0.33 in rural areas.

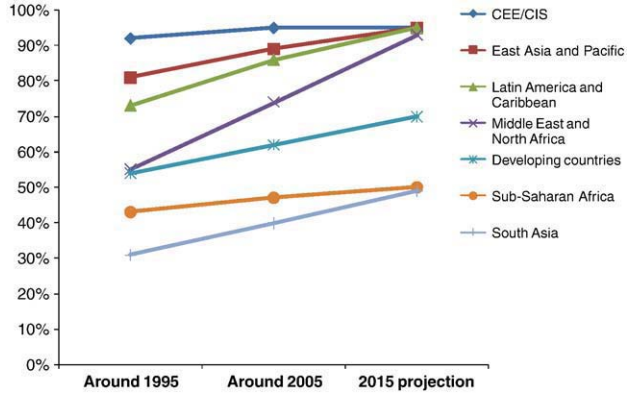

Fig. 6. Time trends in skilled attendance coverage, by region, for 80 countries with trend data (around 1995 and around 2005) with projection for 2015. Source: DHS, MICS, and other national household surveys; for details see www.childinfo.org [89].

2.6.2. The global gap for care at childbirth: Are we making progress?

Gaps in healthcare coverage during the prenatal, intrapartum, and postnatal periods contribute markedly to the inequities in health outcomes. Although some regions have made progress in increasing the coverage of skilled care at birth, the highest mortality regions have seen little progress in the last decade. The coverage gap of skilled birth attendance is widest in certain regions, namely Sub-Saharan Africa and South Asia, where baseline coverage is lowest globally and progress to reaching universal skilled attendance is slow (Fig. 6). The rates of increase for skilled birth attendance in these regions is less than 0.5% per year and at current rates, by 2015, a skilled birth attendant will only reach 1 out of every 2 women in Sub-Saharan Africa and South Asia. This is a priority gap requiring substantial work to define potentially scalable approaches to reaching universal skilled birth attendance in varying contexts [4]. Postnatal care is also a critical, yet neglected, gap in low- and middle-income countries, and coverage is even lower than skilled birth attendance and much lower than prenatal care [2,44]. In the 68 priority countdown countries, a median of only 21% of mothers received postnatal care within 48 hours of birth [72].

Equity gaps in prenatal care and skilled birth attendance are present among the marginalized populations within countries—between rich and poor, between urban and rural. The inequities in access to prenatal care and skilled birth attendance are most pronounced between rich and poor in South Asia and Sub-Saharan Africa, where coverage rates may differ by up to 4-fold (Fig. 7). For

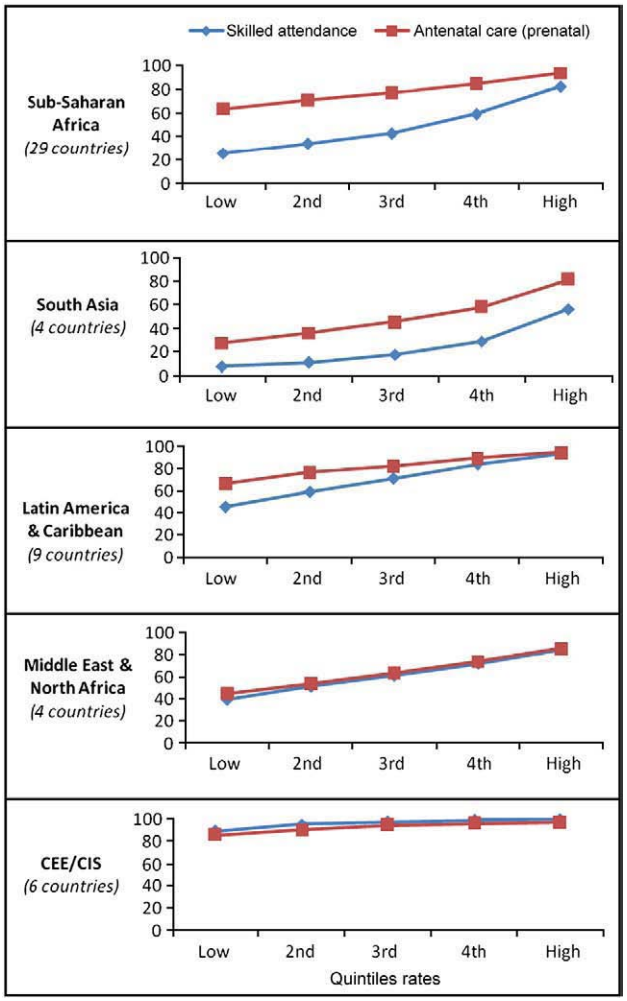

Fig. 7. Skilled birth attendance and antenatal (prenatal) care (at least one visit) by wealth quintiles whereby the low level is the poorest population and the high level is the population best-off. Data based on Gwatkin et al. 2007 [93].

mothers in the lowest wealth quintile in South Asia, skilled birth attendance is less than 10% and prenatal care reaches around 25%, whereas for the wealthiest, skilled birth attendance reaches nearly 60% of mothers and prenatal care coverage is 80%. Similarly, rural mothers have lower access to skilled birth attendance and cesarean delivery than mothers in urban areas [12]. In South Asia, only 33% of rural deliveries are attended by a skilled birth attendant compared with 68% in urban settings [12].

As well as coverage gaps and equity gaps, another critical gap in coverage is the quality gap. For women or neonates who do interact with the health system, the effective interventions may not be provided; for example, at prenatal care there may be a gap between those who come and those whose condition (malpresentation, pre-eclampsia, diabetes) is identified and correctly managed. This missed opportunity in health systems is discussed in the final paper of this series.

3. Solutions to reduce intrapartum-related deaths

3.1. Prevention strategies for intrapartum-related deaths

Interventions to reduce the burden of intrapartum-related complications can act by 3 main mechanisms:

- *Primary prevention of the insult*: Improved maternal health including nutritional status, prenatal recognition of at-risk pregnancies, skilled attendance at birth, and particularly early recognition and timely management for obstetric complications.
- *Secondary prevention after the event*: Resuscitation of the "non-breathing" neonate.
- *Tertiary prevention for the baby with acute complications*: Management of the baby with acute complications of "perinatal asphyxia" such as neonatal encephalopathy, which is complex to address even in well-resourced health systems, and late sequalae such as cerebral palsy.

Of the 3 possible approaches, primary prevention of the insult is likely to have the greatest impact on intrapartum-related mortality [3,73]. Prepregnancy risk factors, such as short inter-pregnancy spacing, low maternal nutritional status, and young age only predict some of the population-attributable risk, and intrapartum complications may occur to mothers without these risk factors (Table 3). In low-resource settings, intrapartum stillbirths may comprise the majority of intrapartum-related deaths [70] and these deaths can only be averted with adequate intrapartum care and timely emergency obstetric care, which must be available for all births [74]. For intrapartum-related neonatal deaths, early recognition and management of women with childbirth complications is expected to have higher efficacy than resuscitation or attempts to manage neonatal encephalopathy after neurological injury has occurred [13,73]. The evidence for facility-based intrapartum care is reviewed in the second paper [12] in this series; risk screening and referral are reviewed in the fourth paper; and the options for community-based recognition and care are covered in the fifth [14].

Secondary prevention of intrapartum-related hypoxic injury through neonatal resuscitation is reviewed in the third paper [10].

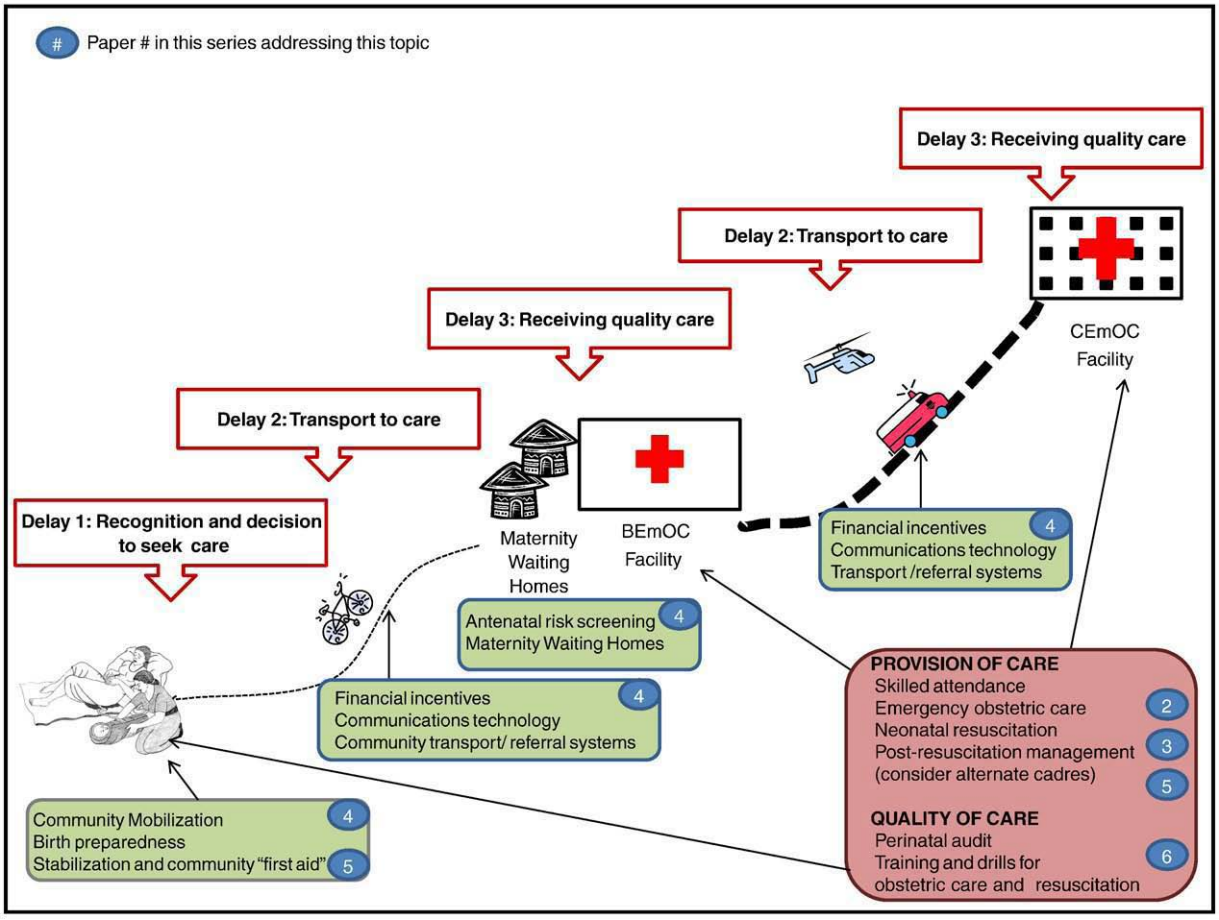

Fig. 8. Reducing delays to emergency obstetric and neonatal care. Abbreviations: BEmOC, Basic Emergency Obstetric Care; CEmOC, Comprehensive Emergency Obstetric Care. For contents of the papers please refer to Table 4. Image of home birth reprinted with permission granted by the American College of Nurse-Midwives.

The potential impact of tertiary prevention is likely to be lower than primary and secondary prevention. Interventions may have marginal effects on disability-free survival even in high-income settings; and in low- and middle-income settings, neonatal intensive care is infrequently available [75]. The management of neonatal encephalopathy in district and referral hospitals is discussed in the third paper.

3.2. Addressing deadly delays: The need for linkages

Delays in receiving appropriate care can be important for many conditions, but delays of even a few hours in addressing an obstetric emergency around the time of birth can be significant. Delays of minutes in resuscitating a non-breathing baby can result in death or major impairment. The "classic" 3 delays were first described in relation to delay for women with obstetric emergencies. The delays include [76,77]: (1) delay in recognition of the problem and the decision to seek care; (2) delay to reach a health facility; and (3) delay in receiving quality care at the facility.

Strategies to reducing these 3 delays are crucial to effectively link mothers and babies to skilled obstetric and newborn care, and are depicted in Fig. 8 and discussed in the fourth paper in the context of improving maternal outcomes and pregnancy outcomes [13]. The continuum from the home, to first-level health clinic, to referral hospital ensures effective linkages from all potential places of care giving. Functional linkages to EmOC are especially crucial for the 60 million women who deliver at home each year [13].

The continuum of care approach is a conceptual framework for integrated maternal, neonatal, and child health that has been defined by the dimensions of time through the lifecycle and levels of care within the health system [2,78,79]. Programs to reduce intrapartum-related injury must address risk factors across the entire continuum of the life cycle from adolescence through pregnancy and childbirth. For example, ensuring adequate child nutrition may reduce rates of maternal stunting, and delayed age of first birth may decrease the risk of obstructed labor [80]. Interventions for the primary prevention of intrapartum-related injury are required during the time of pregnancy and childbirth, while secondary and tertiary prevention measures are needed in the immediate postnatal and neonatal periods.

3.3. Contextualizing local culture and traditions when designing solutions

Communities may have diverse beliefs and customs for the baby who does not breathe at birth [81]. Elucidating local explanatory models for abnormal childbirth and the non-breathing baby are essential to understand behavioral responses and to develop interventions to effectively influence behavior change during pregnancy and childbirth. Panel 1 highlights qualitative data on knowledge, attitudes, and practices from two different South Asian settings with a predominance of home births. In Bangladesh, the mother catching a cold and evil spirits were commonly believed to cause a baby not to breathe, and common responses included stimulating the baby, mouth-to-mouth breaths, or stirring and/or warming the placenta in a bowl of water. In Shivgarh, India, a spiritual healing process was invoked for the non-breathing baby that involved chanting mantras and heating copper coins and placing them on the baby's back [82]. While some traditional practices may stimulate the infant and trigger breathing, others may increase delays to receiving effective care.

4. Methods and overview for this series on intrapartum-related deaths

4.1. Searches and methods

For this series we systematically reviewed the evidence for impact of the interventions and strategies detailed in Table 4. The searches were first conducted in 2002, for a background report for an Expert Meeting in Cape Town [83], and have now been updated to 2009. Searches of medical literature databases were conducted, including PubMed, Popline, EMBASE, LILACS, IMEM, African Index Medicus, the Cochrane library, and WHO documents. Additionally, "snowball searching" was performed, whereby literature referenced in bibliographies of key papers was identified. Attempts were made to identify other relevant literature and non-published data through a survey of experts and program managers [6], directly contacting experts and agencies working in newborn care, and reviewing abstracts published in recent maternal and child health conferences.

Search strategies included various combinations of keywords and MeSH headings relevant for specific interventions. The search terms used are shown in web appendix 1 (available in the online version). Articles were limited to those published after 1960 and involving human subjects. All languages were included and if an article was deemed relevant by title and abstract screening, the full article was translated. All titles were screened for initial inclusion; for those of potential relevance

Table 4
Interventions reviewed in the Supplement to reduce intrapartum deaths.

Paper 2: Obstetric care in low-resource settings [12]
Intrapartum care content to address priority obstetric emergencies/complications
• Breech presentation
• Obstructed/prolonged labor
• Fetal distress
• Severe hypertensive disorders of pregnancy
• Antepartum hemorrhage
• Post-term pregnancy
• Maternal intrauterine infection
Intrapartum care provision strategies
• Emergency obstetric training and drills
• Safety checklists
• Rapid response teams
• Public-private partnerships
• Continuous labor support/continuity of care during labor
• Task shifting and alternative cadres
Paper 3: Neonatal resuscitation in low-resource settings [10]
Neonatal resuscitation
• Resuscitation algorithms and content
• Equipment
• Evidence for resuscitation in facility settings
• Evidence for resuscitation in community settings
• Training, competency, skill retention
Post-resuscitation management
• Serum glucose-fluid management
• Anticonvulsants
• Thermal management
• Therapeutic hypothermia
Paper 4: Linking families and facilities for care at birth [13]
Community reaching towards the facility
• Community mobilization
• Financial strategies
Formal healthcare system reaching towards the community
• Community referral and transport schemes
• Risk screening
• Maternity waiting homes
Paper 5: Delivering care at birth in community settings [14]
• Community midwives and birthing centers
• Trained traditional birth attendants
• Integrated home-based care packages by community health workers
Paper 6: Perinatal mortality audit and scaling up in low- and middle-income countries [15]
• Facility-based audit, quality of intrapartum care
• Community audit, partner defined quality
• Country case studies

the abstract was reviewed to determine whether to review the full article. There were a total of 29 358 hits, with around 5000 abstracts reviewed, and more than 530 articles reviewed. The majority (over 95%) were peer-reviewed papers. The balance was composed of relevant reports and monographs, mainly program reports (Fig. 9).

Identified reports and studies were included in the following categories:

1. Trials, studies with inclusion criteria as follows: a study design using a controlled trial methodology (randomized controlled trial (RCT) design, quasi-experimental design with non-random control, or before-and-after comparison); definition of the intervention; population-based study (either in the community, or in an institution where the majority of the population give birth); and reported perinatal, neonatal, stillbirth, early neonatal, and ideally intrapartum-related mortality rates with a consistent case definition.
2. Systematic reviews of mortality or relevant intermediary outcomes.
3. Reports of effect on important intermediate or process indicators, such as care seeking, facility delivery, and utilization of EmOC, morbidity.
4. Publications detailing relevant program experiences, particularly at scale that may be of relevance for case studies.

Data abstracted included study setting, baseline mortality and skilled birth attendance coverage, postnatal care coverage, study design, intervention description, intermediate outcomes (including changes in knowledge, attitudes, behaviors, and care seeking), and impact outcomes (SBR, ENMR, PMR, NMR, and MMR, as well as intrapartum stillbirth rate and intrapartum-related neonatal mortality rate).

4.2. Grading of evidence and meta-analysis

The level of evidence was assessed using the GRADE system criteria [84], to evaluate the quality of the evidence (strong, moderate, low or very low) based on standard criteria (Table 5). We used an adaptation of GRADE developed by the Child Health Epidemiology Reference Group (CHERG) specifically for low- and middle-income settings [85] and focused on the evidence for effect on cause-specific mortality. As our specific interest is for intrapartum-related ("birth asphyxia") outcomes, this is a particular constraint as cause-specific data are limited [3,4]. Once the level of evidence was assigned, based on group consensus a recommendation for programmatic application was allocated, which may be for or against, and may be strong, weak, or conditional. For many of the interventions that are considered standard practice in obstetric care, there is no high-quality evidence and indeed, often only limited moderate- or low-quality evidence. In some cases, this is because the intervention became standard practice before the RCT was invented; for example, it would now be considered unethical to undertake a RCT of cesarean delivery versus placebo. The advantage of the GRADE system is that for conditions that pass the so-called "parachute test" (it is obvious that a parachute saves lives and an RCT is impossible) [86], it can be stated that evidence grade is low, but the recommendation is strong.

Higher quality studies were included and considered for pooling risk estimates if the study design was an RCT or quasi-experimental study. In the absence of high-quality studies, observational studies of lower quality were considered for meta-analysis if the intervention, study design, and the outcomes of interest were comparable. However, historical or ecologic data were excluded. All analyses were conducted using STATA 10 statistical software (StataCorp, College Station, TX, USA).

4.3. Organization of strategies reviewed in Supplement

Interventions were specifically selected for their potential effectiveness, relevance, and applications in low- and middle-income countries, and are listed in Table 4. The series of papers in this Supplement are structured according to different strategies to avert intrapartum-related injury along the continuum of care (Fig. 8). In the second paper we review improving intrapartum obstetric interventions in health facilities, focusing on the content and impact of individual intrapartum interventions and innovative solutions to provide care in settings with extreme resource constraints [12]. In the third paper we review the evidence and program implications of neonatal resuscitation and post-resuscitation management, in both facility and community settings [10]. In the fourth paper we focus on creative strategies to link families to

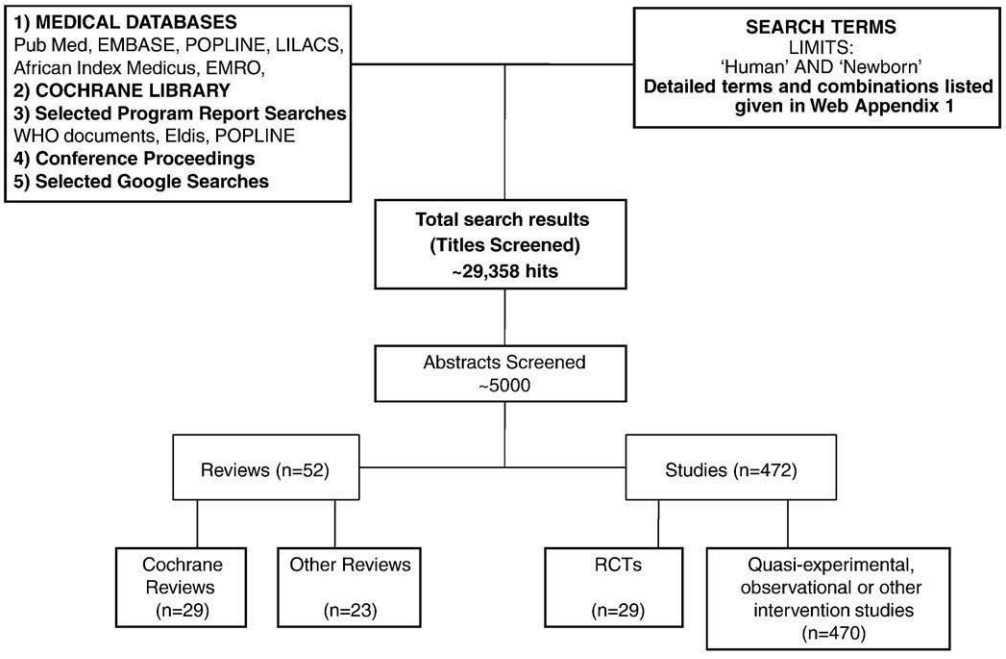

Fig. 9. Summary of the systematic searches undertaken and the reviews and studies of relevance identified.

Table 5
The GRADE criteria for review of the quality of evidence.

Quality of evidence	Study design	Lower the quality when*	Higher the quality when*
High	Randomized trial	**Study limitations:**	**Strong association:**
		−1 Serious limitations	+1 Strong, no plausible confounders, consistent and direct evidence**
Moderate		−2 Very serious limitations	
Low	Observational study	−1 Important **inconsistency**	+2 Very strong, no major threats to validity and direct evidence***
Very low	Any other evidence	**Directness:**	
		−1 Some uncertainty	
		−2 Major uncertainty	
		−1 **Imprecise data**	+1 Evidence of a **Dose response** gradient
		−1 High probability of **Reporting bias**	+1 All **plausible confounders** would have reduced the effect

Source: WHO [111] 2008.

facility-based skilled obstetric care and to reduce the 3 delays, by improving birth preparedness, increasing demand for skilled obstetric care through community mobilization or use of financial incentives, strengthening referral-transport systems, or bringing the mother closer to care before delivery [13]. In the fifth paper we discuss strategies to bring care closer to the community, including use of trained traditional birth attendants, community health workers, or community-based skilled birth attendants [14]. In the sixth paper we highlight strategies to improve health delivery systems and quality of care via perinatal audit and quality improvement. The final paper provides a synthesis of the evidence and discussion of policy and program advances to improve intrapartum-related maternal health and pregnancy outcomes [16] (see Fig. 8 regarding delays).

5. Conclusion

This first paper of the Supplement on "Intrapartum-related deaths: Evidence for action" has brought together data on the size of the global burden related to this silent killer that is responsible for more deaths than childhood malaria, and yet is absent from the global health policy and program agenda. Each year an estimated 904 000 babies die soon after birth due to intrapartum-related injury, particularly childbirth complications, primarily in low- and middle-income countries [1]. These deaths are closely linked to at least 1.02 million stillbirths occurring during labor—a total of nearly 2 million deaths [3]. In addition, an unknown number of babies survive the insult, only to suffer long-term impairment, and are thus unable to reach their full potential [48]. Consensus on definitions surrounding "birth asphyxia" and their wide dissemination across stakeholders is urgently required to build an effective movement to address this huge, yet neglected, problem.

During this same time period, approximately half of the world's half a million maternal deaths occur, as well as many more near-miss maternal deaths and significant maternal morbidity [87]. The time of birth and the immediate postnatal period are crucial as the times of greatest risk for pregnant women and babies (Fig. 5). However, more than 60 million women give birth annually without skilled care at birth, mostly at home, and the majority does not receive early postnatal care. In rich countries, women enter pregnancy in a better nourished condition, and other prepregnancy factors are less common; however, in the last century the advent of modern obstetrics and neonatal intensive care has resulted in dramatic reductions in perinatal and intrapartum-related mortality through primary prevention of the insult and early management with neonatal resuscitation. A recent multicountry analysis suggests that prenatal care is poorly correlated with MMR and SBR, but a rise in coverage of cesarean delivery from 0% to 10% was significantly associated with reductions in MMR and SBR [59]. Furthermore, high-technology innovations have been developed to manage and improve the outcomes for the minority of neonatal encephalopathy cases born in high-income settings. However, these strategies do not reach low- and middle- income countries, especially the poor, who primarily bear the burden of morbidity and mortality from intrapartum-related childbirth complications.

Maternal mortality ratio (MMR) is proposed as a marker of the accessibility and quality of the health system that is required to address maternal deaths due to obstetric causes, including a functioning continuum of care. Given that the MMR globally is 4 per 1000 and the neonatal mortality rate (NMR) is 28 per 1000, NMR may be more readily measurable yet still closely correlated with MMR and also intimately linked to health system performance. Indeed, the United Nations Population Fund (UNFPA) has recently proposed an indicator to track the quality of obstetric care combining intrapartum stillbirth rate with neonatal deaths on the first day [88]. This is currently being tested in a more refined version of the indicator by combining intrapartum stillbirths and predischarge neonatal deaths weighing over 2000 g as a surrogate of intrapartum-related neonatal deaths (Personal communication, R Pattinson). The opportunities for prevention and management of intrapartum-related neonatal deaths or "birth asphyxia" sit primarily in maternal health programs, yet these programs have not received priority among international agencies or in low-resource country programs; within maternal health programs there has been limited attention to these important outcomes, which could increase the imperative for action.

The goal of this series is to call the Maternal Newborn and Child Health communities to collective action, laying out the evidence and actions required to strengthen healthcare delivery systems, and increase community mobilization to reduce the largely preventable and inexcusable 2 million deaths each year that are related to lack of care at birth.

6. Conflict of interest

The authors have no conflicts of interest to declare.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.ijgo.2009.07.016.

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Panel 1. Traditional community knowledge, attitudes, and practices in South Asia for the baby who does not breathe at birth

Qualitative research from India and Bangladesh illustrates some traditional beliefs and practices regarding the baby who does not breathe at birth. In Shivgarh, rural India, household interviews were conducted with pregnant women, fathers, mothers-in-law, female relatives and neighbors, community leaders (e.g. teachers, pundits), and other newborn care stakeholders (e.g. traditional newborn care providers, TBAs, health system workers) regarding common household perceptions and practices [82]. In Bangladesh, a multisite study is ongoing in rural Matlab, urban slums of Dhaka, and rural Dinajpur (Sibley et al. personal communication, June 15, 2009). Cultural domain analysis with case illness narrative and time-event analysis were conducted of laywomen, TBAs, and professional health workers [112].

Cultural explanatory models of a baby who does not breathe at birth

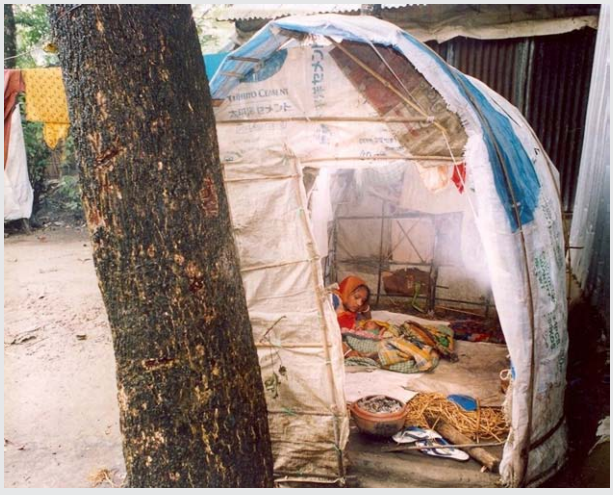
In Shivgarh, India, this condition was not considered a disease, and has no specific name or cause. Approximately 15% of newborns encountered breathing problems at birth, and symptoms commonly recognized by community members included "not crying" immediately after birth and "bluish discoloration of the newborn face." Community members also frequently mentioned observing slow breathing, unconsciousness of the baby, and not sucking on the mother's breast as important signs. Women named various reasons as to what led to a baby not breathing, e.g. bursting of the waters prior to delivery causing the newborn aspirates dirty water, breech delivery, tying of umbilical cord around the neck of the newborn resulting in breathlessness, side effects of medicines consumed by the mother during pregnancy, or a forced delivery using hand, instrument.

In the Bangladesh study, there was an overall high level of agreement and ability to discriminate between a normal baby and one who has difficulty breathing at birth. Signs mentioned by at least 80% of respondents were absent or weak cry, absent or gasping breathing, and skin pallor or cyanosis. Causes of a non-breathing baby mentioned by at least 80% of respondents included prolonged labor, injury to the baby during birth, and a malnourished mother. There were subgroup differences, however. For example, laywomen, TBAs, and village doctors believe that a mother getting cold during pregnancy is a cause of this problem while TBAs and laywomen agree that evil spirits or *alga batas* is a cause.

Traditional practices for the non-breathing baby

In Shivgarh, the majority of community members attempted to address breathing problems with home-remedies before seeking professional care. The most common practices were sprinkling cold water on the baby's face (37%) and patting the baby on the back and soles in the upside down position (34%). Other remedies included wiping the baby's face with a cloth; rubbing the umbilical cord; removing the umbilical cord from around the neck; and massaging of the fontanel, soles, and hands with a mixture of warm water with mustard oil and carom seed. If the newborn still could not recover, then the baby underwent a spiritual healing process, which consisted of heating copper coins and placing them on the baby's back after chanting a mantra, or placing dried egg-yolk in a folded cloth on the baby's epigastrium. If the newborn still did not recover then the community sought unqualified medical practitioners to give the baby oxygen before seeking formal health care.

In Bangladesh, the majority (60%–80%) of respondents agreed that wiping or cleaning the nose and mouth, covering, warming, giving mouth-to-mouth breaths, and stimulating the baby were treatments for a non-breathing baby. Also mentioned were massaging the baby and soaking and stirring the placenta in a bowl of water (the placenta being thought to contain the baby's life force). Respondents generally agreed that care should be sought from an allopathic doctor, followed by a village doctor, TBA, and spiritual healer in that order. Similar findings have been observed by others [113–118]. The beliefs varied by type of respondent, showing the importance in targeting different messages to these different audiences who influence the decision to seek care.



Photograph: A typical shed specially made for delivery in Bangladesh. The mother is 15 years old, it is her first child. Photo reprinted with permission granted by Save the Children.

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INTRAPARTUM-RELATED DEATHS: EVIDENCE FOR ACTION 2

Obstetric care in low-resource settings: What, who, and how to overcome challenges to scale up?

G. Justus Hofmeyr [a,*], Rachel A. Haws [b], Staffan Bergström [c,d], Anne CC Lee [b,e], Pius Okong [f], Gary L. Darmstadt [b], Luke C. Mullany [b], Eh Kalu Shwe Oo [g], Joy E. Lawn [e,h]

[a] Effective Care Research Unit, Eastern Cape Department of Health, Universities of the Witwatersrand and Fort Hare, South Africa
[b] Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA
[c] Averting Maternal Death and Disability (AMDD) Program, Columbia University, New York, USA
[d] Division of Global Health (IHCAR), Karolinska Institute, Stockholm, Sweden
[e] Saving Newborn Lives, Save the Children-US, Cape Town, South Africa
[f] St Raphael of St. Francis Hospital, Nsambya, Uganda
[g] Karen Department of Health and Welfare, Mae Sot, Thailand
[h] Health Systems Research Unit, Medical Research Council of South Africa, Cape Town, South Africa

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ABSTRACT

Background: Each year, approximately 2 million babies die because of complications of childbirth, primarily in settings where effective care at birth, particularly prompt cesarean delivery, is unavailable. *Objective:* We reviewed the content, impact, risk-benefit, and feasibility of interventions for obstetric complications with high population attributable risk of intrapartum-related hypoxic injury, as well as human resource, skill development, and technological innovations to improve obstetric care quality and availability. *Results:* Despite ecological associations of obstetric care with improved perinatal outcomes, there is limited evidence that intrapartum interventions reduce intrapartum-related neonatal mortality or morbidity. No interventions had high-quality evidence of impact on intrapartum-related outcomes in low-resource settings. While data from high-resource settings support planned cesarean for breech presentation and post-term induction, these interventions may be unavailable or less safe in low-resource settings and require risk-benefit assessment. Promising interventions include use of the partograph, symphysiotomy, amnioinfusion, therapeutic maneuvers for shoulder dystocia, improved management of intra-amniotic infections, and continuous labor support. Obstetric drills, checklists, and innovative low-cost devices could improve care quality. Task-shifting to alternative cadres may increase coverage of care. *Conclusions:* While intrapartum care aims to avert intrapartum-related hypoxic injury, rigorous evidence is lacking, especially in the settings where most deaths occur. Effective care at birth could save hundreds of thousands of lives a year, with investment in health infrastructure, personnel, and research—both for innovation and to improve implementation.
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1. Introduction

1.1. Why focus on care at the time of childbirth?

Childbirth is the time of greatest lifetime risk of mortality for a mother and her baby [1]. An estimated 42% of the world's 535 900 annual maternal deaths are intrapartum-related; these deaths are closely linked to the deaths of 1.02 million babies during labor and 904 000 intrapartum-related ("birth asphyxia") neonatal deaths [1–3]. Intrapartum-related insults also result in an unknown burden of disabilities and impairments—perhaps 1 million children each year [4]. In this Supplement, we follow the shift away from the term "birth asphyxia" as recommended by a series of consensus statements [1]. We use the term "intrapartum-related" for cause of death and "neonatal encephalopathy" for the acute complications manifesting soon after birth [5–7].

The advent of modern obstetric care, particularly intrapartum monitoring, the use of forceps and vacuum extraction, and cesarean delivery, has been correlated with historical declines in perinatal mortality in high-resource settings [8–13]. Prompt obstetric interventions are crucial to prevent intrapartum-related fetal hypoxic injury and maternal morbidity and mortality associated with obstetric emergencies. As the first paper in this series indicates, intrapartum obstetric complications are strong predictors of perinatal death [1]. For example, antepartum hemorrhage in the eighth month of pregnancy

* Corresponding author. Effective Care Research Unit, East London Hospital Complex, PB X9047, East London 5201, South Africa/University of the Witwatersrand/University of Fort Hare, South Africa. Tel.: +27 83 280 9402; fax: +27 43 708 761158.
E-mail address: gjh@global.co.za (G.J. Hofmeyr).

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is associated with a 3- to 6-fold increased risk of perinatal death, while obstructed labor, malpresentation, and breech are associated with a 7- to 85-fold increased risk. Furthermore, certain obstetric risk factors, such as maternal pyrexia and chorioamnionitis, may be synergistic with intrapartum hypoxia, markedly elevating the risk of neonatal encephalopathy [14–16]. Intrapartum risk factors more strongly predict perinatal death than prepregnancy (RR range, 1–5) and prenatal risk factors (RR, range 2–14), which have previously been the focus of risk screening tools for obstetric risk and are further examined in the fifth paper in this series [17].

Thus, the prompt emergency management of high priority intrapartum complications, or earlier effective identification and management of the related intrapartum risk factors (RR range, 2-85), may potentially reduce the substantial burden of fetal hypoxic injury [18].

1.2. Current coverage and constraints, key challenges

Neonatal mortality and maternal mortality are inversely associated with coverage rates of skilled birth attendance, emergency obstetric care (EmOC), and neonatal intensive care, at least in ecological analysis [1]. The countries with the highest rates of neonatal mortality (NMR>45) have the lowest rates of skilled attendance (median 46% vs 100% in countries with NMR<5), cesarean delivery (3% vs 17%), and physician density (11 per 100 000 population vs 131/100 000). The density of skilled personnel is 15-fold lower in the highest mortality settings, and in many low-resource settings these are the only personnel legally permitted to perform assisted vaginal delivery or cesarean delivery [19]. Thus, an enormous obstetric care *coverage gap* disadvantages the world's poor—60 million births occur annually outside of hospitals, 52 million of these without a skilled provider [20]. At least three-quarters of neonatal deaths and a similar proportion of maternal deaths occur in these suboptimal care settings [1]. Furthermore, a substantial *quality gap* exists because of failure to monitor pregnancy and labor, identify complications, and provide timely life-saving interventions. Population-level data are not available regarding the quality of obstetric care such as fetal heart rate monitoring and use of the partograph [19], but it is clear in both high-income and middle-income countries [21] that many intrapartum-related neonatal deaths have avoidable factors. Finally, obstetric care coverage has wide urban–rural and rich–poor *equity gaps*. In Sub-Saharan Africa and South Asia, rates of skilled birth attendance are 5-fold higher in the highest versus lowest wealth quintiles [1]. In Sub-Saharan Africa, in rural versus urban areas respectively, rates of skilled birth attendance are 29% versus 75%, and cesarean delivery rates are 1% versus 5% (Fig. 1).

1.3. Objectives of this review

In this paper, the second in a series that focuses on reduction of intrapartum-related deaths, we systematically review approaches during labor and birth to reduce these deaths in low-resource settings, including clinical interventions and strategies to increase coverage and quality. We evaluate impact on mortality outcomes including intrapartum-related neonatal mortality rate, early neonatal mortality rate (ENMR), neonatal mortality rate (NMR), intrapartum-related stillbirth rate, stillbirth rate (SBR), perinatal mortality rate (PMR), and maternal mortality ratio (MMR). We also consider non-fatal intermediate outcomes including neonatal encephalopathy and low Apgar score. We use the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) System to assess evidence quality and make recommendations [22].

This paper interprets available evidence for addressing high risk/high prevalence obstetric complications in the context of constraints in resource-constrained settings. We build on recent comprehensive reviews [23] and previous World Health Organization (WHO) guidelines that have made recommendations for care during normal childbirth [24], emergencies in pregnancy and childbirth [25], and newborn emergencies [26].

While there is a major supply-side gap for obstetric care, with long distances to facilities and lack of staff and equipment, there are also other barriers including financial constraints, cultural practices, and lack of empowerment of women to seek care, as well as wider health systems and governance issues. This paper focuses on supply-side constraints for childbirth care. Other papers in this series review linking families and facilities, including overcoming delays to care [17], and what can be done for 60 million non-facility births [27]. Neonatal resuscitation is an important adjunct to emergency obstetric care and is reviewed in the third paper [28]. Perinatal audit has potential to improve quality of care [29]. The final paper outlines a health systems approach to care at birth [19].

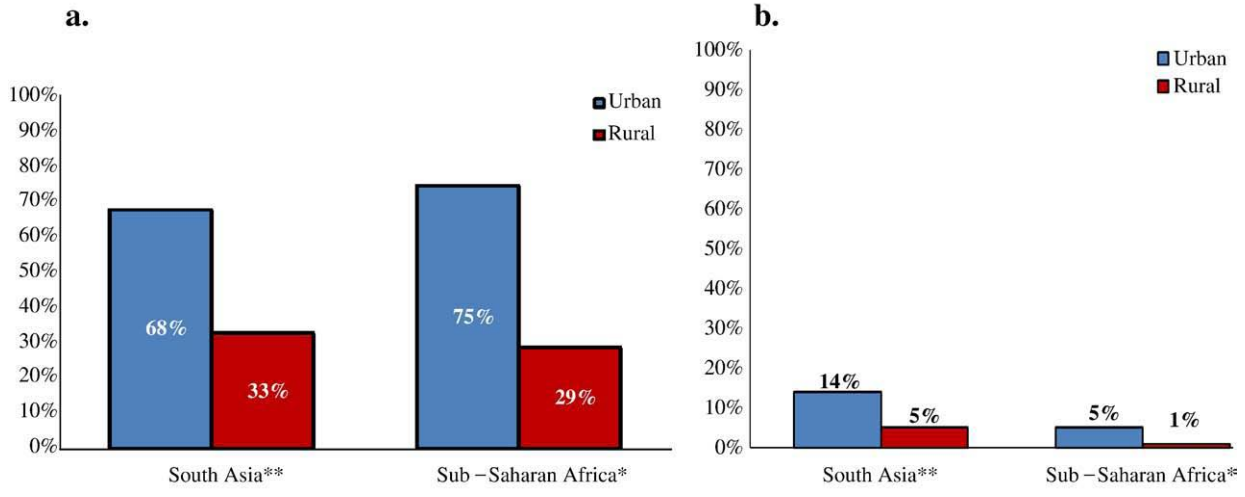

Fig. 1. Variation in rates of cesarean delivery performed for women in urban and rural populations. a. Skilled attendance at birth. b. Cesarean delivery. * Sub-Saharan Africa includes: Benin, Burkina Faso, Cameroon, Chad, Congo, Eritrea, Ethiopia, Gabon, Gambia, Ghana, Guinea, Kenya, Lesotho, Liberia, Madagascar, Malawi, Mali, Mauritania, Mozambique, Namibia, Niger, Nigeria, Rwanda, Senegal, Swaziland, Togo, Uganda, United Republic of Tanzania, Zambia, and Zimbabwe. ** South Asia includes: Bangladesh, India, Nepal, and Pakistan. Source: New analysis based on Demographic and Health Surveys 2000–2007; averages weighted to population.

2. Methods for searches, abstraction, and synthesis

Methods for the literature review are described in detail in the first paper in this series [1]. Searches of the medical literature were conducted using PubMed, Popline, EMBASE, LILACS, IMEM, African Index Medicus, Cochrane, and World Health Organization (WHO) document databases. Initial searches were conducted in November 2002 and September 2007; focused searches were updated in May 2009. Keyword searches for this manuscript are shown in an appendix in the online version (Appendix A). All effect sizes reported are relative percentage mortality rate reduction, as opposed to absolute percentage reduction.

The level of evidence was assessed using the GRADE system [30] criteria to evaluate the quality of the evidence (high, moderate, low, or very low) and given a recommendation for programmatic application (strong, weak, conditional). We use an adaptation of GRADE developed by the Child Health Epidemiology Reference Group (CHERG) specifically for low- and middle-income settings [31]. As our specific interest is for intrapartum-related ("birth asphyxia") outcomes, this is a particular constraint, as cause-specific data are limited [1].

3. Evidence for interventions to prevent and manage intrapartum complications

We review the evidence for impact on intrapartum-related mortality and morbidity of interventions to prevent and manage intrapartum complications, organized by obstetric emergency entry points with priority given to the entry points with the highest risk/population attributable risk for intrapartum-related mortality, notably: (1) obstructed labor; (2) breech position; (3) suspected fetal distress, (4) hemorrhage; (5) severe hypertension/pre-eclampsia; (6) post-term; and (7) intra-amniotic infection (Table 1). There are some important risk factors and complications not covered here, notably maternal diabetes and gestational diabetes. There are very limited data from low-income settings at present on prevalence, risk, and feasible interventions—this is an area to be highlighted for more research, especially in South Asia, which has a high prevalence of type II diabetes.

In reviewing the evidence we pay particular attention to:

1. The possibility that interventions that have not been proven effective in trials from high-resource settings could be effective in low-resource settings where there is greater scope for improvement in care.
2. The effect of the clinical context in shaping risk-benefit calculations regarding specific interventions: for example, availability of safe cesarean delivery. If cesarean delivery is unavailable but the mother's or baby's life would be lost without intervention, interventions that increase the risk of cesarean delivery, such as oxytocin induction with unripe cervix, are discouraged, while alternatives to cesarean delivery may be appropriate.
3. Novel or unexplored solutions to extend coverage of interventions including the need for further testing of these strategies. Such innovations may also have important implications for cost savings and service provision in high-resource settings.

3.1. Obstructed/prolonged labor

Obstructed labor affects between 3%–6% of live births [32], and is a major contributor to maternal and perinatal morbidity and mortality accounting for an estimated 43 000 maternal deaths annually. Obstructed labor is also the highest-risk obstetric condition for perinatal mortality, with reported adjusted odds ratio of up to 80-fold [1]. Obstructed and/or prolonged labor can result from cephalopelvic disproportion, fetal malpresentation or malposition, or inefficient uterine contractions (atony). Obstructed labor is usually managed via instrumental delivery or cesarean delivery, or labor augmentation for uterine atony, although other procedures such as symphysiotomy may have been relatively neglected (Table 1).

3.1.1. Slow progress of labor

3.1.1.1. Presenting problem. The first stage of labor is considered delayed if the rate of cervical dilation in the active phase is lower than 1 cm per hour. A second stage of labor exceeding 2 hours in a primigravida and 1 hour in a multipara (plus 1 hour if epidural anesthesia has been given) is considered delayed [33].

3.1.1.2. Evidence for partograph use. The partograph was designed to monitor the progress of labor where intrapartum surveillance may be limited by staff shortages and lack of experienced staff [34,35]. The partograph (also called the partogram) is a paper form designed to encourage regular assessment of maternal and fetal condition once active labor is established; alert and action lines provide objective guidance for intervention. The alert line reflects the average rate of cervical dilation of the slowest quintile of term primigravidas, if dilation slows or ceases, the partograph plot will cross the alert line [36]. Higher rates of perinatal mortality are associated with delays of 4 hours or more after the alert line, so the action line is 2–4 hours after the alert line, which prompts interventions to accelerate labor or perform cesarean delivery [37–39].

Individually randomized trials of use of the partogram in a clinical trial setting are useful for comparing variations in partogram design. Yet few studies have assessed partograph versus no partograph, the impact of which would be underestimated in higher-resource settings where all women have close surveillance by experienced clinicians, who may make similar decisions whether or not the partograph is used. Several studies examining partograph use have reported perinatal outcomes (Table 2). A Cochrane review of partograph versus no partograph found a non-significant reduced risk of cesarean delivery overall (2 studies, n = 1590; RR 0.64; 95% CI, 0.24–1.7), which was statistically significant in low-income settings (1 study, n = 434; RR 0.38; 95% CI, 0.24–0.61) [40]. There was no effect on the proportion of 5-minute Apgar scores lower than 7; perinatal mortality was not reported. In a large prospective WHO study in South East Asian hospitals (1994) [41], partograph use was associated with reduced prolonged labor (from 6.4% to 3.4%), need for augmentation (20.7% to 9.1%), emergency cesarean delivery (9.9% to 8.3%), and stillbirth (0.5% to 0.3%).

The WHO has developed a simplified partograph without the latent phase of labor [42] that has been shown in one trial to be more user-friendly ($P = 0.002$) and more likely to be completed than the composite partograph, while being associated with fewer cesarean deliveries and comparable perinatal and maternal outcomes. Outcome evaluation of the effectiveness of the simplified partograph at scale is needed, linked with improved fetal heart rate monitoring devices. In low-resource settings, partograph use is recommended for monitoring all women in labor, and can serve as a guide for timely referral to Comprehensive Emergency Obstetric Care (CEmOC) facilities.

3.1.1.3. Evidence for mother's position during labor. A mother's position during labor and birth may affect her comfort, the progress of labor, the baby's position, placental perfusion, and her ability to bear down effectively.

Cochrane reviews have associated upright postures with shorter first stage of labor (mean difference –0.99 hr; 95% CI, –1.60 to –0.39 hr), less use of epidural analgesia (RR 0.83; 95% CI, 0.72–0.96), and a trend toward fewer cesarean deliveries (RR 0.73; 95% CI, 0.51–1.07), with possible increased risk of postpartum hemorrhage [43]. In contrast, supine laboring positions increase the risk of fetal acidosis and prolonged labor [44]. Hands-and-knees position in late pregnancy and/or during labor showed no statistically significant reduction in

Table 1
Summary of interventions (preventive and operative) for reducing intrapartum-related fetal–neonatal death and disability, with GRADE evidence of impact, risk-benefit considerations, and alternatives in low-resource settings.

Obstetric complication entry point	Specific condition or indication	Intervention strategy	Evidence according to GRADE		Impact estimates from Cochrane reviews (if available)	Risk-benefit considerations in low-resource settings	Feasibility issues and alternatives in low-resource settings
			Level of evidence	Recommendation strength			
1. Obstructed/prolonged labor (including malposition/ malpresentation, multiple gestation, cephalopelvic disproportion, uterine atony, etc).	Slow labor/failure to progress (inefficient uterine contractions, uterine atony)	Active management (amniotomy plus oxytocin augmentation) Cesarean delivery for failure to progress	Low (high-resource settings)	Weak	No statistically significant intrapartum-related outcomes [201]	Very modestly decreased risk of cesarean; increased risk of intrauterine infection if aseptic technique cannot be or is not observed; risks of uterine hyperstimulation and fetal distress from oxytocin use [48,201]. Uterine rupture risk of oxytocics with prior uterine incision(s), esp. classical.	Not advised in women with prior cesarean, multiple gestations, or areas with high prevalence of HIV or hepatitis or seropositive patients. May be inadvisable as routine practice where sanitary conditions and/or cesarean access are poor.
	Delayed second stage	Controlled fundal pressure	Low	Weakly not recommended	–	Non-operative, widely used, but theoretical risk of fetal injury including brain damage, risk of maternal uterine rupture or anal sphincter tears; can worsen shoulder dystocia if present	Fundal pressure one of few options where operative delivery unavailable – more research required. See Table 3: Alternatives to cesarean
		Instrumental delivery	Low	Conditional	No RCTs of instrumental delivery versus none	See Table 4: Alternatives to cesarean	See Table 3: Alternatives to cesarean
		Symphysiotomy	Very Low	Strong	–	See Table 4: Alternatives to cesarean	See Table 3: Alternatives to cesarean
	Shoulder dystocia	Prevention by induction for suspected macrosomia*	Low	Weakly not recommended	Shoulder dystocia: RR 1.06 (95% CI, 0.44–2.56) [60] [Among diabetic women] Macrosomia: RR 0.56 (95% CI, 0.32–0.98); 0 vs 3 cases of shoulder dystocia [61]	Benefits of non-operative option, vs risk of inaccurate estimation of fetal size, risks of induction including fetal distress (Table 5)	See Table 3: Alternatives to cesarean
		Management using therapeutic maneuvers with cesarean delivery for failure to deliver	Very low	Strong	5-min Apgar <7: RR 0.44 (95% CI, 0.02–10.61)	Sequence of maneuvers used in clinical practice has never been tested for effectiveness (episiotomy, McRobert, suprapubic pressure, posterior traction, finger traction on arm, rotation of shoulders, and tocolysis followed by cesarean delivery)	Rarely seen, posing challenge for low-volume maternity facilities. Training should include practice on a mannequin and regular obstetric drills
	Uterine rupture	Emergency laparotomy plus uterine repair or hysterectomy	Very low	Strong	No outcome data	Access to cesarean delivery limited, risks of cesarean (Table 4). Greater skill required for emergency hysterectomy	No alternatives in areas lacking cesarean/ hysterectomy capability
2. Breech presentation	Breech identified after 34 weeks of gestation	External cephalic version*	Low-moderate (High-resource setting) Very low (Low-resource setting)	Strong	PMR: RR 0.51 (95% CI, 0.05–5.54) 5-min Apgar<7: RR 0.76 (95% CI, 0.32–1.77) [202]	Reduces risk of breech birth, and cesarean, but no statistically significant impact on perinatal outcome. Risks (cord prolapse, fetal distress, and fetal injury) increase with fetal growth restriction, uterine bleeding, prior cesarean, fetal abnormalities, twin pregnancy, hypertensive disorders. Some breech positions due to position of cord and should not be reversed.	Particularly useful in settings in which safe cesarean is not consistently available, but recommendations suggest continuous ultrasound and a skilled physician to undertake the procedure
		Planned (elective) cesarean section	Moderate (High-resource setting) Low (low-resource setting)	Strong (High-resource setting) Weak-Conditional (low-resource setting)	PM or neonatal morbidity: RR 0.33 (95% CI, 0.19–0.56) PMR: RR 0.29 (95% CI, 0.10–0.86) [203]	Eliminates risk of injury or obstruction of aftercoming head; reduced risk of perinatal or neonatal death. Risk-benefit of cesarean (Table 4)	Risks in subsequent pregnancy where cesarean access poor (see Table 4). Vaginal breech delivery safe and feasible for complete or frank breech **if** provider is skilled, fetal head flexed, and no CPD.
	Breech presentation identified in labor	Emergency cesarean delivery	Low	Strong	–	Higher risk of perinatal morbidity and mortality than planned cesarean	See Table 3: Alternatives to cesarean
3. Suspected fetal distress	Decreased or absent fetal movement, cord accident, fetal heart rate/blood flow changes, thick meconium	Fetal monitoring methods: See Tables 6 and 7					
		Amnioinfusion	Moderate	Weak	*For meconium staining* neonatal encephalopathy: RR 0.09 (95% CI, 0.02–0.49) 5-min Apgar <7 (RR 0.45; 0.27–0.75) and a trend toward reduced PMR (RR 0.34; 0.11–1.06) [82]	Risk of intra-amniotic infection	

					For umbilical cord compression PMR: RR 0.51 (95% CI, 0.11–2.24) Birth asphyxia: RR 0.32 (95% CI, 0.15–0.70) [83] 5-min Apgar <7: RR 0.54 (95% CI, 0.30–0.97)		
		In utero resucitation	Low	Strong	Lower risk of base deficit ≤ 12 mEq/L (RR 0.68; 95% CI, 0.45–1.0) Lower risk of NICU admission (RR 0.47; 95% CI, 0.27–0.81) in resuscitated group [18]	May resolve fetal distress and avoid cesarean delivery, may avoid need for neonatal resuscitation, particularly relevant where cesarean is unavailable and/or great distances to EmOC health facilities	Requires access to tocolytics and capacity to administer
4. Severe hypertensive disorders of pregnancy (esp. pre-eclampsia and eclampsia)	Highly elevated maternal blood pressure, with or without proteinuria (chronic hypertension, pregnancy-induced hypertension, HELLP); seizures (eclampsia)	Antihypertensive drugs if systolic>160 mm Hg or diastolic > 110 mm Hg (no particular anticonvulsant superior)	Low	Weak	PMR: RR 0.98 (95% CI 0.88, 1.10) 5-min Apgar <7: RR 1.02 (95% CI 0.85, 1.22)	Potential toxicity, continuous maternal and electronic fetal monitoring advised.	Adequate fetal monitoring may be unavailable; lack of diagnostic capacity in some settings to monitor maternal organ function
		Anticonvulsant drugs (IV magnesium sulfate)	Very low	Conditional	Eclampsia: RR 0.41 (95% CI, 0.29–0.58, NNT 100) Placental abruption: RR 0.64 (95% CI, 0.50–0.83; NNT 100) [204]	Potential toxicity (rare) vs presence of seizures (or risk of eclampsia in severely pre-eclamptic patients); low cost and availability of MgSO4 in low-resource settings	Many settings lack monitoring capability for oxygen saturation, resuscitative equipment, catheterization, calcium gluconate for hypermagnesemia. NB: Severe malaria can resemble eclampsia.
		Early or rapid delivery for severe pre-eclampsia or eclampsia (Induction or elective or emergency cesarean)	Low (high-resource settings) Very low (low-resource settings)	Strong (high-resource settings) Strong (low-resource settings)	–	Risks and benefits associated with induction and elective cesarean in low-resource settings, especially iatrogenic prematurity (Tables 2 and 7)	Constraints associated with induction and cesarean delivery in low-resource settings (Tables 2 and 7)
5. Antepartum hemorrhage	Suspected placenta previa	Ultrasound confirmation of previa to confirm diagnosis, plan elective cesarean	Low	Moderate	–	Perinatal mortality reduced with diagnosis prior to labor. Ultrasound may not be available. Anticipate hemorrhage with vaginal delivery. Cesarean for previa increases risk of uncontrollable hemorrhage and complications including infection, injury of maternal bowel/bladder, and/or hysterectomy; consider surgical skill and access to safe blood transfusion (Table 4)	Impractical and hazardous at population level to diagnose without ultrasound. Rapid delivery may be risky or impossible where instrumental delivery, blood bank, and/or cesarean are unavailable, but few alternatives exist
		Cervical cerclage	Moderate	Weak. Not recommended in low-resource settings	5-min Apgar <7: RR 0.19 (95% CI, 0.04–1.00) likely attributable to reduced preterm birth, not prevention of hypoxic injury [110].	Procedure can cause hemorrhage or infection; requires diagnosis of placenta previa (difficult in low-resource settings)	Capacity to diagnose previa and insert stitch limited in settings without ultrasound and trained practitioners. No acceptable alternatives
	Placental abruption	Rapid delivery (labor induction or augmentation with or without instrumental delivery; or emergency cesarean), blood transfusion	Very low	Strong	No outcome data [110]	Access to cesarean limited, risks of cesarean (Table 4), access to safe blood transfusion	Alternatives to cesarean (see Table 3)
6. Post-term pregnancy	Suspected post-term pregnancy	Membrane sweeping at or after 41 weeks of gestation	Very low	Weak		Prostaglandin release often induces labor; more likely effective in true post-term pregnancy than pregnancy with incorrect gestational assessment. Risk of infection or premature membrane rupture	Training needed to minimize risks of infection or membrane rupture
		Routine induction of labor at 41–42 weeks	Moderate (high-resource settings) Low (low-resource settings)	Strong (high-resource settings Weak (low-resource settings)	PMR: RR 0.30 (95% CI, 0.09–0.99) Apgar<7: RR 0.85 (95% CI, 0.48–1.48) at 41 completed weeks; RR 0.24 (95% CI, 0.05–1.10) at 42 completed weeks	Reduced PMR and cesarean for fetal distress; reduced meconium aspiration. Risks associated with induction (Table 7)	May be inadvisable where few women have early ultrasound and/or intrapartum fetal surveillance and/or cesarean is unavailable
7. Maternal intrauterine infection	Tender uterus, fever, rapid fetal heart rate, offensive amniotic fluid	Antibiotics plus delivery	Low (indirect from high-resource settings)	Strong	No documented impact on intrapartum-related outcomes; however, reduced risk of chorioamnionitis and/or endometritis	No evidence of impact on all-cause neonatal mortality [122]; low risk intervention, but management depends on gestational age (risk of infection vs risk of prematurity)	Rapid delivery usually indicated; emphasis on prevention may be best strategy in resource-poor settings (prenatal screening for infections, minimal vaginal exams, clean hands, cautious use of amniotomy)

* Preventive interventions.

Table 2
Intrapartum monitoring impact using the partograph.

Intervention/study	Setting	Baseline MMR (per 100 000) and NMR (per 1000)*	% skilled attendance*	Impact percentage reduction in mortality rate (*measure of association, number of deaths*)					Investigator and year
				SBR	ENMR	PMR	NMR	MMR	
Before-and-after comparison of pregnancy outcomes using partograph versus standard intrapartum care	Multicentre trial in 4 pairs of hospitals in SE Asia (Indonesia (2), Thailand (1), Malaysia (1))	MMR: Indo: 450 Malay: 53 Thail: 50 NMR: Indo: 17 Malay: 5 Thail: 9	Hospital-based: 81%	38% (IP SB) (*n* = 148)	-		-		WHO Safe Motherhood program [41] 1994
Comparison of avoidable perinatal deaths in hospital between 1971–76 and 1977–79 (partograph implemented with standard protocols to decrease high rate of avoidable IP SB)	Rural Tanzania, small hospital serving population of 75 000 with ~24% deliveries in hospital	MMR: not available NMR: 35	Deliveries mainly by "medical aides" National rate: 39%	-	-	40% (*n* = 173)	-	-	Van Roosmalen [205] 1989
Comparison of outcomes for women who crossed the alert and action lines on the partograph	Senegal Pikine hospital and four peripheral maternity clinics	MMR: 430 NMR: 35	Midwives and CHWs National rate: 47%	46%[b] (IP SB) (*N* = 10)					Dujardin et al. [206] 1992
Ongoing audit with implementation of changes, including management guidelines, use of partograph, and training	South Africa rural district health service 1991–1995 21 112 births	MMR: 150 NMR: 17	>80% National rate: 84%	-	-	36%[a] (*n* = 653 weight >1000 g)	-	-	Wilkinson [207] 1997
Cluster-RCT comparing the WHO partograph with standard midwifery care	Medan City, Indonesia. 626 pregnant women serviced by midwives	MMR: 420 NMR: 17	Maternity-home-based using midwives National rate: 73%	38% (fetal death; OR 0.62; 95% CI, 0.17–2.19)	30% (OR 0.70; 95% CI, 0.16–3.11)	-	-	-	Fahdhy [208] 2005
Before-and-after study of use of partograph in breech delivery	Indonesia, Thailand, Malaysia, subset of WHO 1994 study	MMR: Indo: 450 Malay: 53 Thail: 50 NMR: Indo: 17 Malay: 5 Thail: 9	Hospital-based, 1740 breech presentations	42% (breech SB, 1.1% (*n* = 8) vs 1.9% (*n* = 16), *P* = 0.163)	-	-	-	-	Lennox [209] 1998

Abbreviations: MMR, maternal mortality ratio; NMR, neonatal mortality rate; SBR, stillbirth rate; ENMR, early neonatal mortality rate; PMR, perinatal mortality rate.
* For MMR, NMR, and skilled birth attendance where data were not reported in the study, we sought data regarding national status on MMR, NMR, and skilled birth attendance from UN databases to give the context.
[a] Avoidable deaths reduced from 19% to 0%, with a high of 30%.
[b] 46% reduction in fresh stillbirth rate if intervention commenced when alert line crossed rather than waiting for action line.

malpresentation, malposition, or operative delivery [45]. The supine position should be avoided during labor and birth; women who wish to be mobile during first stage and upright during second stage of labor should be encouraged and assisted to do so.

3.1.1.4. Evidence for active management of the progress of labor. Active management of the progress of labor (distinct from active management of the third stage of labor to prevent postpartum hemorrhage) may prevent dystocia and reduce cesarean delivery rates. Active management involves strict criteria for the diagnosis of labor, early amniotomy, early oxytocin (with high-dose oxytocin in case of inefficient uterine action), and continuous intrapartum professional support (see item 4.4) [46,47].

A Cochrane review of active management to prevent slow labor among women in spontaneous labor reported a slightly reduced risk of cesarean delivery in the actively managed group (RR 0.88; 95% CI, 0.77–0.99, risk difference 1.47%, NNT = 68) and modestly reduced time from admission to birth (mean difference 1.1 hr; 95% CI, 0.41–1.82 hrs) [48]. There were no differences in perinatal morbidity or mortality indicators. Another Cochrane review of an active management package of care among low-risk women also found a modest reduction in cesarean risk, but no impact on perinatal outcomes (Table 1) [49]. Active management in both studies was associated with increased risk of uterine hyperstimulation and possible fetal heart distress, probably as a consequence of monitoring bias.

In Kalafong, South Africa, because of human resource constraints, nursing staff were insufficient to provide the continuous intrapartum support component of active management. A randomized controlled trial (RCT) was conducted comparing expectant management (vaginal exams every 4 hours, with oxytocin infusion only after the action line was crossed) with a protocol of "aggressive" management (use of the partograph and vaginal exams every 2 hours, with oxytocin infusion if the alert line was crossed). The trial reported a significantly lower risk of cesarean delivery in the aggressively managed group (RR 0.68; 95% CI, 0.50–0.93). Labors were also shorter, but there was no difference in neonatal outcomes; the authors concluded that early oxytocin is more effective than delayed use, but caution that this strategy requires more intensive nursing, although nursing burden is offset by more rapid labors [49].

Because each of the components of active management of labor has associated risks, including infection, hyperstimulation, and fetal distress, and need for cesarean, which may be of greater importance in low-resource settings, active management requires further study in these settings.

3.1.1.5. Evidence for the use of fundal pressure. Fundal pressure, a routine obstetric practice in many low- and high-resource settings, involves application of manual pressure to the uterine fundus directed toward the birth canal to avoid prolonged second stage and/or operative delivery (Table 3).

Fundal pressure is controversial, as anecdotal reports have associated its use, particularly if forceful, with maternal and fetal morbidities. In Turkey, a small RCT (n = 197) of fundal pressure reported no differences in duration of second stage of labor or fetal-neonatal morbidity or mortality between the control and intervention groups; however, mean pO2 was lower and mean pCO2 was higher in the fundal pressure group compared with controls (both measures were still in the normal range) [50]. A possible contributing factor was that fundal pressure was applied in the intervention group regardless of the progress of labor. Another RCT using an inflatable girdle also found no difference in duration of labor [51]. Data on intrapartum-related mortality and non-fatal outcomes associated with fundal pressure for delayed second stage would be particularly relevant to low-resource settings where assisted births or cesarean delivery is unavailable. Fundal pressure is not recommended for routine care, as its effectiveness and safety in women with a prolonged second stage of labor

Table 3
Alternatives to cesarean delivery in low-resource settings.

Alternative option GRADE evidence/recommendation	Description	Evidence of risk and benefit	Advantages and applications	Constraints
Fundal pressure* Low quality of evidence/Weak recommendation against	Application of manual pressure to the top of the uterus toward the birth canal to assist spontaneous vaginal delivery	Anecdotal reports of uterine rupture, maternal anal sphincter tears [210,211], neonatal fractures, or adverse neurological outcome; 2 small RCTs showing no impact of fundal pressure on duration of 2nd stage of labor (when used whether or not labor was delayed) and no neonatal encephalopathy (intervention or control) [50]	- May reduce prolonged labor and/or need for instrumental delivery - Relevant where assisted delivery, cesarean unavailable - Inflatable girdle can be used	Widely practiced but further research needed to determine effectiveness and optimal technique to reduce risk of maternal or fetal injury
In utero resuscitation* Low quality of evidence/Strong recommendation for	If fetal distress likely caused or worsened by uterine hyperstimulation, stopping oxytocin infusion and/or tocolysis can improve placental perfusion. Advised while preparing for cesarean section (ACOG) or during emergency transfer	RCT of in utero resuscitation for non-reassuring cardiotocography indicated lower risk of base deficit ≤12 mEq/L (RR 0.68; 95% CI, 0.45–1.0) and lower risk of NICU admission (RR 0.47; 95% CI, 0.27–0.81) in resuscitated group [18]	- May resolve fetal distress and avoid cesarean delivery - May avoid need for neonatal resuscitation - Particularly relevant where cesarean delivery is unavailable and/or great distances to EmOC health facilities	Requires access to tocolytics and capacity to administer
Instrumental delivery (vacuum extraction or forceps) Moderate quality of evidence/ Conditional recommendation for	Utilization of mechanical methods of traction applied to the fetal head to facilitate delivery	No RCTs of instrumental delivery vs none, only between methods, few with mortality outcomes [212]	- Can avoid cesarean delivery if unavailable or inadvisable - May be best option if fetal station precludes cesarean - Inexpensive manual vacuum extractor available [53]	Availability of equipment Choice of instrument depends on experience and preference of birth attendant
Symphysiotomy* Low quality of evidence/Strong recommendation for	An emergency procedure to widen the pubic symphysis during obstructed labor	No trials of symphysiotomy. Review of 5000 cases found very favorable results [54]	- May be life-saving where cesarean unavailable or culturally unacceptable - Quick, minimal equipment, local analgesia - "Modern" (partial) symphysiotomy has low morbidity and associated maternal mortality - Avoids increased uterine rupture risk in subsequent pregnancies associated with cesarean [213]	Strong global opposition as rarely practiced in high-resource settings, viewed as poor substitute for cesarean. Not an option after failed forceps Provider must be trained (teaching video on WHO Reproductive Health Library)

* Requires further research.

are unknown. Because it is so widely used, further research is important to provide adequate evidence for its use to be discouraged or promoted.

3.1.1.6. Evidence for instrumental birth. Instrumental birth (also called assisted vaginal delivery) utilizes traction applied to the fetal head in cases of obstructed or prolonged second stage of labor to accelerate birth, and is one of the components of Basic Emergency Obstetric Care (BEmOC). Either forceps or a vacuum extraction device (also called a *ventouse*) can be used to provide traction. The use of either instrument has been associated with birth trauma, although rates of injury are extremely low when performed by well-trained practitioners. Instrumental delivery may be conducted in an effort to avoid cesarean delivery or where cesarean delivery is unavailable. The risks and benefits to both mother and baby of cesarean delivery compared with vaginal delivery should be carefully considered in low-resource settings, particularly where cesarean delivery capabilities at facilities are suboptimal or women may not have ready access to safe repeat cesarean delivery during subsequent pregnancies, placing them at risk for uterine rupture and maternal death (Table 3).

Historical data suggest an ecological association between introduction of forceps (with aseptic technique) and declining perinatal mortality [8,12]; however, there are no RCTs of instrumental delivery versus no intervention, and virtually all data comparing forceps to vacuum extraction are from high-resource settings. A Cochrane review of vacuum extraction versus forceps found that few studies reported mortality outcomes; the review identified no statistically significant difference in mortality (OR 0.80; 95% CI, 0.18–3.52) or Apgar scores comparing vacuum versus forceps, respectively [52]. Vacuum extraction was associated with a slight increase in risk of neonatal injury (cephalhematoma and retinal hemorrhage) but a significantly lower risk of maternal trauma (OR 0.41; 95% CI, 0.33–0.50) and a trend toward lower risk of cesarean delivery (OR 0.56; 95% CI, 0.31–1.02). Vacuum extraction attempts were more likely to fail than forceps (OR 1.69; 95% CI, 1.31–2.19). A meta-analysis of vacuum extraction versus forceps found a statistically non-significant reduction in stillbirth risk (OR 0.60; 95% CI, 0.07–5.00) [13].

While instrumental birth clearly has the potential to be life-saving, there is a dearth of evidence comparing any instrumental birth mode with cesarean delivery, other intervention, or non-intervention. The optimal choice of instrument appears to depend largely on provider skill and availability of equipment. Vacuum extraction may be preferable where available based on its association with lower maternal morbidity, fewer cesarean deliveries, and superiority for managing certain fetal malpositions (e.g. deflexed occipital posterior). Inexpensive manual vacuum extractors are available that may expand access to this intervention, which is weakly recommended based on the lack of data on its use from low-resource settings [53].

3.1.1.7. Evidence for the use of symphysiotomy. Symphysiotomy is a surgical procedure to widen the pubic symphysis, which has recently been revisited as an alternative to cesarean delivery in some settings (Table 3). Reviewing more than 5000 documented cases of symphysiotomy in the literature, Bjorklund [54] demonstrated that symphysiotomy: (1) compares favorably with cesarean delivery in terms of risk for the mother's life and is equal to cesarean delivery in terms of risk to the newborn's life as PMR in 4 studies from 1973 to 1995 was 37 out of 307 (12.1%) versus 66 out of 571 (11.6%) in symphysiotomy versus cesarean cases, respectively; (2) confers a permanent enlargement of the mother's pelvic outlet while avoiding a cesarean scar and risk of subsequent uterine rupture; and 3) severe long-term complications are rare. Maternal postoperative pain and discomfort is an issue; however, this may be comparable to post-cesarean section pain. The authors also observed that symphysiotomy has been successfully used for the obstructed aftercoming head of the breech baby, and is appropriate in women who are poor candidates for surgery and/or anesthesia, including those with intrauterine infection. Ersdal et al. [55] confirmed that symphysiotomy results in a permanent widening of the symphysis joint while avoiding a cesarean scar, which facilitates future vaginal deliveries in women with a contracted pelvis. The "modern" form (partial symphysiotomy or Zarate procedure, developed in the early 20th century) has very low risk of maternal morbidity and mortality [56], although fetal and neonatal outcomes are infrequently reported.

When performed by a trained provider, symphysiotomy is a safe and important alternative to cesarean delivery [57]. Unfortunately, global opposition to symphysiotomy has cast the procedure as a poor substitute for cesarean delivery, and many providers are inexperienced with the symphysiotomy technique. Limited available data suggest that symphysiotomy is life-saving; further operational research is needed regarding training of providers and strategies for overcoming biases against the procedure. Symphysiotomy is strongly recommended where cesarean delivery is not available or culturally unacceptable [58,59] or the balance of risks may differ (Table 4). In its forthcoming version of the IMPAC manual, the WHO is endorsing symphysiotomy as a valuable additional management alternative in selected cases of prolonged labor. Further research on safety and effectiveness is encouraged.

3.1.2. Shoulder dystocia

3.1.2.1. Presenting problem. Shoulder dystocia occurs when birth becomes obstructed after birth of the baby's head and is fatal for the baby if not quickly resolved; various obstetric maneuvers have been described to overcome the obstruction.

3.1.2.2. Evidence for prevention of shoulder dystocia. Strategies to prevent shoulder dystocia include early induction of labor for suspected macrosomia (especially in women with gestational diabetes mellitus) and a prophylactic McRobert maneuver (flexion of the woman's thighs towards her chest during the second stage of labor, performed with or without suprapubic pressure to dislodge the anterior shoulder).

A Cochrane review of induction for suspected macrosomia found a trend toward reduced neonatal trauma (brachial plexus injury or fracture) in induced versus expectantly managed groups (0/183 vs 6/189) [60]. Another Cochrane review of elective induction at 38 weeks in diabetic women documented a reduced risk of macrosomia in the active induction group (RR 0.56; 95% CI, 0.32–0.98); all 3 cases of mild shoulder dystocia occurred in the expectantly managed group [61]. A Cochrane review of the prophylactic McRobert versus therapeutic maneuvers found a non-significant reduction in cases of shoulder dystocia (RR 0.44; 95% CI, 0.17–1.14) and proportion of infants with 5-minute Apgar score less than 7 (RR 0.44; 95% CI, 0.02–10.61) [62]. There is insufficient evidence to recommend any preventive procedures; larger trials are needed.

Table 4
Cesarean delivery in low-resource settings: Balancing risks and benefits.

Risk-benefit considerations
• Elective/planned safer than emergency if cesarean delivery is inevitable • Consideration of alternatives to cesarean delivery (Table 3) • Maternal age and future childbearing intentions ◦ Consider access to safe cesarean delivery for future pregnancies (risk of uterine rupture) • Availability of safe blood transfusion in case of hemorrhage • Simplified cesarean (Misgav-Ladach/modified Misgav-Ladach) vs conventional (Pfannensteil-Dorffler/traditional lower midline cesarean) ◦ Simplified procedure associated with shorter operating time, less blood loss, and shorter postoperative maternal fever and complications [214] ◦ Insufficient data to assess risk of intrapartum-related perinatal outcomes or risk of uterine rupture in subsequent pregnancy by method ◦ Observational data suggests less risk of subsequent uterine rupture with double layer closure of the myometrium

Alternatives to general anesthesia
• Spinal anesthesia • Ketamine • Local anesthesia: WHO recommends local anesthesia as a safe alternative, especially in emergency situations, where general anesthesia/spinal/ketamine, or anesthetist, not available [25].

Advantages of local anesthesia	Disadvantages of local anesthesia
Does not require transfer from facility if local anesthetics available	Delivery is more challenging, as bowel and omentum may interfere, adhesions from prior cesarean delivery may cause difficulty, and delivery of baby in deep transverse arrest more difficult [215] Mother may experience more pain
Lower risk of fever, headache, pain and nausea after procedure	Pfannensteil incision should not be performed with local anesthesia (takes longer, retraction poorer, requires more anesthetic)

3.1.2.3. Evidence for management of shoulder dystocia. A sequence of maneuvers to manage shoulder dystocia (Table 1) has been developed in clinical practice but never assessed for effectiveness [63,64]. Despite this lack of evidence, because shoulder dystocia is rapidly fatal for the baby all birth attendants should be trained in empirical methods of resolving shoulder dystocia, including practice on a mannequin and regular obstetric drills [65,66]. This is particularly critical for small obstetric care centers, as shoulder dystocia may be rarely encountered where caseloads are light, thus requiring frequent refresher trainings to maintain competence.

3.1.3. Uterine rupture

3.1.3.1. Presenting problem. Uterine rupture is loss of integrity of the myometrium that may result from dehiscence of a prior cesarean delivery scar, dysfunctional or obstructed labor, uterine hyperstimulation with uterotonics, and high parity. When oxytocin or other uterotonic drugs are administered inappropriately to induce or augment labor, particularly by unskilled attendants, there is a risk of uterine hyperstimulation or rupture, increasing the risk of intrapartum hypoxic injury [67,68]. Traditional herbal uterotonics place both the mother and the fetus at risk for hypoxic insult and increase the risk of intra-amniotic infection when inserted directly into the vagina [69–71].

3.1.3.2. Evidence for management of uterine rupture. Uterine rupture is a life-threatening condition that is diagnosed clinically, and accepted standard of care is laparotomy and uterine repair or hysterectomy. Strategies to reduce the risk of uterine rupture include avoidance or reduced dosage of uterotonic agents for labor induction or augmentation (Table 5), use of the partogram to diagnose prolonged labor, and avoidance of "unnecessary" cesarean deliveries to reduce the risk of

Table 5
Induction of labor in low-resource settings: Balancing risks and benefits.

When induction may be unwise	
Absolute risk reductions in perinatal mortality after induction are small (e.g. for post-term pregnancy, 368 labor inductions needed to avoid one perinatal death) [216]. Induction in low-resource settings may pose more risk than benefit: • Where gestational age is not confirmed via ultrasound early in pregnancy. • Where Bishop score<6 and/or cervical ripening fails. • Where tocolytics are not available to counteract uterine hyperstimulation. • In HIV-positive patients (if amniotomy is performed). • For multiple pregnancy or grand multiparity [217,218]. • Where intrapartum monitoring capability is limited or ineffective. • Where safe cesarean delivery is unavailable. • In primiparous women (lower success rate of induction than in multiparas).	
Potential risks of induction	**Potential benefits of induction**
Increased risk of perinatal mortality or disability due to: • Uterine hyperstimulation from labor induction (risk greatest when prostaglandins and/or oxytocin are induction agents). • Iatrogenic prematurity from incorrect gestational estimation [219].	Decreased complications of postmaturity, including meconium aspiration and fetal distress.*
Increased risk of cesarean delivery due to induction-related suspected fetal distress or failed induction.	Reduced perinatal mortality when used for certain indications (e.g. post-term, term PROM)* [128].
Avoiding uterine hyperstimulation and fetal distress	
A premium should be placed on avoiding uterine hyperstimulation in settings without safe cesarean capacity when inducing with unfavorable cervix. Membrane sweeping is one safer option; alternatively, a Foley catheter with extra-amniotic saline infusion (EASI) 50 mL/hr can be supplemented with intravenous oxytocin if necessary, which is as or more effective than prostaglandins when oxytocin is administered (GRADE evidence level: Moderate; Recommendation: Conditional)	
If EASI is not feasible, oral misoprostol 25 μg (dosage may be prepared accurately by dissolving 200 μg tablet in 200 mL potable water and administering 25 mL 2-hourly) can be used with careful fetal surveillance and established protocol [220]. Oral misoprostol has lower risk of uterine hyperstimulation (RR 0.37; 95% CI, 0.23– 0.59) than vaginal misoprostol [221] (GRADE evidence level: Low; Recommendation: Conditional)	

* Studies from high-resource settings.

rupture in subsequent pregnancies (Table 4). There is no evidence from rigorous trials for the optimal management of uterine rupture.

3.2. Breech birth

3.2.1. Presenting problem

Approximately 3%–4% of pregnancies are complicated by breech presentation at term (37–42 weeks), [72] which is associated with an elevated risk of perinatal mortality up to 10-fold compared with normal delivery [1] and of long-term disability or developmental delay (18.7%) [73]. External cephalic version and planned cesarean delivery at term may reduce these risks.

3.2.2. Evidence for external cephalic version for breech presentation

External cephalic version involves manual manipulation of the baby from the breech to the cephalic presentation, with or without the use of tocolytic agents to relax the uterus, with careful fetal heart rate monitoring. Ideally, ultrasound is used to exclude fetal anomalies, multiple pregnancy, and placenta previa and to identify the position of the umbilical cord because external cephalic version should not be performed on some breech-position fetuses. It is usually performed between 36 and 40 weeks of gestation.

A Cochrane review of external cephalic version at term [72] reported a significantly reduced risk of non-cephalic birth (RR 0.38; 95% CI, 0.18–0.80) and cesarean delivery (RR 0.55; 95% CI, 0.33–0.91), but a non-significant reduction in risk of perinatal mortality (RR 0.51; 95% CI, 0.05–5.54) and 5-minute Apgar score less than 7 (RR 0.76; 95% CI, 0.32–1.77). Commencing external cephalic version before term may be more effective; another Cochrane review [74] of 3 RCTs with women at 34–35 weeks of gestation found a decreased risk of non-cephalic birth and cesarean delivery compared with no external cephalic version at term, but no differences in intrapartum-related mortality outcomes were reported. Where access to safe cesarean delivery for breech is limited or unavailable, or where a trial of cephalic vaginal labor is desired, external cephalic version is an important alternative, but requires further testing in settings where ultrasound and cesarean delivery are not available.

3.2.3. Evidence for planned Cesarean delivery for breech presentation at term

Planned cesarean delivery is a strategy to avoid obstructed labor or fetal injury/compromise arising during vaginal breech birth, particularly associated with delivery of the aftercoming head.

A Cochrane review found that compared with planned vaginal breech delivery, planned cesarean delivery was associated with substantially reduced risk of perinatal mortality (excluding fatal anomalies) (RR 0.29; 95% CI, 0.10–0.86) [75]. Risks of complications and perinatal mortality were lower for elective than emergency cesarean delivery; ideally, breech presentation should be diagnosed prenatally to permit planned elective cesarean delivery. Reduction in relative risk of perinatal death was smaller and not significant in countries with a high PMR (RR 0.66; 95% CI, 0.35–1.24) than a low PMR (RR 0.07; 95% CI, 0.02–0.29).

Considering the small absolute risk reduction and no differences in long-term outcomes attributable to planned cesarean, selected vaginal breech delivery may be preferable in some low-resource settings, if the provider has sufficient skills (Tables 3 and 4).

3.3. Suspected fetal distress

3.3.1. Presenting problem

Intrapartum fetal distress has been presumed to indicate fetal hypoxia, which is associated with perinatal morbidity/mortality and long-term disability [76]. In South Africa, the Perinatal Problem Identification Programme found that inadequate intrapartum fetal heart rate monitoring, and consequent failure to identify intrapartum fetal distress and subsequently intervene, were common factors in neonatal deaths [18,77]. Accurate assessment of fetal well-being can improve recognition of and response to suspected distress. However, assessment relies on indirect and complex evidence including fetal movements, heart rate, vascular flow, and/or blood oxygenation, as well as amniotic fluid volume and appearance. The prevalence of diagnoses of fetal distress is directly proportional to the intensity of intrapartum monitoring.

Suspected fetal distress suggests the need for immediate delivery, often by cesarean, although amnioinfusion and in utero resuscitation have been proposed as alternative interventions to resolve distress (Table 1). An important consideration with fetal monitoring is the high rates of false positives for fetal distress associated with most intrapartum fetal monitoring methods, coupled with the poor ability to interpret monitoring results, that may both contribute to unnecessary cesarean deliveries [78].

3.3.2. Evidence for fetal monitoring to identify fetal distress

If continuous cardiotocography were affordable, systematic reviews comparing it with intermittent auscultation found increased rates of cesarean delivery and instrumental deliveries without evidence of long-term benefits (Table 6). Where safe cesarean delivery is not readily available, investment in such costly intrapartum monitoring equipment is not advisable (Table 4). Few options exist for fetal monitoring that are effective, simple, *and* affordable, but some promising monitoring strategies should be implemented and tested in low-resource settings, while others should be avoided (Tables 6 and 7).

Table 6
Fetal monitoring methods to identify fetal distress not recommended for use in low-income settings.

Monitoring strategy GRADE evidence/recommendation	Reasons for not recommending use
Continuous electronic fetal heart rate monitoring (cardiotocography) Moderate evidence/Strongly not recommended	• Expensive equipment and hard to sustain (e.g. expert maintenance, requires disposables). • Requires skill to interpret. • No impact on PMR compared with intermittent auscultation (RR 0.85; 95% CI, 0.59–1.23, n = 33 513, 11 trials). • Significant increase in cesarean delivery (RR 1.66; 95% CI, 1.30–2.13, n = 18 761, 10 trials) and instrumental birth (RR 1.16; 95% CI, 1.01–1.32, n = 18 151, 9 trials). • Reduction in neonatal seizures (RR 0.50; 95% CI, 0.31–0.80, n = 32 386, 9 trials) but trend toward increased risk of cerebral palsy (RR 1.74; 95% CI, 0.97–3.11, n = 13 252, 2 trials) [222].
Electronic fetal electrocardiogram assessment Moderate evidence/Strongly not recommended	• Complex and costly equipment, including scalp electrode. • Requires high level of expertise. • Risk of infection, requires ruptured membranes. • No advantage over cardiotocography alone in reducing PMR (RR 1.64; 95% CI, 0.5–5.28), neonatal encephalopathy (RR 0.37; 95% CI, 0.14–1.00), or 5-min Apgar <7 (RR 0.78; 95% CI, 0.56–1.08) [223]. • Inappropriate for settings with high HIV or hepatitis prevalence.
Fetal pulse oximetry Low evidence/Strongly not recommended	• Expensive equipment. • Technical problems obtaining adequate quality records [224]. • Slight reduction in risk of cesarean delivery (RR 0.68; 95% CI, 0.47–0.99); no impact on PMR, neonatal encephalopathy (RR 0.34; 95% CI, 0.01–8.44), or 5-min Apgar<7 (RR 0.71; 95% CI, 0.17–2.91) compared with cardiotocography alone
Assessment of amniotic fluid for meconium as indicator of distress Very low evidence/Weakly not recommended	• Very poor correlation between meconium staining and fetal condition [225–227]. • Meconium passage may be related to fetal maturity, transplacental exposure to smooth muscle stimulants such as herbal alkaloids, castor oil, rather than distress; alternatively, may be response to short-lived episode of fetal hypoxia.

Optimal monitoring options need not be expensive or intensive: an RCT in an urban hospital in Harare, Zimbabwe, found that intermittent use of the hand-held Doptone device compared with continuous cardiotocography led to similar rates of cesarean delivery (28% versus 24%) and comparable fetal outcomes [79]. A robust hand-held Doptone using wind-up technology rather than batteries has been developed for use in low-resource settings. In a limited clinical trial, women in labor preferred it to the Pinard stethoscope or cardiotocography [80]. A key research gap in the available arsenal of fetal monitoring is techniques to assess fetal distress in low-resource settings.

3.3.3. Evidence for amnioinfusion

Amnioinfusion refers to the augmentation of amniotic fluid with sterile saline, which may dilute meconium (if present) and thereby reduce the risk of meconium aspiration, and/or alleviate cord compression to correct fetal hypoxia. Amnioinfusion has been piloted in a low-resource setting without electronic fetal monitoring using a low-cost catheter [81].

One Cochrane review studied amnioinfusion for meconium staining [78]. Two studies in settings with limited peripartum surveillance reported a lower risk of meconium aspiration syndrome (RR 0.25; 95% CI, 0.13–0.47); neonatal ventilation or neonatal intensive care unit admission (RR 0.52; 95% CI, 0.37–0.73); and a trend toward reduced perinatal mortality (RR 0.37; 95% CI, 0.13–1.01). Neonatal encephalopathy was substantially reduced in one trial (649 women; RR 0.07; 95% CI, 0.01–0.56). In well-resourced settings, amnioinfusion for meconium-stained amniotic fluid had no statistically significant effect on substantive maternal or perinatal outcomes other than

Table 7
Fetal monitoring methods to identify fetal distress recommended for use in low-income settings.

Monitoring strategy GRADE evidence/recommendation	Description	Feasibility in low-income settings	Constraints
Intermittent auscultation Very low evidence/Strong recommendation	Listening to fetal heart with Pinard stethoscope to detect the baseline heart rate as well as early or late fetal heart rate decelerations.	• Inexpensive, non-invasive. • Preserves freedom of movement. • Essential for confirmation that baby is alive.	• Requires well-trained practitioner. • Less comfortable for mother than monitoring with Doptone. • Effectiveness in improving perinatal outcome not yet assessed.
Simplified umbilical artery Doppler Moderate evidence/Strong recommendation	Abnormal umbilical artery waveforms have been linked with adverse perinatal outcomes [228] and Doppler in high-risk pregnancies has been linked with reduced risk of perinatal death (RR 0.71; 95% CI, 0.50-1.01) compared to no ultrasound [229]. A simplified version of the Doppler ultrasound is a portable, continuous wave apparatus without ultrasound imaging.	• Less expensive than traditional Doppler; low-cost personal computer screen can be used as display. • Requires minimal training for low-level health workers [230]. • Could also be used as a screening test for fetal well being in early labor.	• More research needed to develop low-cost Doppler devices for low-income settings. • Effectiveness of simplified device in setting has not been tested.
Fetal blood sampling Low evidence/Conditional recommendation	Used to detect hypoxia and regarded as "gold standard" of fetal well being, involves oxygenation analysis of blood sample from fetal scalp.	• Recommended if equipment is available and infection risk to fetus is minimal.	• Requires expensive blood gas analyzer equipment and trained technician. • Requires ruptured membranes. • Fetal infection risk in areas with high HIV or hepatitis.
Doptone (hand-held Doppler) Moderate evidence/Weak recommendation	Hand-held device to detect fetal heart movement and count the fetal heart rate, either manually or displayed on an LED screen.	• Less technically challenging than auscultation. • Can identify late fetal heart rate decelerations. • Lower PMR (2/312 vs 14/625) and neonatal encephalopathy (1/312 vs 17/625) than with auscultation [79].	• Requires considerable provider training and skill to interpret. • Dependent on batteries/electricity, but robust wind-up version available.

neonatal ventilation or neonatal intensive care unit (NICU) admission (3 studies, 472 women; RR 0.45; 95% CI, 0.23–0.90) [82] and cesarean delivery (RR 0.70; 95% CI, 0.49–1.00). A second Cochrane review of amnioinfusion for umbilical cord compression [79] found a statistically non-significant reduction in perinatal mortality (RR 0.51; 95% CI, 0.11–2.24); however, significant reductions in risk of "birth asphyxia" (RR 0.32; 95% CI, 0.15–0.70) [83] and 5-minute Apgar less than 7 (RR 0.54; 95% CI, 0.30–0.97). For managing fetal distress, amnioinfusion is a weakly recommended intervention, and a priority area for further research.

3.3.4. Evidence for in utero resuscitation

In utero resuscitation (intrauterine resuscitation) is a strategy to minimize or resolve fetal distress likely caused or worsened by uterine hyperstimulation, whereby oxytocin infusion is stopped and/or tocolytics and respired oxygen are administered with the mother in the left lateral recumbent position, theoretically allowing time and improved placental perfusion for the baby to recover from fetal acidosis. The procedure can be performed in conjunction with amnioinfusion if membranes are ruptured. In utero resuscitation is advised by the American College of Obstetricians and Gynecologists (ACOG) while preparing for cesarean delivery or during emergency transfer [84,85].

There is no evidence from rigorous trials for an impact of in utero resuscitation on intrapartum-related outcomes, but an RCT of in utero resuscitation for non-reassuring cardiotocographic tracings showed that the resuscitated group had a lower risk of base deficit of 12 mEq/L or lower (RR 0.68; 95% CI, 0.45–1.0) and lower risk of NICU admission (RR 0.47; 95% CI, 0.27–0.81) [18]. Further research on in utero resuscitation is urgently needed.

3.3.5. Further research areas

In addition to further operational and effectiveness research on the recommended strategies in Table 7, other options hold promise for identifying and/or managing fetal distress in low-income countries (presented below in order of feasibility and promise), but cannot yet be recommended:

- ***Clinical fetal arousal tests:*** Noise or vibration can be used to stimulate fetal response (movement or heart rate changes) as reassurance of fetal well being; there is a high level of correlation in fetal condition assessment between fetal arousal testing and fetal blood sampling [86]. Minimal or no electronic equipment is needed (e.g. electric shaver or toothbrush, a soft drink can, or physically jostling the baby or stimulating the fetal scalp) [87–90]. Effectiveness of this strategy has not been assessed in RCTs but is promising.
- ***Amniotic fluid volume assessment*:** While abnormal amniotic fluid levels are clearly associated with adverse perinatal outcomes, ultrasound assessment of amniotic fluid volume has not demonstrated an impact on perinatal outcome [91]. Further research is needed on the accuracy of clinical assessment of amniotic fluid volume and the impact of subsequent interventions.
- ***Enquiring about fetal movement on admission:*** In cases of inadequate placental perfusion and infections, fetal movements usually decrease then cease some days before intrauterine death [92,93]; maternal perception of decreased movement may provide early warning of fetal distress. The intervention requires no equipment and minimal training but does require uniform prenatal education of mothers. A large cluster RCT in Europe included in the systematic review [89] found that prenatal fetal movement counting identified babies at risk of death, but had no impact on the actual number of deaths. It is possible that the effect of the intervention was obscured by contamination, as informal fetal movement counting could not be prevented in the control group. Rates of unexplained fetal death were considerably lower in both groups than before commencement of the trial. The scope for inquiry about fetal movements to improve outcomes may be greater in settings where general knowledge of the significance of fetal movements is lower. This would need to be confirmed by trials in such settings.

3.4. Management of hypertensive disorders in pregnancy

3.4.1. Presenting problem

High blood pressure with or without proteinuria complicates 5% of all pregnancies and 11% of first pregnancies [94]. Pre-eclampsia (high blood pressure with proteinuria) and eclampsia (seizures) occur in 2%–8% of pregnancies [95] and increase the risk of maternal death, premature delivery, and perinatal mortality [96] associated with impaired utero-placental blood flow causing fetal hypoxia or placental abruption [97]. Risk of perinatal mortality may be increased 2- to 14-fold, also varying with severity of the condition [1].

Antiplatelet agents and calcium supplementation have been shown to prevent pre-eclampsia [98], but the only known cure for severe pre-eclampsia and eclampsia is giving birth, which increases the risk of neonatal morbidity and mortality in preterm pregnancies [99]. Antihypertensives and anticonvulsants can be used in pregnancy to treat hypertensive disorders, but some anticonvulsant and antihypertensive drugs cross the placenta and may harm the fetus.

3.4.2. Evidence for use of antihypertensives

Well-designed, large trials that evaluate the effect of antihypertensives on maternal, fetal, and neonatal outcomes are lacking. A Cochrane review of all trials of antihypertensives found that all drugs substantially reduced high blood pressure, but found no statistically significant differences in rates of perinatal or neonatal morbidity or mortality between any two antihypertensives [97]. The review recommended that high-dose diazoxide, ketanserin, nimodipine, chlorpromazine, and magnesium sulfate (except to prevent eclamptic seizures) should be avoided owing to the increased risk of other adverse events. Additionally, extreme and/or rapid lowering of blood pressure can compromise utero-placental blood flow and fetal oxygenation.

3.4.3. Evidence for use of anticonvulsants

Intravenous or intramuscular magnesium sulfate is the anticonvulsant of choice, superior to diazepam or phenytoin, for preventing and treating eclamptic fits [100], and appears to neither cause harm nor confer benefit to the fetus. A Cochrane review of magnesium sulfate to prevent eclampsia in women with pre-eclampsia found no impact on stillbirth (RR 0.99; 95% CI, 0.87–1.12), perinatal death (RR 0.98; 95% CI, 0.88–1.10), neonatal death (RR 1.16; 95% CI, 0.94–1.42), or 5-minute Apgar score less than 7 (RR 1.05; 95% CI, 0.52–2.12) [101]. For women with severe pre-eclampsia at risk of seizures, magnesium sulfate is inexpensive and suitable for use in low-resource settings, and should be considered if there is concern about the risk of eclampsia. However, use of magnesium sulfate remains limited in many low-resource settings owing to lack of availability, fear of adverse effects, confusion regarding routes of administration, and dosing uncertainty [102].

Preliminary evidence suggests that the antihypertensive drug labetalol may reduce the risk of eclampsia in women with pre-eclampsia [103]. As oral labetalol would be easier to administer in low-resource settings that magnesium sulfate (which requires parenteral administration and intensive monitoring), research to determine its effectiveness is a priority.

3.4.4. Evidence for early or rapid birth

The mode of birth in severe pre-eclampsia and eclampsia (after stabilization of blood pressure, administration of anticonvulsants, and in utero resuscitation) is still controversial. Observational studies suggest similar outcomes of planned cesarean delivery versus induction [104], with worse outcomes for emergency cesarean [105], which is indicated for fetal distress. Pre-eclampsia usually resolves after birth, though close monitoring of maternal blood pressure and

neurological status for 24–48 hours postpartum is strongly advised [106].

3.5. Antepartum hemorrhage

3.5.1. Presenting problem

Antepartum hemorrhage, or significant vaginal bleeding in the second half of pregnancy, occurs in 3.5%–5% of all pregnancies and is an important contributor to maternal and perinatal morbidity and mortality [1,107]. Half of all cases are caused by placenta previa (where a placenta partially or completely overlies or is implanted in the cervix, around 0.5% of pregnancies) or placental abruption (separation of the placenta from the uterus, 1%–2% of pregnancies) [108]; less commonly, uterine rupture or placenta accreta are implicated [109]. Patients with placental abruption usually present with bleeding, uterine contractions (unless the uterus has ruptured), abdominal tenderness, signs of fetal distress, and/or hypovolemic shock.

3.5.2. Evidence for mortality effect or intermediary outcomes

There is little evidence for optimal management of pregnancies at risk of antepartum hemorrhage, although immediate delivery is commonly undertaken, either via induction and/or active management of labor (often with instrumental delivery), or cesarean delivery. Intravenous fluids or blood transfusion may be needed to restore blood volume.

3.5.3. Evidence for management of placental abruption

Placental abruption is diagnosed clinically, and its usual management is rapid birth. There is no evidence from RCTs for the optimal management of placental abruption in any setting [110].

3.5.4. Evidence for management of placenta previa

Ultrasound has radically improved screening, diagnosis, and management of placenta previa and placenta accreta, and perinatal mortality associated with placenta previa has subsequently declined [107]. Cervical cerclage (a stitch to hold the cervix closed) is thought to prevent or slow the dilation of the cervix, which may reduce the incidence of detachment and hemorrhage in case of a low-lying placenta. A Cochrane review of cervical cerclage versus no cerclage in placenta previa cases found a borderline significant reduction in Apgar score less than 6 at 5 minutes (RR 0.19; 95% CI, 0.04–1.00), but this was likely mediated more by prevention of prematurity rather than reduction in intrapartum-related neonatal deaths [110].

3.6. Post-term pregnancy

3.6.1. Presenting problem

Perinatal mortality risk increases in pregnancies that progress beyond 42 weeks of gestation, which has led to policies of labor induction between 40 and 42 weeks to reduce risks of postmaturity, meconium aspiration, and cesarean deliveries for fetal distress [111,112]. The risk is moderate compared with many of the other conditions listed here (aOR 1.5) but the prevalence may be high, so the population level effect is likely significant [1].

3.6.2. Evidence for membrane sweeping

Sweeping of the placental membranes, performed at or beyond term, entails inserting a finger through the cervix and separating the membranes from the lower uterine segment with a circular motion. Membrane sweeping disrupts decidual cell lysosomes and releases prostaglandins, in some cases stimulating cervical ripening and/or the initiation of labor. A Cochrane review found that membrane sweeping was significantly associated with reduced risk of pregnancy continuation beyond 41 weeks (RR 0.59; 95% CI, 0.46–0.74) and 42 weeks (RR 0.28; 95% CI, 0.15–0.50) [113], but no difference in perinatal outcome was observed. However, all pregnancies in the trial settings were closely monitored, and both intervention and control groups were offered routine labor induction at 41 or 42 weeks. Where medical labor induction is unavailable or inadvisable (Table 5), routine membrane sweeping could potentially hasten onset of labor and improve perinatal outcome. Membrane sweeping is more likely to be effective in true post-term pregnancy than pregnancies with incorrectly estimated gestational age and is weakly recommended at or beyond 40 weeks of gestation if early ultrasound dating of gestational age is available. Membrane sweeping requires rigorous trials in low-resource settings.

3.6.3. Evidence for elective induction of labor

Many physicians in high-resource settings routinely induce labor at 41 or 42 completed weeks of gestation to reduce the risks of fetal morbidity and mortality. A Cochrane review of labor induction in normal pregnancies at or beyond term found a non-significant reduction in PMR at 41 completed weeks (RR 0.25; 95% CI, 0.05–1.18) or 42 completed weeks (RR 0.41; 95% CI, 0.06–2.73), but when all post-term inductions at 41 completed weeks or more were analyzed together, a statistically significant reduction in PMR was observed (RR 0.30; 95% CI, 0.09–0.99) [114]. Risk of meconium aspiration syndrome was also significantly reduced in the group induced after 41 weeks (RR 0.29; 95% CI, 0.12–0.68) and non-significantly after 42 weeks (RR 0.66; 95% CI, 0.24–1.81). A trend toward reduced risk of 5-minute Apgar score less than 7 was also reported (RR 0.24; 95% CI, 0.05–1.10). While evidence is moderate for labor induction at 41–42 weeks of gestation in high-resource settings, absolute risk reduction is small and multiple factors should be considered in decisions to induce labor in low-resource settings, including difficulty in precisely determining gestational age [115] (Table 5).

3.7. Maternal infection

3.7.1. Presenting problem

Intra-amniotic infection (chorioamnionitis) and fetal cerebral hypoxia be a synergistic for brain injury and neonatal encephalopathy [116–118]. Clinical diagnosis is based on presence of unexplained maternal fever, rapid fetal heartbeat, tender uterus, and/or foul-smelling amniotic fluid. Although prevalence data are poor, both subclinical and symptomatic intra-amniotic infections have been associated with preterm prelabor rupture of membranes (pPROM) and preterm labor [119,120], as well as labor abnormalities, increased need for oxytocin, and increased risk of cesarean delivery. In addition, maternal fever alone has been shown to be an independent risk factor for intrapartum-related mortality and neonatal encephalopathy, with an adjusted OR of approximately 10-fold [15,121].

3.7.2. Evidence for antibiotics for chorioamnionitis and prelabor rupture of membranes

Research on treatment of chorioamnionitis has investigated different parenteral antibiotic treatment regiments and the effect on neonatal and maternal morbidity [122–124]. In one small study (n = 45) comparing intrapartum versus postpartum ampicillin and gentamycin for the treatment of intraamniontic infection, there was a non-significant reduction of neonatal mortality, sepsis, and pneumonia [125]. There were no studies that reported the effect on intrapartum-related outcomes.

A Cochrane review of antibiotic administration for pPROM reported that antibiotic treatment was associated with a significant reduction in risk of chorioamnionitis (RR 0.57; 95% CI, 0.37–0.86), and longer time to delivery (RR 0.71; 95% CI, 0.58–0.87), as well as major markers of neonatal morbidity, but no statistical differences in perinatal mortality were reported (RR 0.90; 95% CI, 0.74–1.10) [126].

A Cochrane review of prophylactic antibiotics in cases of prelabor rupture of membranes (PROM) found no statistically significant differences in perinatal mortality (RR 0.98; 95% CI, 0.14–6.89), 5-minute Apgar score less than 7 (RR 0.98; 95% CI, 0.28–3.34) [122,127], or chorioamnionitis (RR 0.60; 95% CI, 0.30–1.18) [127]. However, risk of endometritis was significantly reduced (RR 0.09; 95% CI, 0.01–0.73).

A Cochrane review of antibiotics to manage intra-amniotic infection reported a non-significant reduction in all-cause neonatal mortality (RR 0.25; 95% CI, 0.01–5.75), but the sample size was very small [122].

Although the evidence is low, treatment of chorioamnionitis with antibiotics and delivery should be standard of care for all pregnant women and is strongly recommended for low-income settings given the high case-fatality rate of early onset neonatal sepsis. Antibiotic therapy (excluding clavulanic acid) is beneficial for the management of preterm PROM, but not for preterm labor with intact membranes. There is insufficient evidence to recommend antibiotic prophylaxis or immediate delivery for term PROM [128], but research for interventions to prevent PROM and prevent and treat chorioamnionitis or maternal pyrexia, particularly with ruptured membranes, is needed. As digital vaginal examinations increase the risk of ascending infection, they should be avoided or minimized in patients with pPROM and PROM, especially in latent phase labor.

3.8. Summary of evidence for intrapartum care interventions

Rigorous evidence for interventions during labor to reduce the risk of perinatal death and particularly intrapartum-related deaths is scarce. While data from high-resource settings support planned cesarean for breech presentation and post-term induction, data from low-income countries are severely lacking, and risks of these interventions in low-resource settings may outweigh the small absolute reductions in risk (Tables 3 and 5). Several alternatives to cesarean delivery (Table 3), including instrumental delivery and symphysiotomy, are life-saving and scalable, but have not been tested in rigorous RCTs, and would require investments in equipment and/or training. Evidence for some benefit of amnioinfusion in middle-income settings is promising, but comes primarily from a meta-analysis of small studies; further research is needed to determine whether amnioinfusion is safe, effective, and feasible in low- and middle- income countries. Simple and inexpensive interventions such as partograph use, external cephalic version, and in utero resuscitation have shown no impact on perinatal mortality outcomes in high-resource settings, but require further investigation of potential impact in resource-constrained settings. Finally, there is a dearth of simple, feasible, effective interventions for several important risk factors for intrapartum-related injury, such as antepartum hemorrhage and intra-amniotic infection.

4. Delivery of intrapartum care in low-resource settings

The global deficit of more than 4 million trained health workers is most acute where maternal and perinatal mortality are highest, especially in Sub-Saharan Africa and much of South Asia [129]. For example, Malawi has 1.1 doctors and 25.5 nurses per 100 000 population, compared with 230 doctors and 1212 nurses per 100 000 population in the United States [129]. In the highest mortality settings, skilled birth attendant (SBA) coverage reaches only 46%, and median coverage of cesarean delivery is 3%, well below the minimum expected 5% level recommended by the UN [1].

The prevailing challenge for low- and middle- income regions is how to increase the supply, quality, and equity of obstetric care in settings of extreme human resource constraints. In this section, we address innovative supply-side strategies to strengthen Emergency Obstetric Care (EmOC) at the facility level, which is merely one aspect of the strengthening activities needed globally to reach the poor. Later in this series, we address demand-side strategies to increase care seeking and utilization of obstetric services, and link families to facility-based obstetric care [17]; provision of skilled childbirth care within the community [27]; and perinatal audit as a quality-improvement strategy [29].

4.1. Intrapartum care packages

The two primary maternal health strategies promoted by the United Nations to reduce intrapartum-related maternal mortality are: (1) universal access to a skilled birth attendant for all mothers during childbirth; and (2) ensuring prompt, universal access to EmOC [130]. A skilled birth attendant is a facility-based or community-based medically trained provider with midwifery skills including monitoring the progress of labor, augmenting labor, normal childbirth using aseptic technique, actively managing the third stage of labor, newborn resuscitation, and appropriate referral for mothers requiring advanced interventions [131].

Specific packages and standards for EmOC have been defined for different levels of the health system, although overlap and ambiguity in contents of various obstetric care packages have generated substantial confusion and debate [132,133]. Ideally, all women would have access to essential obstetric care, which includes intrapartum monitoring with early detection and management or referral of complications. BEmOC is comprised of 6 key non-surgical "signal functions": the use of intravenous/intramuscular antibiotics, intravenous/intramuscular oxytocics, intravenous/intramuscular anticonvulsants, manual removal of retained placenta, removal of products of pregnancy, and assisted vaginal delivery. CEmOC functions include all BEmOC functions plus cesarean delivery (which typically requires an operating theater) and blood transfusion [133]. One CEmOC and 4 BEmOC facilities are recommended per 500 000 population to adequately service the 15% of deliveries estimated to experience complications (Fig. 2) [134].

The evidence for the impact of EmOC packages has recently been systematically reviewed [135]. Evidence of the impact of the package on perinatal mortality has not been evaluated as a whole and hence data are based primarily on low-quality historical trends and ecologic data. An expert Delphi process estimated that universal application of BEmOC and CEmOC packages together may avert 75% of intrapartum-related neonatal deaths—very high impact yet currently low coverage (Fig. 1) [135] (GRADE evidence level: Low; Recommendation: Strong).

4.2. Strategies to improve quality of EmOC packages

4.2.1. Strategy definition

Delay in diagnosis, failure to implement appropriate interventions correctly or at all, and poor teamwork have been shown to contribute to suboptimal outcomes in obstetric emergencies [136]. Several innovative strategies, including in-service training, obstetric simulations and drills, rapid response teams, safety checklists, and intrapartum risk assessment aim to minimize delay and error in EmOC provision by improving knowledge, competency, and skill retention of providers. Training courses, such as ALARM, ALSO, and Life-Saving Skills, can train providers to better manage obstetric emergencies [137–139]. Obstetric simulations and drills involve the practice of specific clinical algorithms or action plans in response to simulated obstetric complications and emergencies to identify deficiencies and improve teamwork (Panel 1) [65]. Educational tools for training courses and drills may include formal classroom lectures, internet modules, computer-based simulations, model-based simulations with medical equipment, and real-time observed experiences on the maternity ward [140]. Surgical Safety Checklists have been shown to reduce surgical complications (half of which are preventable), iatrogenic infection, and anesthesia-related errors by improving team communication [141].

4.2.2. Evidence for in-service training, obstetric simulations and drills, and rapid response teams

Only two studies reported perinatal outcomes associated with training, obstetric drills, and/or rapid response teams. In a tertiary care hospital in Bristol, UK, the Practical Obstetric Multi-Professional Training (PROMPT) Course was used to train midwives to monitor labor and manage obstetric emergencies including shoulder dystocia,

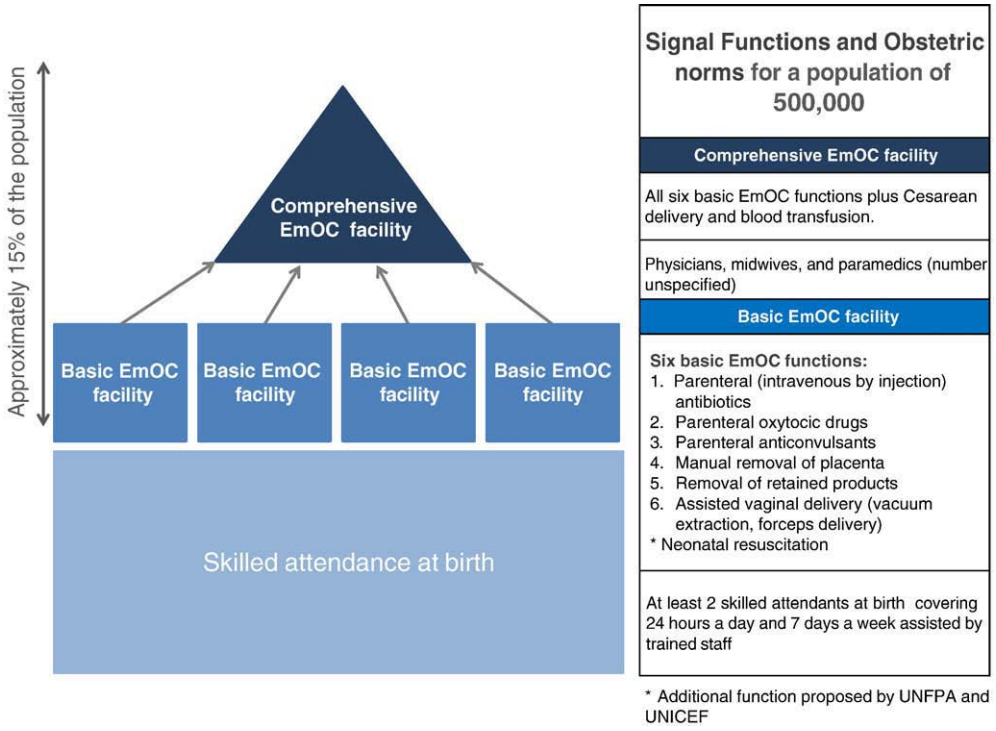

Fig. 2. Summary of United Nations standards for provision of obstetric care services. Source: UNICEF, WHO, UNFPA [133] 1997.

postpartum hemorrhage, eclampsia, twin/breech delivery, and neonatal resuscitation. Before-and-after training comparisons showed a significant reduction in 5-minute Apgar scores less than 6 (86 versus 44 per 1000 births, RR 0.50; 95% CI, 0.26–0.95) and neonatal encephalopathy (27 versus 14 per 1000 births, RR 0.51; 95% CI, 0.35–0.74) [142]. Rates of emergency cesarean delivery increased from 9.3% to 11.4%, potentially owing to improved monitoring and early recognition of complications. The same Bristol-based investigators also assessed the impact of shoulder dystocia drills; standardized procedures and checklists included in these training exercises improved physician practices and skill retention for up to 1 year [143–145]. A before-and-after comparison associated shoulder dystocia drills with reduced risk of neonatal injury and brachial plexus injury at birth (RR 0.25; 95% CI, 0.11–0.57 and RR 0.31; 95% CI, 0.13–0.72, respectively) [146].

A recent review of EmOC training programs in hospitals that have reported subsequently improved outcomes identified labor wards as more effective training settings than simulated facilities. The review identified the following common features of successful programs: institution-level incentives for training; multi-professional training; integration of teamwork training with clinical instruction; and use of high-fidelity simulation models such as mannequins [136].

In southern Vietnam, an EmOC Life-Saving Skills and refresher cesarean delivery training course was given to midwives and physicians [147]. Recognition and appropriate management of life-threatening obstetric emergencies improved in both intervention primary clinics and secondary hospitals; no intrapartum outcome data were reported.

Rapid response capability appears critical (Panel 1); a small prospective study in Finland reported significantly shorter decision-to-delivery intervals when an emergency cesarean team was available in-hospital versus on-call (13.5 ± 0.7 min vs 23.6 ± 0.9 min). Significantly fewer intrapartum stillbirths occurred among cases managed by the in-hospital versus the on-call team (0/60 vs 3/41, $P = 0.05$). Most adverse outcomes occurred after delays of 20 minutes or more; one case of neonatal encephalopathy occurred in the control group [148] (GRADE evidence level: Low; Recommendation: Strong).

4.2.3. Evidence for safety checklists

Implementation of the WHO Surgical Safety Checklist in 8 hospitals led to significantly reduced surgical mortality (from 1.5% to 0.8%, $P = 0.003$), and surgical morbidity (from 11% to 7%, $P < 0.001$) [141]. In each facility, deficiencies in baseline practices were identified and a surgical checklist, including 19 items covering the basic practices of safe anesthesia, infection prophylaxis, and effective teamwork, was implemented. Complication rates were reduced most in low-income settings, and 6 process indicators of quality of care significantly improved across all sites (GRADE evidence level: Moderate; Recommendation: Strong).

4.2.4. Evidence for intrapartum risk screening and preparedness for neonatal resuscitation

Anticipating which infants may require neonatal resuscitation could aid EmOC teams in emergency preparedness, but 20%–76% of infants requiring neonatal resuscitation have no risk factors [149,150]. An intrapartum risk stratification system to triage a "Neonatal Resuscitation Team" attending primarily moderate and some high-risk deliveries in a Canadian hospital [151–153] identified 80% of newborns requiring positive pressure ventilation (PPV). The strongest predictors of need for PPV (OR>2) included multiple pregnancy less than 35 weeks, maternal hypertension, preterm birth less than 34 weeks, use of general anesthesia, shoulder dystocia, meconium stained liquor, and emergency cesarean delivery. A similar approach of risk stratification with modified risk factors could assist in triaging limited staff skilled in resuscitation to attend deliveries (GRADE evidence level: Very Low-Low; Recommendation: Weak-conditional).

4.2.5. Implications

There is limited evidence, primarily from high-resource settings, that quality improvement measures may improve provider recognition and management of obstetric complications and subsequent perinatal outcomes. Most life-threatening intrapartum complications become clinically apparent either during or just before labor, and treatment is time-dependent [154]. Quality-improvement strategies could speed the delivery of appropriate interventions and save lives [155]. Training programs in neonatal resuscitation in low-resource

facility settings have resulted in improvements in provider competency and intrapartum-related outcomes [28]. EmOC training could have similar or greater impact but these programs have yet to be evaluated for outcome effects. Team preparedness, risk screening, and appropriate triage could target rapid intervention to urgent cases. Safety checklists can be used with any of the above strategies as a tool to decrease preventable and/or iatrogenic morbidity and mortality. Application of this concept to childbirth care is in process, with WHO leading development of a Safe Childbirth Checklist.

4.3. Continuous labor support/continuity of care in childbirth

4.3.1. Strategy definition

Shortages of physicians and nursing cadres in many low-resource settings lead to low staff-to-patient ratios, which preclude one-to-one support and monitoring of labor [156]. Shift changes further diminish the likelihood that women will receive care from the same provider(s) throughout labor. Hospital policies in many low-income countries prohibit companions of laboring women from entering the maternity ward, leaving many women to labor unattended. This lack of continuous care stands in stark contrast to the widespread custom of traditional birth attendants and/or female relations providing touch, verbal encouragement, assistance with birthing positions, and food/drink to women during labor and the early postpartum period at home [157]. A lack of continuous intrapartum care in an unfamiliar environment has been theorized to contribute to increased maternal stress, anxiety, and exhaustion, prolonged labor [158], and suboptimal intrapartum monitoring [159,160].

4.3.2. Evidence for mortality effect or intermediary outcomes

A Cochrane review of 13 RCTs in multiple countries (Table 8) found that compared with no support, presence of a female supportive companion was associated with shorter labor duration (mean difference 0.42 hrs, 95% CI, −0.83 to 0.04), reduced risk of cesarean delivery (RR 0.91; 95% CI, 0.83–0.99), 5-minute Apgar score less than 7 (RR 0.72; 0.51–1.02), intrapartum analgesia (RR 0.89; 95% CI, 0.82–0.96), instrumental vaginal delivery (RR 0.89; 95% CI, 0.82–0.96), and dissatisfaction with the birth (RR 0.73; 95% CI, 0.65–0.83). Benefits were greater if the companion was not a hospital employee: in this subgroup, the reduced risk of poor 5-minute Apgar was statistically significant (RR 0.36; 95% CI, 0.14–0.90). Investigating the impact of non-hospital employees as companions, an RCT in an urban Botswana hospital found that female relatives providing intrapartum support were associated with a lower risk of intrapartum analgesia (53% vs 73%), augmentation (13% vs 30%), amniotomy (30% vs 54%), vacuum extraction (4% vs 16%), and cesarean delivery (6% vs 13%) [161].

Other studies from urban high-resource settings corroborate the positive impact of providing continuous support to women in labor, including significantly lower rates of cesarean delivery [162] and meconium staining [163] (RR 0.51; 95% CI, 0.28–0.94), with higher maternal satisfaction with birth (GRADE evidence level: Low; Recommendation: Strong) [163,164].

4.3.3. Implications

Continuous intrapartum support is associated with decreased stress, pain, and anxiety during labor, and subsequent decreased intervention, modest improvements in neonatal outcomes, and higher maternal

Table 8
Evidence for the effect of continuous support during labor on intermediate outcomes.

Intervention/study	Setting and population	Intermediate Outcomes	Investigator & year
Meta-analysis on the effects of continuous, one-to-one intrapartum support on maternal and infant outcomes. Support included nurses, midwives, doula, family member or friend (a childbirth professional or an individual with knowledge about the process of labor). Control groups did not have continuous intrapartum support.	16 trials from 11 countries including 13 391 women (4 trials from Mexico, Guatemala, South Africa, Botswana)	Supported women had: • Shorter labor (mean difference 0.42 hrs, 95% CI, 0.83–0.04). • Higher likelihood of spontaneous vaginal delivery (RR 1.07; 95% CI, 1.04–1.12). • Lower risk of intrapartum analgesia (RR 0.89; 95% CI, 0.82–0.96). • Lower risk of instrumental birth (RR 0.89; 95% CI, 0.82–0.96). • Lower risk of cesarean birth (RR 0.91; 95% CI, 0.83–0.99). • Less dissatisfaction with childbirth (RR 0.73; 95% CI, 0.65-0.83). • Greater benefits when provider was not hospital staff, and started early in labor. • Not associated with significantly decreased low 5-min Apgar scores (RR 0.72; 95% CI, 0.51–1.02), although sub-analysis of trials using non-hospital caregiver yielded significantly lower risk (RR 0.36; 95% CI, 0.14–0.90). • No differences in perineal trauma.	Hodnett et al. [157] 2006
RCT of continuous female family member present during labor.	Hospital setting, Urban Gaborone, Botswana	Mothers with companions had: • Higher rate of spontaneous vaginal delivery (91 vs 71%). • Less intrapartum analgesia (53 vs 73%). • Less augmentation of labor (oxytocin 13 vs 30%; amniotomies 30% vs 54%). • Fewer assisted (vacuum 4% vs 16%) and cesarean (6% vs 13%) deliveries.	Madi et al. [161] 1999
Follow-up evaluation of postpartum outcomes after RCT of continuous labor support by lay doula. Pregnancy outcomes included in Cochrane review.	Urban hospital, New Jersey, USA	• Doula supported women were more likely to report positive prenatal expectations about childbirth. • More positive perceptions of infants, support from others, and self-worth. • More likely to breastfeed within first hour of life and by time of postpartum interview.	Campbell et al. [164] 2007
RCT of presence of companion during labor and delivery. Companion of choice was most frequently child's father or pregnant woman's mother.	Urban hospital, Sao Paulo, Brazil	• Women with companion had greater satisfaction with care received, medical guidance, and delivery experience for vaginal deliveries. • No significant differences in type of delivery, fetal heart rate, Apgar scores, NICU admission, birth weight, breastfeeding initiation, or mortality. • Lower rate of meconium stained fluid in support group (RR 0.51, 95% CI 0.28-0.94)	Bruggemann et al. [163] 2007
Retrospective evaluation of birth outcomes with and without doula support over 7-year program. Multivariate regression models to control for confounding factors.	Urban hospital, Boston, USA	• Statistically significant reduction in cesarean birth for primiparous women cared for by midwives. • Higher rates of breastfeeding intent and early initiation rates.	Mottl-Santiago et al. [162] 2007

satisfaction with birth. Providing or permitting continuous dedicated intrapartum support bridges the gap between traditional intrapartum care practices and hospital policies. Culturally sensitive intrapartum support could encourage more women to give birth in facilities.

Barriers to widespread implementation of continuous support include resistance from healthcare providers; additionally, in over-burdened health facilities, space and sanitation considerations may hinder implementation [156]. Support appears to lead to fewer interventions, with associated cost savings for health systems, and impact appears to be higher when the provider is familiar to the woman; a doula or female relation may be more effective than hospital-based providers, alleviating some portion of the caregiving burden on nursing staff at little or no cost. This promising and highly feasible intervention warrants more widespread implementation and evaluation.

4.4. Task-shifting and use of alternative cadres to provide EmOC

4.4.1. Strategy definition

Task-shifting maximizes available human resources by redistributing specific tasks from highly qualified professionals to the least-specialized professional capable of performing the task safely and reliably, including general practitioners or non-physician clinicians (NPCs) such as nurse-aides, midwives, surgical technicians, medical or clinical officers, and community-based workers. Task-shifting has been widely embraced in Sub-Saharan Africa, where numbers of NPCs exceed physicians [165] in several countries. Ethiopia, Mozambique, Zambia, and Malawi have accelerated training of NPCs [166]. In some Sub-Saharan countries (including Ethiopia, Malawi, Mozambique, and Tanzania), the national training curriculum for NPCs includes training in cesarean delivery; NPCs perform cesarean deliveries in at least 5 African countries [165,167,168]. Task-shifting may also mean having midwives perform instrumental deliveries, or using nurse-aides to provide intrapartum supervision to enable midwives or physicians to handle obstetric emergencies [140]. In other cases, new cadres of workers, such as surgical technicians, may be created to bridge the human resource gap [169,170].

4.4.2. Evidence for mortality effect (including safety) or intermediary outcomes

Population-level data are lacking (Table 9), but several studies report promising results of shifting intrapartum care functions to general practitioners or NPCs.

In Mozambique, assistant medical officers (*tecnicos de cirurgia*, or TCs) are the principal providers of emergency surgical care, including cesarean delivery. TCs receive 3 years of training in general surgery, obstetrics/gynecology, orthopedics, trauma, emergency and intensive care, with biweekly supervised clinical emergency shifts. An evaluation comparing cesarean deliveries (n = 2071) conducted by TCs versus obstetricians found no clinically significant difference between

Table 9
Evidence for alternative cadres for intrapartum care.

Intervention/study	Setting	Skilled attendance and cesarean delivery rates (%)	Intermediate outcomes	Investigator and year
Analysis of 2071 consecutive cesarean deliveries comparing outcomes by medical assistants trained for surgery versus obstetricians at Maputo Central Hospital.	Mozambique	National SBA: 44% Cesarean delivery: 1.9%	• 46% of surgeries performed by assistant medical officers, 53% by obstetricians. • No difference in indications for surgery. • Increased risk in superficial wound separation in assistant medical officer-conducted surgeries (OR 2.2; 95% CI, 1.3–3.9) • No other significant differences in other outcomes (total wound rupture, SBR, ENND, prolonged hospital stay or maternal death)	Pereira et al. [171] 1996
Prospective evaluation of 2131 consecutive obstetric surgeries comparing outcomes by clinical officers (non-physician mid-level providers) versus medical officers in 38 district hospitals	Malawi	National SBA: 54% Cesarean delivery: 3.1%	• 88% of emergency obstetric operations performed by clinical officers; 12% by medical officers. • No significant difference in SBR or ENND between surgeries by clinical vs medical officers. • No significant difference in maternal postoperative outcomes (fever, infection, wound dehiscence, or maternal death).	Chilopora et al. [174] 2007
Cross-sectional study of 12 178 consecutive obstetric operations by "tecnicos de cirurgia" (TCs) (non-physician mid-level providers) versus medical officers in 34 health units.	Mozambique	National SBA: 48% Cesarean delivery: 1.9%	• TCs performed 57% of major obstetric surgeries in Mozambique. • TCs perform 92% of surgeries in rural district hospitals. • Higher retention of TCs in district hospitals (88% after 7 years), compared with medical officers who tended to move to urban, provincial hospitals (0% retention after 7 years).	Pereira et al. [183] 2007
Evaluation of cesarean deliveries (n = 2305) conducted by obstetricians, general practitioners, and district clinical officers with 6 months' training in emergency surgery	Burkina Faso	National SBA: 54% Cesarean delivery: 0.7%	• Neonatal CFR 99 per 1000, 125 per 1000, and 198 per 1000 in surgeries conducted by obstetricians, general practitioners, and district clinical officers, respectively. • Authors estimate refresher courses and closer supervision could reduce the higher CFR among clinical officer-led cesareans to 161.5 per 1000 [176].	Hounton et al. [176] 2009
Description of experiences and outcomes of surgical procedures by nurse-surgeons at 2 rural hospitals	Rural northwest Zaire	National SBA: 70% Cesarean delivery: 4.0%	• 321 cesarean deliveries, 87% by nurse-surgeons. • CFR for cesarean by nurse was 1%. • 13 nurse-surgeon-led laparotomies for uterine rupture with 1 death.	White et al. [231] 1987
Historical description of rural health service in Malaysia, tiered pyramidal system task-shifting to medical auxiliary staff (indigenous midwives, junior laboratory assistants) to reach majority of rural population.	Rural Malaysia	National SBA ~25% *[from article; 1957]*, Cesarean delivery: undocumented	• Indigenous midwives attended 32% of registered births in 1970. • 46% reduction in IMR, 54% reduction in MMR* (from baseline IMR 75.5 per 1000, MMR 320 per 100 000 in 1957).	Chen et al. [232] 1973

Abbreviations: MMR, maternal mortality ratio; NMR, neonatal mortality rate; SBR, stillbirth rate; ENMR, early neonatal mortality rate; PMR, perinatal mortality rate.
Historical data should be interpreted with caution as many other factors may have influenced the reduction.
* For MMR, NMR, and skilled birth attendance where data were not reported in the study we sought data regarding national status from UN databases to give the context.

TCs and obstetricians in indications for cesarean, associated interventions, or serious complications including stillbirth and neonatal or maternal death [171]. Complication rates were low at 0.4%, postoperative mortality was 0.1%, and TCs could competently conduct complicated surgeries, including obstetric hysterectomies [172]. To alleviate the heavy workload on TCs (who manage all types of surgeries), qualified midwives with 3 years' midwifery training are now being given 4 years' additional training in obstetric surgery to become maternal health nurses (*enfermeiras de saúde maternal*). Assessment of retention in rural and hard-to-serve areas showed a zero retention rate for obstetricians at 2 years, but 88% for NPCs.

In Malawi, where there are fewer than 5 national obstetricians in public service, non-physician clinical officers perform most cesarean deliveries at district hospital level. An evaluation of their performance found a maternal case fatality rate (CFR) of 1.3% and a perinatal CFR of 13.6%, which may be higher than if a fully qualified surgical team had been in place, but well below rates where cesarean is unavailable [173,174].

In rural Zimbabwe, nurse-aides were trained to conduct low-risk deliveries to enable doctors and nurses to manage primigravidas and high-risk deliveries. Nurse-aides conducted 57% of all deliveries with a PMR of 5 per 1000, suggesting that nurse-aides could competently attend appropriately identified low-risk births in this setting [175].

In Burkina Faso, an evaluation of cesarean deliveries (n = 2305) conducted by obstetricians, general practitioners, and district clinical officers (who had 6 months' training in emergency surgery) found neonatal CFRs of 99 per 1000, 125 per 1000, and 198 per 1000, respectively, although case fatality rates are notoriously hard to assess between cadres of workers at different sites owing to many confounding factors. The authors suggest that refresher courses and closer supervision could reduce the higher CFR among clinical officer-led cesareans and also show that the cost per newborn death averted is much lower for the NPCs at 200 international dollars, compared with 11 757 for the obstetricians [176].

South Asian countries have also been utilizing task-shifting to address specialist shortages. Throughout India, general practitioners with MBBS degrees are being trained in surgery, obstetrics, and anesthesiology to alleviate shortages of specialists [177–179], although only a small number are currently performing these tasks. Nurses are being trained to administer magnesium sulfate for eclampsia and misoprostol to prevent postpartum hemorrhage [180]. Other South Asian countries have undertaken task-shifting to expand access to anesthesia (including training nurse-anesthetists, medical officers, and anesthesia assistants); evidence from Nepal and Bangladesh suggests that these efforts have resulted in expanded coverage of EmOC [179].

In a politically unstable part of Burma where facility-based care is infeasible, task-shifting of EmOC functions to first-level health workers, community health workers, and traditional birth attendants has resulted in an innovative mobile health system (Panel 2).

Task-shifting employing EmOC teams has also shown promise. In Senegal, teams comprised of an anesthetist, a general practitioner with 6 months' training in obstetrics including cesarean delivery, and a nurse-auxiliary trained as a surgical assistant were introduced as part of a national plan to provide EmOC at new operating theaters, a plan operationalized in only 3 districts [168]. In one district for which baseline data were available, the proportion of stillbirths during cesarean delivery declined non-significantly from 23 per 100 cesarean deliveries in referral hospitals to 12 per 100 in all hospitals after the opening of the operating theatre; overall rates of stillbirth remained unchanged (GRADE evidence level: Low; Recommendation: Conditional).

4.4.3. Evidence regarding cost-effectiveness

General practitioners and NPCs are cheaper to train and pay than specialists, with lower turnover, particularly in rural areas. In Mozambique, cost per major obstetric surgery for TCs was $39 versus $144 for obstetricians/gynecologists [181]. In Burkina Faso, the estimated average cost per averted newborn death for an obstetrician-led team compared with a general practitioner-led team was 11 757 international dollars (due largely to personnel availability and larger teams in urban settings), and 200 international dollars for a general practitioner-led team versus a clinical officer-led team. An international dollar is a hypothetical unit of currency with the same purchasing power of the US dollar in the US in the year 2000. Improving CFRs among clinical officers through training and supervision could make them even more cost-effective.

4.4.4. Implications

Mounting evidence supports task-shifting in the provision of life-saving intrapartum care, particularly for providing cesarean delivery or other EmOC functions such as managing antepartum or postpartum hemorrhage or pre-eclampsia/eclampsia in areas with poor access to EmOC. Although successful examples of safe task-shifting exist, ensuring quality of care requires standardized and rigorous training and supportive supervision, a lack of which often underlies health workforce shortages. Additionally, individuals with low status (e.g. midwives, nurse-aides) may be denied learning opportunities or adequate supervision [167]. In Malawi, NPCs who felt they were treated fairly by their managers reported high job satisfaction and eagerness to take on new responsibilities [182].

Even where providers can be capably trained to perform new tasks, logistical and health systems issues pose challenges to task-shifting schemes. Providing EmOC in unstable regions like Burma requires mobile and rapid response of providers. The Senegal experiment documented failures in meeting obstetric need, attributable to delays between training and readiness of operating theaters, limitations of centralized training, slow scale up, career path dissatisfaction, and absent team members who rendered the team non-functional [168]. Achieving sustainability requires incentivization (including adequate salary increases) and a clear career path for providers, especially physicians. As in Senegal, Burkina Faso has experienced a high turnover of physicians with additional training owing to lack of reward and heavy workload [168,176]. Dissatisfaction is less common among non-physicians; surgical assistants in Senegal were pleased with their training, and Mozambique has seen higher retention of TCs than physicians in rural areas and district hospitals [168,183].

Evidence suggests that team-building is paramount to effective task-shifting, as scalability and sustainability of these initiatives require immense dedication, coordination, and leadership [168]. Task-shifting often garners resistance from specialists and professional groups, who fear that NPCs cannot provide high-quality care or being replaced by NPCs [167]. A district surgery training program that included task-shifting in Ethiopia failed during follow-up when specialists refused to supervise trained general practitioners [184]. NPCs have been most accepted in circumstances where needs are great, NPCs prove they can provide safe and effective care, and skills are perceived as shared rather than encroached upon [185–187]. Alternative cadres need defined roles with standardized and assessed competency levels, which will facilitate recognition of their legitimacy. Regulations regarding specific tasks they may perform, as well as strategies to protect them from liability, are also needed. Although seen largely as a supply-side strategy, task shifting has demand-side implications; NPCs including nurse-aides, health officers, midwives, and community-based workers might enhance acceptability and lead to improved care seeking.

4.5. Summary of intrapartum care provision strategies

A recent review linked staff shortages with poor quality EmOC, and warned that poor quality services discourage facility use [188]. Promising supply-side strategies should be employed more widely to improve both the quality and coverage of EOC and EmOC in settings "where there are no doctors." Comprehensive strategies are needed including early identification of complications, rapid transfer and

Table 10
Summary of GRADE recommendations for care in childbirth to reduce intrapartum-related adverse outcomes.

Strongly recommended	Conditionally recommended	Weakly recommended (effectiveness, feasibility or risk-benefit concerns)	Possible options: not currently recommended; more research needed
Clinical intrapartum care interventions			
• Use of the partograph • Intermittent assessment of fetal heart rate • *In utero* resuscitation • Simplified umbilical artery Doppler • Symphysiotomy • Maneuvers to manage shoulder dystocia • Emergency laparotomy plus uterine repair or hysterectomy for uterine rupture • External cephalic version for breech presentation • Early delivery for severe pre-eclampsia or eclampsia • Early delivery for placental abruption • Antibiotics and early delivery for intra-amniotic infection	• Instrumental delivery • Planned Cesarean for breech presentation • Anticonvulsant drugs for pre-eclampsia/eclampsia • Ultrasound confirmation of placenta previa with planned Cesarean section	• Active management of labor • Use of Doptone • Fetal scalp blood sampling • Amnioinfusion for meconium stained amniotic fluid and umbilical cord compression • Antihypertensive drugs for severe hypertension • Cervical cerclage for suspected placenta previa • Membrane sweeping for post-term pregnancy[a] • Routine induction for post-term pregnancy[a]	• Fundal pressure • Clinical fetal arousal tests • Amniotic fluid assessment • Induction for suspected macrosomia[a]
Intrapartum care provision strategies			
• Obstetric drills on labor wards with high-fidelity simulations (for shoulder dystocia, Cesarean section) • Rapid response teams • Safety checklists (surgical safety, Cesarean, general childbirth) • Continuous intrapartum support from a familiar individual	• Task-shifting to NPCs for Cesarean section, anesthesia, and intrapartum monitoring		

[a] Provided that early-gestation ultrasound dating is available.

referral, and infrastructural investment to ensure widespread availability of quality life-saving interventions delivered with minimal delay and error [155,189]. Training programs and drills have shown some evidence of reduction of intrapartum-related morbidity; however, training strategies and materials are still needed for low-resource settings. Surgical checklists have been shown to reduce surgical complications, and are being adapted for cesarean delivery and general intrapartum care. Continuous intrapartum support from a relative can improve cultural acceptability of facility-based births and cost-effectively reduce the need for interventions, while reducing the care-giving demands on overburdened nursing staff.

Public-private partnerships such as the Chiranjeevi Scheme in India can incentivize private practitioners to serve poor and marginalized populations and increase access to skilled attendance and EmOC [190–192]. However, long-term assessment of impact on perinatal health outcomes is lacking and more rigorous operational research is needed. Task-shifting may increase availability of EmOC and life-saving interventions in remote, low-resource settings where interventions are needed most. NPCs in some settings have been shown to perform obstetric surgeries as competently as and more cost-effectively than obstetricians. As with the other strategies reviewed, task-shifting is not a stand-alone solution and cannot remedy the gaping deficit of well-trained health professionals in resource-poor settings; rather, it should complement comprehensive plans for human resource capacity-building [193].

5. Considerations for programs

5.1. Summary of evidence

There is a dearth of evidence supporting the effectiveness of obstetric interventions in the reduction of intrapartum-related injury, and yet, this evidence gap is worse in low-resource settings where the deaths are highest. None of the intrapartum interventions reviewed showed strong evidence of impact for reducing intrapartum-related mortality from trials in low-resource settings. Few studies reported perinatal mortality let alone intrapartum-specific outcomes. Evidence from RCTs in high-resource settings may not be directly applicable to low-resource settings (Tables 1, 2, 4, 6 and 7). Other interventions, such as amnioinfusion, show statistically significant positive impact on intermediate intrapartum outcomes in middle-income countries, but feasibility, scalability, and effectiveness questions require operational research in low-resource settings.

We placed a premium on highlighting interventions that would be expected to be effective in a setting of suboptimal background care, even if the level of evidence is low, or trials in high-resource settings indicate negligible impact. In summary, some interventions with low levels of evidence from high-resource settings, such as use of the partograph, in utero resuscitation, management of shoulder dystocia, and symphysiotomy, still merit conditional or strong GRADE recommendations (Table 10). Simple, low-cost interventions requiring minimal training inputs may be safer and/or more feasible alternatives to resource-intensive interventions such as cesarean delivery, although virtually all require further effectiveness and operational research. It is possible that for some interventions we considered, such as the use of the partograph or external cephalic version, that absolute risk reductions would be greater and reach statistical significance in well-designed trials in low-resource settings, but further research is required. Disappointingly few evidence-based options exist for some important causes of intrapartum injury and death in low-resource settings, including intrauterine infection and antepartum hemorrhage.

Some interventions for which evidence is strongest may not be justifiable in light of the small absolute risk reductions that have been observed in high-resource settings and heightened risks in low-income settings e.g. risk of iatrogenic prematurity of induction in the absence of accurate gestational age dating; or risks of unsafe cesarean delivery for breech, particularly if a provider skilled in vaginal breech deliveries is available (Tables 3 and 5).

Some promising strategies to increase coverage of emergency obstetric care with demonstrated benefit to health outcomes include obstetric drills, safety checklists, continuous intrapartum support, and task-shifting (Table 9). Immediate and substantial investment is needed to fund research on efficacy, effectiveness, and feasibility of delivering such interventions at scale and especially in rural and hard to reach areas, and in settings with recent or ongoing conflict.

Devices and Tools	Current technology for possible use in low-resource settings	Development needs before device can be employed at scale
Prenatal screening		
Fundal height assessment tools	- Fundal height assessment	- None needed
Ultrasound	- Hand-held, portable ultrasound , including models with USB connection using PC monitor display (with adequate resolution for diagnostic accuracy)  - Ultrasound belt to minimize need for skilled operator [197]	- Field trials of usage - Distribution (has US FDA clearance and Asian distributor) - Training aids for ultrasound technicians
Umbilical artery Doppler ultrasound	- Simplified Doppler umbilical artery ultrasound (using PC monitor)	- Field trials needed, widespread distribution - Simple training aids (operation manual, interpretation of waveforms)
Intrapartum fetal monitoring		
Monitoring labor progress devices/tools	- Partograph 	- Standard, simplified partograph with outcome-validated action points
Fetal heart rate monitoring Auscultation Doptone Cardiotocography	- Auscultation using Pinard stethoscope  - Hand-held wind-up Doptone Doppler [198, 199] 	- Simple training aids for Pinard stethoscope and Doptone interpretation - Field trials of wind-up Doptone devices, widespread distribution - Additional user-friendly, low-cost, durable, accurate alternative-powered fetal heart rate monitors capable of detecting late decelerations without need for complex interpretation
Acid-base balance / Pulse oximetry monitoring	- Wind-up pulse oximeter (oxygen saturation monitor) (under development) [199]	- Field trials of wind-up oxygenation monitor, distribution
Oxygen condenser	- None available	- Oxygen condenser using alternative power (solar or wind-up)
EmOC devices		
Intravenous magnesium sulfate for eclampsia	- Pre-dosed magnesium sulfate delivery device without power dependence and with minimal risk of misuse (e.g. Springfusor; Go Medical, Subico, Australia; a spring-driven infusion pump for continuous infusion) 	- Springfusor currently being tested by Gynuity Health Projects). - Packaging this device or pre-dosed magnesium sulfate vials in "eclampsia treatment packs" with calcium gluconate [102] and intramuscular + intravenous supplies, with administration info.
Vacuum extractor (not portable; electricity-dependent)	- Portable, manually-powered, disposable or easily sanitized and reusable vacuum extractor [53, 200] 	- Trials at scale; widespread distribution - Development and trials of symphysiotomy kits with appropriate training aids where cesarean delivery unavailable or not culturally acceptable
Supportive devices to improve quality and availability of EmOC		
High-fidelity training mannequins for managing normal and abnormal birth, shoulder dystocia, vaginal breech delivery, neonatal resuscitation [28]	- Standard birthing simulators current cost over US$3,500 	- Significantly lower cost, durable, easy-to-disassemble-and-sanitize high-fidelity mannequins with culturally appropriate features
Devices for surgery and obstetric emergencies (refrigeration, communication, lighting)	- Solar-powered lighting for surgery when power unpredictable/ unavailable - Solar-powered refrigeration for blood banking • Alternative-powered walkie-talkies to summon EmOC teams	- Pilot projects but needs scaled-up production and broader distribution if successful

* Note reference to specific devices or use of images does not constitute endorsement

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Fig. 3. Equipment and devices for intrapatum care in low-resource settings: Available options and needed inoovations and actions [197–200].

5.2. Innovation for equipment and devices

Intrapartum care in high-resource settings, including fetal monitoring, diagnostic testing, and operative delivery is an increasingly technology-dependent enterprise focused on assuring fetal well being, with early intervention for complications. These technologies are often unavailable, unaffordable, or impractical in low-resource settings. Several promising examples of feasible, low-cost alternatives have been identified in this review that could facilitate expanded coverage of evidence-based intrapartum interventions (Fig. 3). Some require little more than standardization (partograph) or broader production and distribution (portable ultrasound, simplified Doppler waveform analysis, manual vacuum extractor). Others remain to be developed, such as symphysiotomy kits, and affordable, culturally-appropriate versions of high-fidelity training mannequins, or improved and feasible diagnosis of fetal distress. Additionally, there remains a need for broader adaptation and piloting of training curricula to improve quality of care, including obstetric drills and safety checklists.

5.3. Specific data tracking gaps

Few of the studies we reviewed reported stillbirths disaggregated from composite perinatal mortality; when stillbirths were reported, intrapartum stillbirth rates were seldom provided, and cause-specific mortality data were rarely available for intrapartum fetal deaths or early neonatal deaths. Rates of intrapartum stillbirths are a sensitive measure of the quality of intrapartum care [1]; thus, this data tracking gap perpetuates the invisibility of intrapartum deaths and impedes efforts to prioritize interventions in response to these deaths. A universal cause-specific classification system for stillbirth that is implementable in low-resource settings is urgently needed [23]. Furthermore, the use of an aggregate measure of intrapartum stillbirths and intrapartum-related neonatal deaths should be considered, has been proposed by the UNFPA [194], and is discussed in further detail in the last paper in this series [19].

6. Conclusion

Global policy consensus surrounds the importance of increased skilled attendance at birth as a priority to reduce both maternal and fetal–neonatal complications. Experts broadly agree that a system providing access to EmOC is required to manage obstetric emergencies and that generating demand for services within communities is crucial to reduce delays in access to care [17]. However, universal coverage of CEmOC and skilled birth attendance remain unrealized goals hampered particularly by human resource shortages, but also by lack of evidence and consensus on how to accelerate progress.

In a recent Delphi expert consensus survey, CEmOC was estimated to avert 75% of neonatal deaths due to intrapartum events [135]. New analysis for 193 countries suggests that CEmOC could save an estimated 495 000 neonatal lives per year that are currently being lost to intrapartum-related causes [19]. This analysis is based on national-level modeling and inputting the most recent NMR and cause-of-death estimates, and applying mortality effect estimates in the Lives Saved Tool (LiST) [195] while considering current coverage [196]. These estimates do not include the effect of neonatal resuscitation, which is estimated to avert an additional 30% of intrapartum-related neonatal deaths after the CEmOC effect has been included [19].

In order to close gaps in coverage, quality, and equity for intrapartum care, new recognition is required of the importance of care at the time of birth, and the potential to save hundreds of thousands of newborn lives as well as stillbirths and maternal lives. No time in the human lifecycle is so critical—investment is urgently needed in health infrastructure, personnel, and implementation research in the settings where risk is highest and yet the gaps in care are widest.

7. Conflict of interest

The authors have no conflicts of interest to declare.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.ijgo.2009.07.016.

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Panel 1. Obstetric simulations, drills, and rapid response teams to minimize delay and maximize quality

Obstetric simulations and drills

Obstetric simulations and drills are increasingly advocated as a strategy to reduce provider error and improve team performance in response to time-sensitive scenarios that are too rare, grave, or costly to recreate in real life [233]. In conjunction with these strategies, rapid response teams may be used to coordinate and rapidly mobilize the multiple personnel needed during a specific obstetric emergency [234].

Obstetric simulations and drills are specifically recommended by ACOG and the Joint Commission to improve management of shoulder dystocia, neonatal resuscitation, cesarean delivery, and maternal hemorrhage [66]. They have been most commonly implemented to strengthen and maintain provider skills in managing shoulder dystocia, but are increasingly used to manage other complications such as hemorrhage, eclampsia, and vaginal breech delivery [235–239], as well as more common obstetric procedures such as cesarean delivery [65,240,241].

Simulations and drills may be conducted either in training centers or *in situ* in hospital wards using actors or high-fidelity mannequins. Most employ an algorithm specifying the responsibilities of each team member and a clinical action plan. After the drill, participants analyze video recordings or notes taken during the exercise to identify areas for improvement.

Obstetric simulations and drills have been shown to:

- Improve clinical management of complications, including individual provider technique and team coordination and efficiency [241,242].
- Help develop evidence-based standard management protocols [234,240].
- Reveal deficiencies in supplies and equipment, and encourage preparedness (e.g. “eclampsia boxes”) [240,242].
- Suggest changes to hospital policy [242].

Nursing staff and physicians have responded positively to obstetric drills [65,242] and several studies have shown improvement in post-training management of simulated or actual cases [240].

Rapid response teams

Modeled after code teams for cardiac arrest, obstetric rapid response teams involve a range of personnel capable of rapidly mobilizing administrative support as well as specialists to provide anesthesia, blood transfusion, obstetric nursing and surgical care, and perinatal care. Teams in tertiary facilities in high-resource settings in the United States have used rapid response teams, who can be summoned with a single call to the hospital operator, to implement clinical protocols for early diagnosis and rapid treatment for time-sensitive complications such as emergency cesarean delivery and hemorrhage, including preparedness for surgical intervention in high-risk patients. These teams have led to positive impacts on maternal mortality [243], and in one study, recognition of obstetric emergencies and use of the rapid response team increased 4-fold [244]. In low-resource settings where delays are even more common, formation of such teams may lead to reductions in adverse mortality and non-fatal outcomes, but may be challenging from a human resource perspective.

Panel 2. Providing care for obstetric emergencies in settings with humanitarian crises: The MOM Program in Burma

Of the 20 countries with the highest NMRs and MMRs, almost all are either currently experiencing or have recently experienced conflict, famine, or other humanitarian emergencies. Provision of care in such settings often focuses on interventions that are commodity-based such as water purification or immunizations. Providing care during childbirth is a particular challenge, and innovative service delivery approaches are urgently needed.

Decades of conflict between the Burmese military junta and armed rebels in eastern Burma and oppressive policies against minority populations have led to more than 2 million refugees and 560 000 internally displaced persons. Permanent health facilities and referral systems are not viable. A pilot project, the Mobile Obstetric Maternal Health Workers (MOM) Program, is meeting this challenge by providing mobile, community-based EmOC services. Training in essential maternal health care, including BEmOC, has been provided to 33 first-tier lay Maternal Health Workers (MHWs) at the central Mae Tao Clinic. MHWs can administer intramuscular/intravenous antibiotics and magnesium, perform manual vacuum aspiration and manual removal of placenta, and provide active management of the third stage of labor with misoprostol as there is no cold chain for oxytoxin. In addition to providing 5 of the 6 signal functions of BEmOC, MHWs also utilize "walking blood banks" (pre-typed volunteer donors) and sequential blood screening using heat-stable rapid diagnostic tests to provide direct person-to-person blood transfusion. Subsets of these EmOC services are delivered by second-tier CHWs (antibiotics, misoprostol) and third-tier traditional birth attendants (misoprostol) [245], who also act as referral links to the MWHs. Most services are provided in the home or in thatched huts, which serve as birthing centers. Supervision is provided by the central clinic, with intermittent refresher courses.

The number and type of complications, as well as coverage of the program are monitored through annual population-based cluster-sample surveys and a pregnancy-tracking log. Preliminary comparison with baseline data [246] indicates that in only 1.5 years there has been a substantial increase in EmOC access, from 5.1% skilled attendance to EmOC-trained MHWs attending 59.7% of births. Active management of the third stage of labor with misoprostol increased from near zero to 79.5% [247]. During this period, MHWs provided 25 emergency blood transfusions for pregnancy-related malaria (n = 10), postpartum hemorrhage (n = 4), and complications of abortions n = 6) [248].

Mobile service provision *in* the community rather than centralized services accessed *by* the population was a practical necessity in eastern Burma, and this experience suggests that with careful training and supervision, community-based workers can play a critical role in providing childbirth care including EmOC for those with no services currently. Establishing a 3-tier network of community providers linked to a clinic, and gaining community buy-in required mobilization, trust-building, and time [5]. Further evaluation, especially of outcomes and cost, is required.

Photographs: Maternal Health Workers providing obstetric care for internally displaced villagers in eastern Burma. (Photographs reprinted with permission granted by MOM project, 2009)* *The MOM project is a collaborative effort of the Burma Medical Association, the Mae Tao Clinic, Global Health Access Program, the Johns Hopkins Center for Public Health and Human Rights, and health organizations of Karen, Shan, Karenni, and Mon States; it is funded by the Bill & Melinda Gates Institute for Population and Reproductive Health.*

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INTRAPARTUM-RELATED DEATHS: EVIDENCE FOR ACTION 3

Neonatal resuscitation in low-resource settings: What, who, and how to overcome challenges to scale up?

Stephen N. Wall [a], Anne CC Lee [a,b], Susan Niermeyer [c], Mike English [d], William J. Keenan [e], Wally Carlo [f], Zulfiqar A. Bhutta [g], Abhay Bang [h], Indira Narayanan [i], Iwan Ariawan [j], Joy E. Lawn [a,*]

[a] Saving Newborn Lives/Save the Children USA, Washington DC and Cape Town, South Africa
[b] Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA
[c] Department of Pediatrics, University of Colorado Denver School of Medicine, Aurora, CO, USA
[d] KEMRI-Wellcome Trust Research Programme, Nairobi, Kenya
[e] St Louis University, St Louis, MI, USA
[f] University of Alabama at Birmingham, AL, USA
[g] Division of Women and Child Health, the Aga Khan University, Karachi, Pakistan
[h] Society for Education, Action and Research in Community Health, Gadchiroli, Maharashtra, India
[i] USAID/BASICS, Washington DC, USA
[j] PATH, Indonesia

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ABSTRACT

Background: Each year approximately 10 million babies do not breathe immediately at birth, of which about 6 million require basic neonatal resuscitation. The major burden is in low-income settings, where health system capacity to provide neonatal resuscitation is inadequate. *Objective:* To systematically review the evidence for neonatal resuscitation content, training and competency, equipment and supplies, cost, and key program considerations, specifically for resource-constrained settings. *Results:* Evidence from several observational studies shows that facility-based basic neonatal resuscitation may avert 30% of intrapartum-related neonatal deaths. Very few babies require advanced resuscitation (endotracheal intubation and drugs) and these newborns may not survive without ongoing ventilation; hence, advanced neonatal resuscitation is not a priority in settings without neonatal intensive care. Of the 60 million nonfacility births, most do not have access to resuscitation. Several trials have shown that a range of community health workers can perform neonatal resuscitation with an estimated effect of a 20% reduction in intrapartum-related neonatal deaths, based on expert opinion. Case studies illustrate key considerations for scale up. *Conclusion:* Basic resuscitation would substantially reduce intrapartum-related neonatal deaths. Where births occur in facilities, it is a priority to ensure that all birth attendants are competent in resuscitation. Strategies to address the gap for home births are urgently required. More data are required to determine the impact of neonatal resuscitation, particularly on long-term outcomes in low-income settings.
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1. Introduction

Each year an estimated 10 million babies require assistance to initiate breathing (Fig. 1). Between 5%–10% of all babies born in facilities need some degree of resuscitation, such as tactile stimulation or airway clearing or positioning [1,2], and approximately 3%–6% require basic neonatal resuscitation, consisting of these simple initial steps and assisted ventilation [3,4]. The need for neonatal resuscitation is most urgent in low-resource settings, where access to intrapartum obstetric care is poor and the incidence, mortality, and burden of long-term impairment from intrapartum-related events is highest [5,6]. Delays in assisting the non-breathing newborn to establish ventilation, as may happen in many low-resource country settings, may exacerbate hypoxia, increase the need for assisted ventilation, and contribute to neonatal morbidity and mortality. Each year there are an estimated 904 000 intrapartum-related neonatal deaths, previously loosely termed "birth asphyxia" [7]. The first paper in this series discusses this shift in terminology in more detail [5]. Although "birth asphyxia," as applied to the non-breathing newborn, is an important clinical problem, it is not a specific cause of death. A series of international consensus statements have recommended the shift to the term "intrapartum-related deaths" when used for cause of death, and "neonatal encephalopathy" for the acute complications manifesting with a neurologically abnormal state soon after birth. Case definitions should exclude preterm babies and other causes of death where possible, such as congenital anomalies.

* Corresponding author. Saving Newborn Lives/Save the Children USA, 11 South Way, Cape Town 7405, South Africa. Tel.: +27 21 532 3494.
E-mail address: joylawn@yahoo.co.uk (J.E. Lawn).

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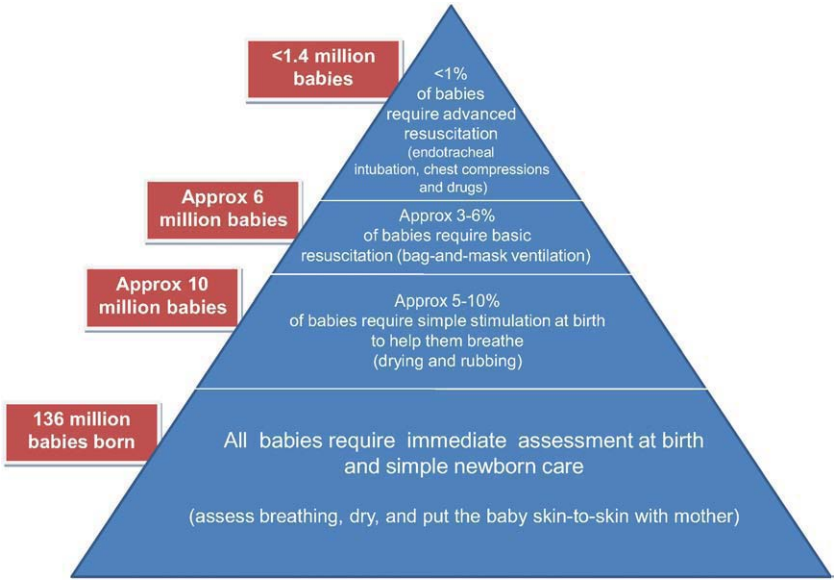

Fig. 1. Estimates of global numbers of babies undergoing resuscitation at birth. Source: Estimates based on references [1–4,8,9].

Advanced resuscitation (i.e. chest compressions, intubation, or medications) is required for around 2% of all babies who do not breathe at birth [4,8], and less than 1% of all babies born [2,9]. Furthermore, in many cases, babies who require advanced resuscitation may not survive without ongoing ventilation and neonatal intensive care. Therefore, basic neonatal resuscitation, including bag-and-mask ventilation, is sufficient for most babies who would be saved by resuscitation in low-resource settings. Recently, Newton and English [10] reviewed the evidence for neonatal resuscitation and concluded that effective resuscitation was possible with basic equipment and skills in low-resource settings. Training providers in neonatal resuscitation in health facilities may prevent 30% of deaths of full-term babies with intrapartum-related events, as well as 5%–10% of deaths due to preterm birth [11]. Therefore, universal application of basic resuscitation may save hundreds of thousands of newborn lives currently lost each year, and contribute significantly to progress toward Millennium Development Goal 4. To achieve impact, the challenge is to improve obstetric care and provide universal coverage of basic resuscitation where resources are limited and where many, even most, babies are born at home.

1.1. Current coverage, constraints, key challenges

In low-resource settings where the burden of intrapartum events is the greatest, the capacity to provide adequate neonatal resuscitation is lacking. For example, in South East Asia where over one-third of all intrapartum-related neonatal deaths occur, rates of skilled birth attendance are among the lowest in the world (34% for 2000–2007) [12]. For the babies born in hospitals, staff are frequently not trained in resuscitation and equipment is not available. In National Service Provision Assessments in 6 African countries, only 2%–12% of personnel conducting births in facilities had been trained in neonatal resuscitation and only 8%–22% of facilities had equipment for newborn respiratory support (Fig. 2). If these limited data were generalizable for Africa, less than one-quarter of babies born in facilities would have access to resuscitation, and because only about half of births are in facilities, only one-eighth of babies who require resuscitation may receive this intervention. Clearly a major increase in coverage is required. The key challenges are how to seize the missed opportunity to ensure adequate provision of basic resuscitation in facility settings, including equipment and competent personnel, and how to address the gap for neonatal resuscitation for 60 million non-facility births each year.

1.2. Objective

In this paper, the third in a series that focuses on reduction of intrapartum-related neonatal deaths, we review the current evidence for neonatal resuscitation and post-resuscitation management. Several publications have recently analyzed the level of evidence for specific components of neonatal resuscitation in settings with limited

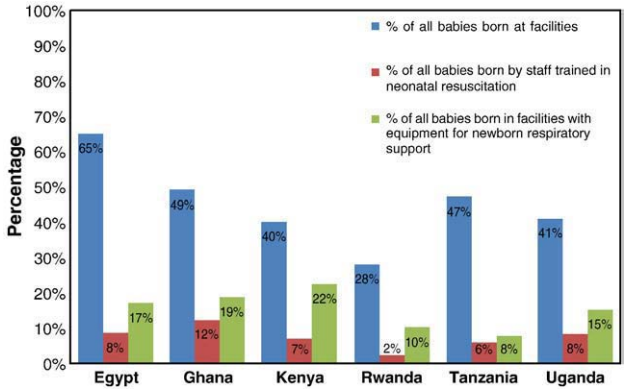

Fig. 2. Estimates from 6 countries for the percentage of babies born in facilities, and the percentage of facilities with staff trained in neonatal resuscitation and with bag-and-mask. Source: **Egypt:** Ministry of Health and Population, El-Zanaty Associates, and ORC Macro. *Egypt Service Provision Assessment Survey 2004: Key Findings.* Calverton, Maryland, USA: Ministry of Health and Population and ORC Macro; 2005. **Ghana:** Ghana Statistical Service (GSS), Health Research Unit, Ministry of Health, and ORC Macro. *Ghana Service Provision Assessment Survey 2002.* Calverton, Maryland: Ghana Statistical Service and ORC Macro; 2003: 135. **Kenya:** National Coordinating Agency for Population and Development (NCAPD) [Kenya], Ministry of Health (MOH), Central Bureau of Statistics (CBS), ORC Macro. *Kenya Service Provision Assessment Survey 2004.* Nairobi, Kenya: National Coordinating Agency for Population and Development, Ministry of Health, Central Bureau of Statistics, and ORC Macro; 2005. **Rwanda:** National Institute of Statistics (NIS) [Rwanda], Ministry of Health (MOH) [Rwanda], and Macro International Inc. *Rwanda Service Provision Assessment Survey 2007.* Calverton, Maryland, USA: NIS, MOH, and Macro International Inc; 2008. **Tanzania:** National Bureau of Statistics [Tanzania], Ministry of Health and Social Welfare [Tanzania], and Macro International Inc. *Tanzania Service Provision Assessment Survey 2006: Key Findings on Family Planning, Maternal and Child Health, and Malaria.* Dar es Salaam, Tanzania: National Bureau of Statistics and Macro International, Inc; 2006:13. **Uganda:** Ministry of Health (MOH) [Uganda] and Macro International Inc. *Uganda Service Provision Assessment Survey 2007.* Kampala, Uganda: Ministry of Health and Macro International Inc. 2008; 132.

resources [10,13,14]. Here we focus on the evidence for neonatal resuscitation and post-resuscitation care in low-resource settings, the evidence for impact in different settings, and a series of national case studies to synthesize the implications for scaling-up neonatal resuscitation. The major focus is on evidence and feasibility of interventions most relevant to the lower levels of the health system including:

- the first level of the health system providing basic emergency obstetric and neonatal care;
- health posts, maternity clinics, or home births with skilled birth attendants; and
- community settings without skilled birth attendants.

A complete discussion of resuscitation interventions for referral facilities is beyond the scope of this paper; however, some selected referral-level interventions and relevant issues for programs and scaling up are included, particularly regarding management of neonatal encephalopathy.

2. Methods

Details of the searches undertaken and the selection criteria are described in the first paper of this series [5]. In brief, searches of the following medical literature databases were conducted: PubMed, Popline, EMBASE, LILACS, IMEM, and African Index Medicus, Cochrane, and World Health Organization (WHO) documents. Initial searches were conducted in November 2002 and these were updated in May 2009. Keyword searches relevant for this paper included various combinations of the keywords: "birth asphyxia/asphyxia neonatorum/birth asphyxia," "neonatal mortality," "hypoxic ischaemic encephalopathy/hypoxic ischemic encephalopathy and developing countries," "neonatal encephalopathy," "newborn/neonatal resuscitation," "skilled birth attendant," "traditional birth attendant," "community health worker," "post-resuscitation management," "hypothermia," "fluid restriction," and "anticonvulsants." Modified GRADE criteria were used to evaluate the level of evidence [15], applying methods adapted by the Child Health Epidemiology Reference Group as detailed in an earlier paper in this series [5].

3. Results

3.1. Neonatal resuscitation algorithms and actions

Since the formation of the International Liaison Committee on Resuscitation (ILCOR) in 1992, there have been a number of international consensus statements regarding resuscitation standards. The first statement on neonatal resuscitation was in 1999 and this was updated in 2005 [2,16]. These guidelines are intended for settings with highly-skilled personnel, and focus on advanced resuscitation with use of endotracheal intubation, cardiac massage, and epinephrine. However, some of the principles, particularly the focus on effective ventilation, apply to low-resource setting [17]. Fig. 3 illustrates a variation of the ILCOR guidelines, published by the American Heart Association and the American Academy of Pediatrics [18]. The WHO guide "Basic newborn resuscitation: a practical guide" is aimed at first-referral level and higher in low-resource settings [3]. The more recent WHO Hospital Pocket Book [19] provides a more specific algorithm that includes ventilation and cardiac massage rates, shown in Fig. 4 with minor adaptations to make it consistent with ILCOR [17,18]. The American Academy of Pediatrics is currently field testing a new educational program entitled "Helping Babies Breathe," to promote neonatal resuscitation at lower levels of the health system in low-resource settings [20]. Fig. 5 shows the field test version, which includes pictorial depictions of each step in resuscitation up to the assessment of heart rate in a baby who has received ventilation.

An increasing number of algorithms and guidelines for neonatal resuscitation at varying levels of the health system are available. Many of these are based more on expert consensus than on rigorous evidence, partly because of the ethical issues surrounding randomized trials of an already established practice. While many detailed questions remain around the minutiae of these algorithms, the big question is how to reach the estimated 6 million newborns each year who require basic neonatal resuscitation and "how to implement" questions such as the where, who, and what of neonatal resuscitation.

3.1.1. Which newborns should be resuscitated?

There is little systematic evidence to guide criteria to determine which newborns should be resuscitated. The ILCOR statement emphasizes that the decision is based not on a single sign but on a "compound assessment" of a sign complex, including initial cry, breathing, tone, heart rate, maturity, and response to stimulation [16]. This requires a high level of skill for complex and rapid clinical assessment, judgment, and decision making. The WHO guide [3] recommends a simple, more feasible clinical criterion based on assessment of breathing alone: all babies who do not cry, do not breathe at all, or who are gasping 30 seconds after birth should be resuscitated with bag-and-mask ventilation. This simple indication for resuscitation is similar to the signs that were listed as most useful and feasible in a survey of program managers [21]. Several studies have assessed the predictive value of specific newborn symptoms compared with low cord pH or neonatal death [22–25]. The symptom of "no cry at birth" had a moderate positive predictive value for neonatal death, but was not specific for intrapartum hypoxia [22]. Other symptoms that have been evaluated include delayed or absent breathing, limpness or inactivity, pallor or cyanosis, irregular breathing, and cord pulsation. One study suggested that the combination of poor cry, color, and activity was the best predictor of abnormal cord pH (correlation coefficient 0.71; r=0.38); however, complex scoring systems are not feasible in low-resource settings, particularly at community level [23–25]. Therefore, the simple assessment advocated by WHO appears to be the best practice for now, but there remains a need for a systematic clinical definition of the baby who needs resuscitation and a simplified, but acceptably specific, case definition for resuscitation at the community level.

3.1.2. How should the newborn with meconium staining of the liquor be managed?

Routine intrapartum perineal suctioning for meconium-stained amniotic fluid is no longer recommended after a multicenter randomized controlled trial found no significant benefit [26]. However, these data are from high-income countries with low incidence of meconium aspiration, and may not be generalizable to low-income countries where meconium aspiration may be more common. If the baby is vigorous at delivery (breathing well, good tone, heart rate >100 beats per min), suctioning of the trachea is not required and may be harmful [27,28]. Thus, the indication for endotracheal suctioning at delivery is staining of the liquor with meconium in a nonvigorous baby [2]. If the baby is not breathing, the trachea should be suctioned until clear or until the baby's heart rate falls below 60 beats per minute, in which case the baby should be ventilated. Tracheal suctioning requires advanced skill and frequent practice, is associated with hazards [3], and is not usually recommended, even for physicians at health facilities unless they are specifically trained. Where endotracheal intubation with suctioning is not feasible, it is unclear whether babies with meconium staining should undergo suctioning before birth, after birth, or not at all [29].

3.1.3. What equipment should be used for suction and on whom?

Healthy, vigorous newborns do not require suctioning. Indeed routine oro–naso–pharyngeal suctioning may have potential adverse effects (apnea, upper airway damage, bradycardia, and delays to establishing breathing) [26,29,30]. The WHO Basic Resuscitation Guide only recommends suctioning with a mechanical suction device, electrical

or foot-pedal operated, where possible, when there is meconium and the newborn does not cry. Even in facilities, options for suctioning may be limited because of the cost of mechanical equipment or a lack of appropriate catheters. Risk of cross-contamination of reused catheters is a concern. There are also concerns that excessive negative pressures may be used in mechanical suctioning, resulting in mucosal injury. WHO discourages the use of a cloth to clean the mouth because of a lack of evidence indicating benefit and potential mucosal damage [3]; however, this practice is still common in the community [21]. Mucus extractors with one-way valves are also commonly used, although the operator may be at risk for infection. Rubber bulb suction devices are frequently used, but represent infection hazards when reused because the interior cannot be cleaned and dried adequately. Development of safe, inexpensive, and easily-cleaned suction devices is required.

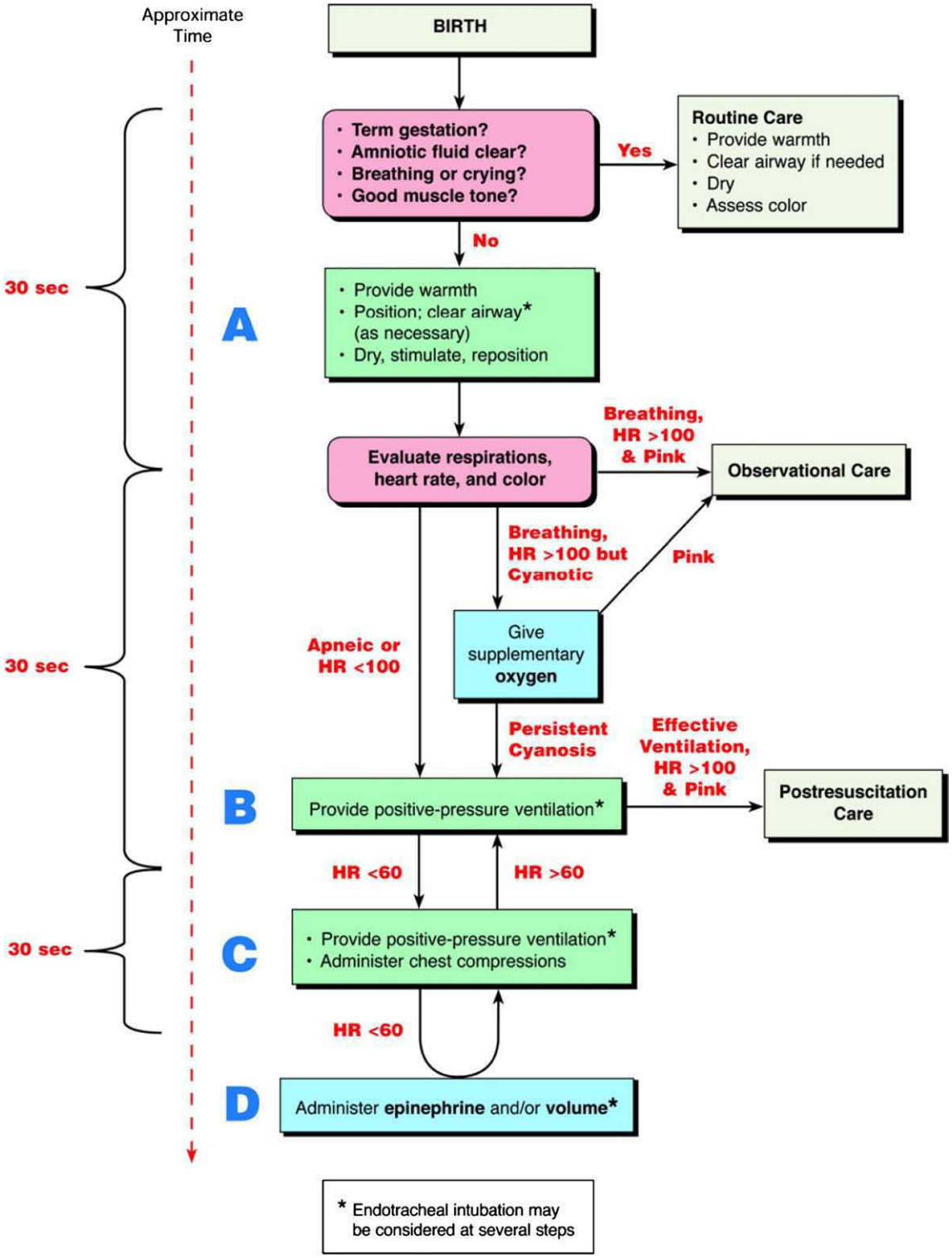

Fig. 3. Neonatal algorithm for advanced resuscitation according to the American Heart Association and the American Academy of Pediatric's updated version of the original ILCOR algorithm. Reprinted with permission from Pediatrics, 117, e1029-e1038, Copyright ©2005 by the American Heart Association and American Academy of Pediatrics. Source [18].

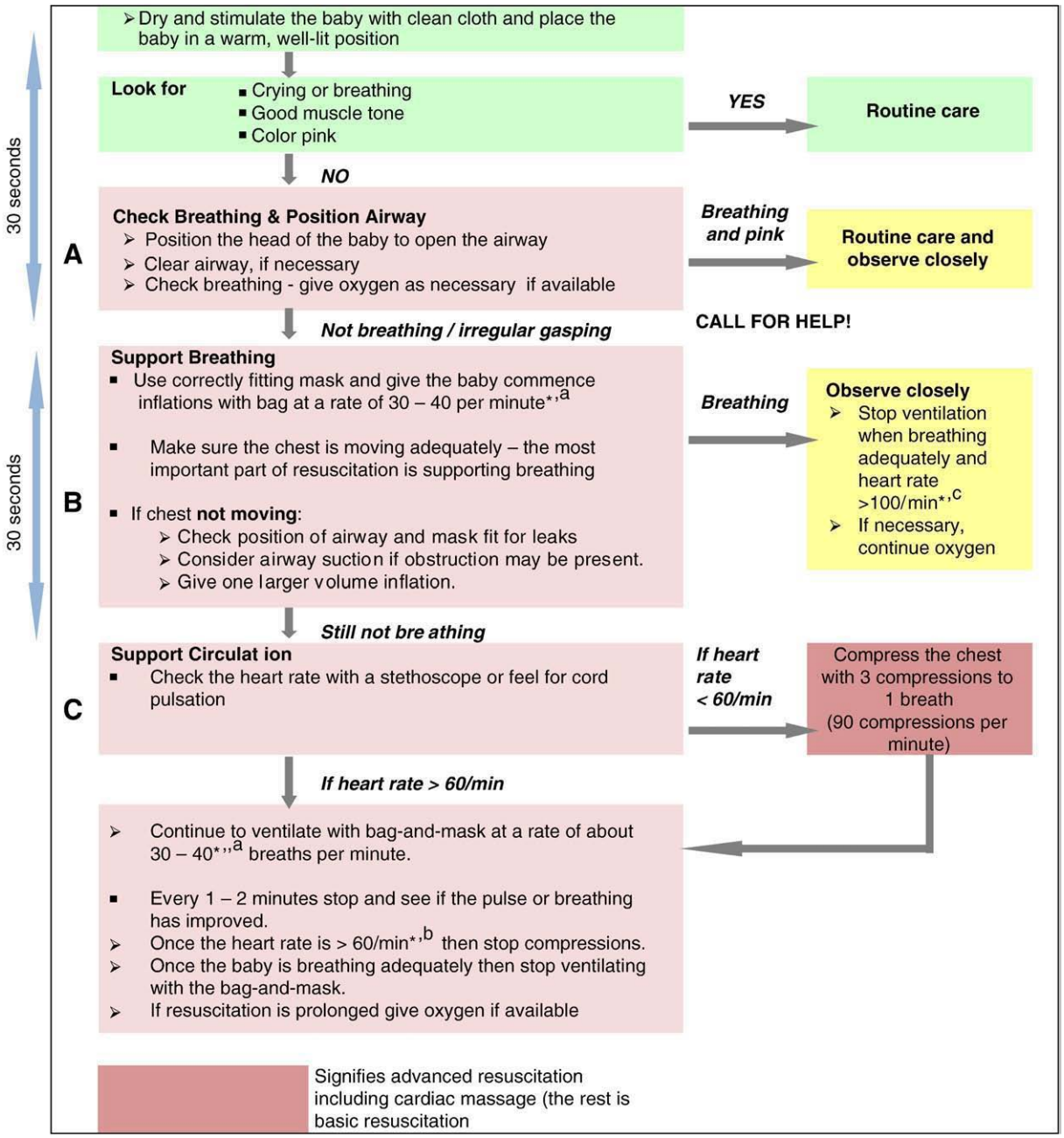

Fig. 4. Neonatal Resuscitation Algorithm based on WHO Pocketbook of Hospital Care for Children and updated with ILCOR 2005 Recommendations. Source [19]. *Items altered from the original for consistency with ILCOR. *[a] Changed instruction for 5 initial inflations to beginning regular ventilations as the 5 inflations based on just one study. Altered ventilate rate to a range of 30–40 instead of 40 based on more recent ILCOR guidelines. *[b] Changed heart rate to stop cardiac massage at from 100 per minute (WHO) to 60 per minute.*[c] Added criteria for stopping ventilation. Color coding added to be consistent with Integrated Management of Childhood Illness (green = well; yellow = ongoing care; pink = add now).

3.1.4. What equipment is needed for resuscitative ventilation?

3.1.4.1. Type of pressure control resuscitation device. The key equipment for neonatal resuscitation is a self-inflating bag-and-mask, first invented by Ruben in 1954 using bicycle parts [31]. Several studies have shown that for the majority of babies who do not breathe at birth, initial ventilation with a self-inflating bag-and-mask is adequate, and there is little difference in the time to first breath whether using ventilation by bag-and-mask or endotracheal intubation by an experienced provider [1,32]. Endotracheal intubation may be more effective than bag-and-mask ventilation for severely depressed babies, but this is often not an option in low-resource settings because of a lack of available equipment (working laryngoscope, supply of endotracheal tubes in a variety of sizes) and skills. In addition, these babies may require ongoing ventilation, which is usually not an option.

The WHO guide still recommends that "every birth attendant should be trained in mouth-to-mouth ventilation in case there is no equipment or equipment fails" [3]. This recommendation needs to be balanced against the possible risk of transmission of serious infections to the provider based on local prevalence of HIV and other infections.

In the 1970s, when bag-and-mask devices were still costly, mouth-to-mask and tube-and-mask devices were developed as a low-cost alternative, with the potential to reduce infection transmission compared with mouth-to-mouth resuscitation. Use of a prototype mouth-to-mask device with a short tube was compared with use of a self-inflating bag-and-mask device in two teaching hospitals: Dar es Salaam, Tanzania and

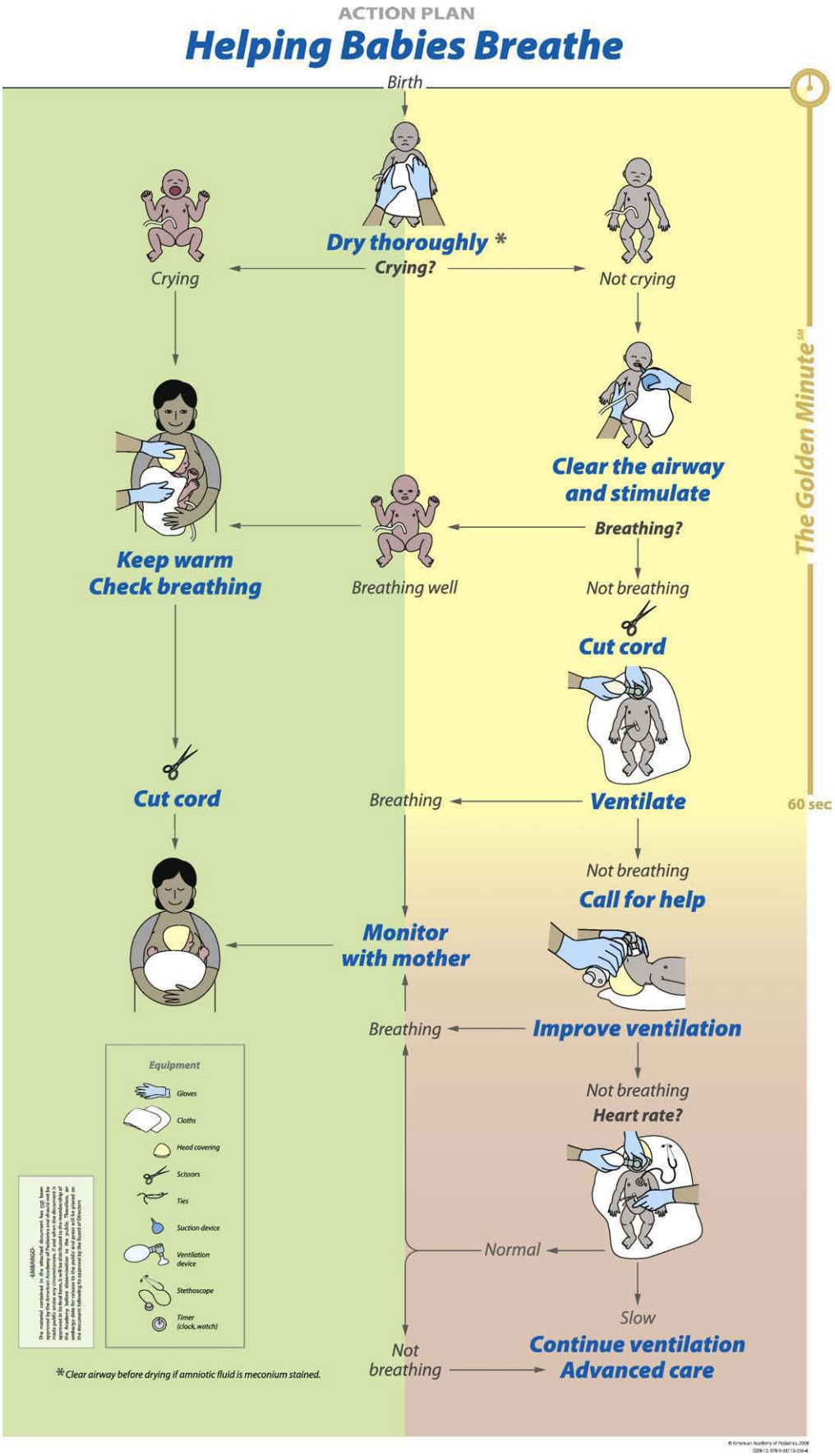

Fig. 5. Action Plan for Helping Babies Breathe for lower levels of the health system. Reprinted with permission granted by American Academy of Pediatrics, 2009 [20].

Bombay (now Mumbai), India [33]. Newborns were non-randomly (according to predetermined time periods) allocated to bag-and-mask (Dar es Salaam n=56, Bombay n=24) or mouth-to-mask device groups (Dar es Salaam n=64; Bombay n=30). No significant differences were detected between the two methods as determined by Apgar scores at 5 and 10 minutes, time to first gasp, incidence of neonatal convulsions, and neonatal death. However, the study lacked sufficient power to detect differences for most outcomes. This study reported that the mouth-to-mask method "was tiring and uncomfortable for the resuscitating personnel," as the provider's breathing had to regulate pressure as well as rate. The study's conclusions were corroborated by a survey of 173 program managers who rated the mouth-to-mask device as having low program feasibility [21].

In Indonesia, Program for Appropriate Technology in Health (PATH) compared 4 different neonatal resuscitation devices: 2 bag-and-mask devices and 2 tube-and-mask devices (1 with a short tube and 1 with a long tube) [34]. Trained community midwives used a computerized resuscitation doll and found no significant differences among the devices for tidal volume or ventilatory rate. Midwives preferred the bag-and-mask device for ease of use, their belief in greater efficacy, and safety with regard to transmission of infections. Challenges to using the tube-and-mask devices included fatigue and difficulties in visualizing the neonate during resuscitation, ascertaining appropriate pressure, and communicating during resuscitation. When device costs were also considered, the long tube-and-mask device was selected because it was substantially cheaper at the time. While the long tube-and-mask device was considered overall to be feasible and affordable, the short-tube device, also affordable, was rated unfavorably by the midwives. The tube-and-mask devices were also considered to be easier to clean than the bag-and-mask devices.

For home deliveries attended by community health workers (CHWs) in rural India, the Society for Education, Action and Research in Community Health (SEARCH) trial compared tube-and-mask with bag-and-mask ventilation over sequential time periods [35]. A tube-and-mask device with a long tube was used by CHWs during the earlier time period (1996–1999), whereas a self-inflating bag-and-mask device was used in the later period (1999–2003) when an affordable device became available locally. Comparing the before-and-after data, there were non-significant trends toward lower case fatality rates for "severe asphyxia" (39%)—not breathing at 5 minutes—and apparently fresh stillbirths (33%) during the period when the bag-and-mask device was used. Moreover, CHWs reported that the bag-and-mask was easier to use. CHWs also noted difficulty in bending forward to ventilate with the tube-and-mask device, especially if prolonged (up to 15 minutes) assisted ventilation was required. SEARCH investigators concluded that the bag-and-mask device was more acceptable to providers, and potentially more effective at saving lives.

Hence, the self-inflating bag-and-mask device remains the standard of care. While the typical self-inflating bag-and-mask devices used in high-income countries are expensive, there are affordable versions now available in many low-income settings. Key considerations are that the bag-and-mask device is designed to be reusable and easily cleaned for safe reuse. In certain community-based settings, a tube-and-mask device, while probably less effective, may be considered as a temporary alternative.

3.1.4.2. Should air from the room or oxygen be used? Whether resuscitation should be initiated with air from the room or oxygen has been previously reviewed, and will be briefly discussed here. A recent meta-analysis pooling data from 4 trials [36–39] found a significant reduction in mortality for newborns who were resuscitated with room air versus 100% oxygen (RR 0.71; 95% CI, 0.54–0.94) [40]. There was also evidence that the recovery time was shorter for newborns who received room air, including shorter time to first breath and sustained respirations, as well as higher Apgar scores. The authors estimated that one death could be prevented for every 20 newborns resuscitated with room air versus 100% oxygen (95% CI, 12–100).

Although ILCOR states that there is "insufficient evidence to specify the concentration of oxygen to be used at initiation of resuscitation" [17], WHO recommends air for resuscitation of "most babies," also citing the unavailability and expense of oxygen. It is reasonable to recommend the use of air for resuscitation at community level and in facility settings without routine availability of oxygen. Further research is required to refine the recommendations for use of supplemental oxygen at resuscitation in facility settings where oxygen is available. However, given these data, it is clear that nonavailability of oxygen is not the limiting factor for the implementation of neonatal resuscitation.

3.1.5. Should chest compressions be performed in basic resuscitation?

There are no human studies that assess the benefit of chest compressions used in neonatal resuscitation [10]. Reported experience with 30 839 consecutively born newborns in a tertiary center noted that chest compressions were employed on only 39 occasions (0.12%) [9]. The authors note that 31 of the 39 babies who received chest compressions were believed to be have been inadequately ventilated [9]. The WHO guide does not include chest compressions in basic resuscitation unless the baby has persistent bradycardia "despite adequate ventilation," and as long as two trained providers are present and the heart rate has been "assessed correctly" [3]. There are 4 arguments to support omission of chest compressions, at least for first-level facilities and community level:

(1) chest compressions are not necessary for the majority of babies who will survive [1,9], suggesting that the focus should be on ensuring *effective* ventilation;
(2) a second trained person to perform chest compression while the baby is ventilated is frequently unavailable in low-resource settings;
(3) studies have shown that even skilled personnel are often inaccurate in assessing the heart rate/pulse of newborns [41]; hence, a lesser skilled practitioner under stress may be considerably less able to assess heart rate and make correct decisions; and
(4) babies who require chest compressions often require ongoing intensive care support post resuscitation—a level of care not available at first-level facilities or at many referral facilities in low-income settings.

3.1.6. Which, if any drugs, are useful in basic neonatal resuscitation?

Both the ILCOR guidelines and the WHO guide agree that drugs are rarely indicated in neonatal resuscitation [3,16,42] and that ventilatory support should be the priority. The rare use of epinephrine for neonatal resuscitation, even in a tertiary care setting (18 uses in 30 839 deliveries), indicates a low priority for use of medication in neonatal resuscitation within limited-resource settings [9]. The ILCOR guide, intended for advanced resuscitation, gives details of the evidence for drugs such as epinephrine and dextrose (Fig. 3) [17]. With the priority being ventilation, followed by chest compressions, drugs should probably not be considered, except in circumstances where 3 trained providers are available: a person to continue ventilation, a person to perform compressions, and a third person to administer drugs. Thus, there is probably no role for drugs in low-income settings except in advanced resuscitation in referral facilities.

3.1.7. When should resuscitation not be initiated, and when should it be stopped?

This is a difficult ethical question, particularly regarding resuscitation of babies with malformations or extreme prematurity. There is a significant body of literature, almost all relevant to settings with neonatal intensive care. Only one paper was identified that was specifically related to low-income country settings [43]. A detailed discussion is beyond the scope of the present paper. The WHO guide recommends that the following should not be resuscitated: stillbirths that are not fresh; the newborn with a "severe malformation" (hydrocephaly, anencephaly, trisomy 13 or 18, short-limbed dwarfism, multiple defects); "extremely low gestational age" to be determined by local policy and probability of survival [3].

In addition to addressing extremely low gestational age, resuscitation protocols at peripheral levels of the health system will need to consider the skill level and experience of the personnel who will make the decision whether or not to resuscitate. One approach is to begin resuscitation for all babies who may appear lifeless, within locally determined gestational age limits, as long as there are no major malformations (such as anencephaly) and no evident maceration. Monitoring and infant follow-up are essential to ensure appropriate practices by peripheral-level providers and to determine whether neurological disability might be increased. The current ILCOR guidelines recommend that after 10 minutes of continuous and adequate resuscitative efforts, neonatal resuscitation may be discontinued if there are no signs of life (no heart beat and no respiratory effort). If the baby is still not breathing after 10 minutes, even if there may be a heart rate, some experts advocate that if there are no facilities for intubation and ventilation then resuscitation should be stopped unless there are clear indications that there is a modifiable factor involved, such as opioid administration to the mother during labor.

3.2. Evidence for the impact of neonatal resuscitation training

3.2.1. Resuscitation in health facilities

We recently conducted a systematic review of the evidence for neonatal resuscitation and a meta-analysis showing that neonatal resuscitation training at the facility level averts 30% of intrapartum-related neonatal deaths [11]. The studies of facility-based neonatal resuscitation from low- and middle-income countries are shown in Table 1.

There were 6 observational before-and-after studies of primary neonatal resuscitation training programs for delivery room personnel (nurses, midwives, and doctors) that reported impact on intrapartum-related neonatal mortality (IPR-NMR). In rural China, a training program in modern resuscitation at the primary county maternal health centers was associated with a reduction in intrapartum-related case fatality rate from 7.1% to 0.45% [44]. In Zhuhai, China, a program training all delivery room staff in the American Academy of Pediatrics-American Heart Association National Resuscitation Program (NRP) resulted in a 63% reduction in early neonatal mortality [4], from 9.9 per 1000 before training to 3.4 per 1000 after training. Results from a nationwide program to scale up the training program in China are highlighted in Panel 1 at the end of the paper. The National Neonatology Forum of India initiated a national Neonatal Resuscitation Training Program in 1990 that was evaluated in 14 teaching hospitals [8]; the intrapartum-related neonatal mortality rate fell significantly from 1.6 per 1000 to 1.1 per 1000, comparing the surveillance period before to after training. Intrapartum-related morbidities including neonatal encephalopathy did not change significantly, although long-term follow-up assessing disability is not available. In Bulgaria, a national resuscitation training program for all delivery room staff in the country was associated with a significant 13% reduction in neonatal mortality and suggestive of declines in the early neonatal and intrapartum-related neonatal mortality rates [45]. A trial of midwife training in the WHO Essential Newborn Care Package (including basic newborn resuscitation with the bag-and-mask device) was taught to midwives in 18 low-risk delivery/health centers in Zambia [46], and demonstrated a 43% reduction in intrapartum-related neonatal deaths. Macedonia implemented a comprehensive perinatal training strategy of doctors and nurses that included a module on neonatal resuscitation, and observed a 21% reduction in perinatal mortality rate (PMR) over 2 years from before-to-after training, although cause-specific mortality was not available and

Table 1
Evidence for the impact of neonatal resuscitation at the facility level: Mortality effect.

Intervention/study (date order)	Setting	Baseline mortality rates	Mortality Effect: Percentage relative reduction in mortality rate (*number of deaths in intervention or end line group*); RR or OR (95% CI)				Investigator and year
			Early neonatal mortality rate (ENMR)	Perinatal mortality rate (PMR)	Neonatal mortality rate (NMR)	Intrapartum-related neonatal mortality (IPR-NMR)	
Before-and-after baseline surveillance of 1722 newborns followed by 2-year prospective study of 4751 newborns while instituting standardized resuscitation guidelines	China Urban hospital	ENMR 34	66% *(16)* RR 0.34 (0.17–0.67)	–	–		Zhu et al. [4] 1997
Before-and-after surveillance of American Academy of Pediatrics' National Resuscitation Program training of village health center physicians, nurses, birth attendants in 1996	Peripheral health centers, Kerala India	IPR-NMR 5.4				32% *(2)* RR 0.68[a] (0.15–3.04)	Tholpadi et al. [105] 2000
Before-and-after surveillance in 14 teaching hospitals for 3 months before institution of National Resuscitation Program and 12 months after	14 University Hospitals, India	NMR 37 IPR-NMR 16	–		No significant change	30% *(283)* RR 0.70 (0.56–0.87)	Deorari et al. [8] 2001
Before-and-after assessment of 10 month perinatal training program of 115 doctors and nurses (neonatal resuscitation, thermal care, jaundice, respiratory distress syndrome, infection control) in 1999	Tertiary care hospitals, Macedonia	PMR 27.4		28% RR 0.72 (0.66–0.78)	36% RR 0.64 (0.56–0.72)		Jeffery et al. [47] 2004
Before-and-after surveillance of perinatal outcomes while instituting nationwide training of neonatal resuscitation for all delivery room personnel in Bulgaria from 2001–2003	National study. All hospitals Bulgaria	PMR 12.3 NMR 7.8 ENMR 5.1	14% RR 0.86 (0.74–1.01)			17% *(38)* RR 0.83 (0.54–1.27)	Vakrilova et al. [45] 2005
Before-and-after surveillance of WHO Essential Newborn Care Package, including basic resuscitation with bag-and-mask	Low-risk maternity centers, Zambia	IPR-NMR 3.2	44% *(127)* RR 0.56 (0.43–0.73)			43% *(37)* RR 0.57 (0.34–0.93)	Chomba et al. [46] 2008
Before-and-after evaluation of nationwide educational program of neonatal resuscitation training program started in 2004. Before-after comparison of incidence rates of babies not breathing (Apgar <7) and intrapartum-related neonatal mortality in 10 provinces	40 hospitals in China	IPR-NMR (delivery room) 3.3				33% *(163)* RR 0.67[b] (0.34–1.30)	Wang et al. [100] 2008

[a] Authors report change in definition of "asphyxia" before-versus-after intervention.
[b] Definition of IP-mortality was death in the delivery room of an infant with 1 minute Apgar<7.

the intervention included multiple concurrent strategies [47]. Finally, in a national program of neonatal resuscitation training in Malaysia, initiated in 1996, national trends in neonatal mortality rates and perinatal mortality rates were observed to decline over an 8-year period [48]. However, it is difficult to attribute this effect to resuscitation training because intrapartum-related specific neonatal mortality was not available, and many other improvements in obstetric and newborn care likely occurred over the 8-year study period.

3.2.2. Neonatal resuscitation in the community

In the community, home births may be attended by persons with various skills and experience, ranging from skilled birth attendants to trained or untrained TBAs, community health workers, or family members (Table 2).

3.2.2.1. Community midwives. A study of training midwives in neonatal resuscitation in Cirebon district, West Java, Indonesia, is highlighted in Panel 2 at the end of the paper.

3.2.2.2. Trained traditional birth attendants. Several evaluations from India have assessed the roles of traditional birth attendants (TBAs) in neonatal resuscitation. In the 1980s, Daga et al. [49] trained TBAs in essential newborn care including mouth-to-mouth resuscitation of babies not breathing. At the start of the program the perinatal mortality rate was 75 per 1000 live births (1987) and this had reduced to 29 at the end of the program in 1990, although the effect of resuscitation training cannot be isolated as several interventions were delivered simultaneously. In the early 1990s, Kumar et al. [50,51] at Chandigarh, India, trained TBAs in the recognition of "birth asphyxia" by clinical assessment and newborn resuscitation, including use of a cloth to wipe the baby's mouth, and mouth-to-mouth ventilation. A subset of nonrandomly selected TBAs were trained in "advanced" resuscitation techniques, including use of a mucus extractor and a self-inflating bag. The prevalence of the non-breathing baby was lower (0.9%) in the advanced resuscitation group compared with the basic group (2.4%), and there was a 20% reduction in case fatality rate among newborns with TBAs trained in advanced resuscitation had a 20% reduction in case fatality rate; however, this was not significant. The definition of "asphyxia-specific mortality" included preterm infants. Thus, while the difference in case fatality was reported to be statistically significant, it could have been due to improved management of the preterm baby, a reduction in the severity of the initial intrapartum insult, as well as a better resuscitation technique. A recent study evaluated the effect of training community birth attendants (TBAs and nurses) in essential newborn care (ENC), including basic neonatal resuscitation. ENC training was provided in 95 communities in 6 countries (Argentina, Democratic Republic of Congo, Guatemala, India, Pakistan, and Zambia). In a before-and-after comparison, stillbirth rates declined from 23 to 16 stillbirths per 1000 live births (RR 0.63; 95% CI, 0.44–0.88). The authors speculated that the decrease in stillbirths may have resulted from effective resuscitation of newborns who would have been classified as stillborn pre-ENC training [52].

3.2.2.3. Community health workers. In a study from Gadichiroli, India, training of village health workers in neonatal resuscitation was feasible and associated with significant reductions in intrapartum-related mortality (see Panel 3).

3.2.2.4. Family member. We did not identify any studies of training family members in neonatal resuscitation. School-aged children have been trained to effectively perform adult CPR in several settings [53–55]. A family member may certainly provide the essential first steps of neonatal resuscitation (drying, warming, stimulation, airway positioning), and in a recent expert Delphi process, an estimated 10% of intrapartum-related neonatal deaths could be averted by the immediate steps of drying and stimulating a baby who is not breathing [11].

3.3. Post-resuscitation management

Post-resuscitation management can improve survival and long-term outcomes of newborns who have survived intrapartum hypoxia and received neonatal resuscitation. However, the evidence regarding effect and capacity for implementation is primarily from high-income settings. Selected post-resuscitation interventions that may apply to district and referral-level hospitals in low-resource settings are summarized in this section.

Babies who required extensive resuscitation should have ongoing assessment for at least 12–24 hours after birth. Even those who have responded appropriately to resuscitation may need further intervention to support breathing, achieve adequate oxygenation, avoid hyperthermia, and maintain glucose and fluid balance. Many of the gains from successful neonatal resuscitation can be lost by poor aftercare and not attending to potential complications. Limited studies indicate that long-term neurological outcomes may be modified by corrective responses to clinically important issues, such as thermal balance, serum glucose levels, oxygen use, seizure control, and medication dosing. Management of neonatal encephalopathy is not feasible in community settings, and requires referral to a district- or tertiary-level facility. In a series of 98 newborns who were transported for specialty care after resuscitation, Portman et al. [56] observed that 61% required continued assisted ventilation, 45% had renal dysfunction, 27% had abnormal liver function tests, and 53% had low blood pressure.

3.3.1. Breathing and oxygenation

Newborns who have experienced intrapartum hypoxia have a high frequency of apneas in the hours following birth and may require supplemental oxygen [57], especially if there is hypoxic lung injury or meconium aspiration. Apnea can be associated with periods of hypoxemia and hypotension [58]. Treatment with methylxanthines or management of underlying causes may reduce apnea [59]. However, mechanical ventilatory support with nasal continuous positive airway pressure (CPAP) or intermittent mandatory ventilation may be necessary for newborns with severe intrapartum hypoxia, which may not be an option in many low-income settings.

While hypoxemia should be avoided, hyperoxia has been associated with cerebral vasoconstriction in preterm babies and lambs [60,61] and with central nervous system cell death in rat pups [62]. Ahdab-Barmada et al. [63] reported a pattern of ponto-subicular necrosis in critically ill newborns with PaO2 higher than 150 torr. These data suggest that excessive oxygen use should be avoided, particularly in the newborn with neonatal encephalopathy, and that these babies receiving supplemental oxygen should have regular oxygen saturation monitoring.

3.3.2. Serum glucose and fluid management

Hypoglycemia can cause neuronal injury and potentiate the injury associated with neonatal encephalopathy [64]. There is considerable uncertainty as to the lowest safe level of serum glucose in healthy newborns. Even though definitive data about the immediate management of glucose levels are lacking, both hypoglycemia and hyperglycemia may be associated with adverse outcomes [65,66]. Since many newborns with neonatal encephalopathy have a period of significant gastrointestinal dysfunction, parenteral glucose administration should be considered if feasible.

Current recommendations for neonatal encephalopathy also include fluid restriction and avoidance of fluid overload to avert cerebral edema [67] and overcome the effect of excessive vasopressin release after intrapartum hypoxia [68,69]. A recent Cochrane review [70] evaluated all randomized or quasi-randomized trials of fluid restriction in term newborns suffering intrapartum-related hypoxia, but found no studies that met the criteria for inclusion. This lack of evidence necessitates well-designed studies investigating the effects of fluid management on outcomes such as mortality, seizure activity, evidence of cerebral damage, electrolyte status, and multiorgan dysfunction. Until such clear guidelines

Table 2
Evidence for mortality effect of neonatal resuscitation in community-based settings.

Intervention/study (date order)	Setting	Percentage skilled attendance	Baseline mortality rates	Mortality Effect: Percentage relative reduction in mortality rate *(number of deaths in intervention or end line group)*; RR or OR (95% CI)					Investigator and year
				Stillbirth rate (SBR)	ENMR	PMR	NMR	IPR-NMR	
Nonrandomized comparison of perinatal outcomes between subset of TBAs trained in "advanced" resuscitation with suction and bag-and-mask as opposed to usual TBA training with mouth-to-mouth resuscitation	Rural India	<10%		–	–	19%[a] *(4)* RR 0.82 (0.56–1.19)	–	70% *(5)* RR 0.3 (0.1–0.8)	Kumar [24] 1995 Kumar [106] 1998
Package of newborn home-based care. Longitudinal study; pre-post comparison. Baseline period (1993–1995): trained TBA using mouth-to-mouth resuscitation. Intervention: team of TBA and semi-skilled village health workers; training of village health workers in tube-and-mask (1996–1999) and later bag-and-mask (1999–2003) ventilation.	Rural India Maharashtra state 39 villages: total population 38 998; 4033 home deliveries during study period	89%–95% Home deliveries, 92%–97% conducted by TBAs; 77%–84% attended by VHW's	NMR 52/1000 IPR-NMR 10.5/1000 Incidence: "Mild birth asphyxia" 14.2% "Severe birth asphyxia" 4.6%	32.6%[b] reduction in fresh stillbirth rate				48% reduction in case fatality of "severe asphyxia" cases[c] 65% reduction in IPR-NMR[c] RR 0.35 (0.15–0.78) 42%[d] reduction in IPR-NMR with tube-and-mask *(37)* and insignificant 12% [e] reduction with mouth-to-mouth resuscitation *(56)*	Bang et al. [35] 2005
Training of Bidan di Desa (village midwives) in neonatal care, including management of neonatal resuscitation using tube-and-mask resuscitators. Refresher 5-minute video distributed with tube-and-mask devices. Before and after comparison of midwife knowledge, observed skills, and neonatal mortality rates.	Rural Cirebon, West Java Indonesia Pop: 2 million	80% of deliveries attended by health provider (midwives, doctors), 70% deliveries attended by midwives. 75% deliver at home	NMR 15 PMR 21 IPR-NMR 5.1	No significant change Baseline 8/1000 End-line 6/1000		29%[f]	40% [f] reduction in overall NMR (No.) not reported	47%[f] reduction in IPR-NMR	Ariawan PATH [34] 2006
Training of birth attendants (TBAs, nurse midwives, and physicians) from rural communities in 6 countries in WHO essential newborn care and basic resuscitation, including bag-and-mask resuscitation. Prospective pre and post PMR and stillbirth rates comparison.	Rural Argentina, DR Congo, Guatemala, India, Pakistan, Zambia	NS	PMR 46/1000 SBR 23/1000	31% *(557)* RR 0.69 (0.54–0.88)	NS RR 0.99 (0.81–1.22)	PMR 15% *(1367)* RR 0.85 (0.70–1.02)			Carlo et al. [52] 2008

[a] Comparison of advanced neonatal resuscitation with bag-and-mask versus traditional neonatal resuscitation with mouth-to-mouth; "Asphyxia mortality" defined previously as the non-breathing baby without exclusion of preterm. Thus, effect may reflect some reduction in preterm neonatal mortality.
[b] Before and after comparison period of 1996–1999 versus 1999–2003.
[c] "Severe asphyxia" defined as not breathing at 5 minutes. "Mild asphyxia" defined as not breathing at 1 minute. Before and after comparison period of 1995–1996 versus 1996–2003.
[d] Comparison of intervention versus comparison areas from 1995–1999.
[e] Comparison of intervention versus comparison areas from 1993–1995.
[f] Number and confidence intervals not reported. Number of births based on estimates of births with crude birth rate.

become available, the subsequent management of newborns after intrapartum hypoxia must consist of close monitoring of fluid and glucose infusion needs, balanced against renal function and electrolyte status. There is an urgent need for developing and recommending appropriate evidence-based algorithms for fluid (or feeding) management of newborns with intrapartum hypoxia in the first 72 hours after resuscitation in district hospital settings.

3.3.3. Anticonvulsants

Neonatal seizures occur in 50% of newborns with neonatal encephalopathy as a consequence of intrapartum hypoxia. Results from both human and animal studies are consistent with the hypothesis that seizures themselves accentuate the cerebral injury of neonatal encephalopathy [71,72]. Anticonvulsive medications are indicated for neonatal seizures. There is consensus that parenteral phenobarbitol is the treatment of choice despite a relatively slow onset of action. Diazepam is not recommended as first-line therapy because of the higher risk of respiratory depression in the newborn [73].

The routine use of anticonvulsant therapy to prevent seizures following intrapartum hypoxia has been evaluated [74]. Of 7 randomized or quasi-randomized controlled trials, none was of sufficient methodologic quality and size to demonstrate a valid, clinically significant change in the risk of mortality or severe neurodevelopmental disability. The author's meta-analysis combining 5 studies comparing barbiturates with conventional therapy demonstrated no difference in risk of death (RR 1.13; 95% CI, 0.59–2.17) or severe neurological disability (RR 0.61; 95% CI, 0.30–1.22). Currently, routine anticonvulsant therapy for term newborns in the period immediately following intrapartum-related hypoxia cannot be recommended. However, as resuscitation strategies are scaled up, there is a need for well designed, suitably powered studies to address whether anticonvulsant therapy can reduce mortality and severe neuro-developmental disability.

3.3.4. Other potential drugs for neonatal encephalopathy

Most medications administered to newborns are modified and/or excreted by the liver and/or kidney. Neonatal encephalopathy has been associated with elevated liver enzymes in one study (27%) [56] and significant renal dysfunction in several studies [75]. Hence, clinicians should carefully consider the selection, dose, and administration frequency for all medication given to a baby who is not breathing. Given the improved understanding of the mechanisms affecting cerebral metabolism of babies who are not breathing, several new drugs have been tested but have not yet shown convincing evidence of benefit, including naloxone [76,77], xanthine oxidase inhibitors (allopurinol) [78], and dopamine [79]. Furthermore, while used in the past, there is no evidence to support the use of corticosteroids to treat neonatal encephalopathy [80], although animal data indicate that pretreatment with corticosteroids may be neuroprotective [81].

3.3.5. Thermal management and hypothermia for neonatal encephalopathy

Minimization of neonatal heat loss and cold stress at birth and providing a neutral thermal environment during care after delivery have been shown to reduce mortality [82,83]. Conversely, hyperthermia has been shown in animal models and human newborns to be physiologically destabilizing [84], to increase the risk of apnea [85], and to aggravate neonatal encephalopathy-induced central nervous system injury [86], with potentially fatal consequences [87]. The use of higher thermal control set points or an uncontrolled warming device should be avoided in babies with neonatal encephalopathy. Carefully controlled environmental temperature or skin-to-skin care may offer safer alternatives.

There has been considerable interest in evaluating the role of mild hypothermia in reducing neurologic sequelae after neonatal encephalopathy [88]. A recent Cochrane review [89] evaluated 8 randomized controlled trials that included 638 term newborns with moderate/severe encephalopathy and evidence of intrapartum hypoxia, and concluded that therapeutic hypothermia was associated with a reduction in mortality (RR 0.74; 95% CI, 0.58–0.94) as well as the combined outcome of mortality or major neuro-developmental disability to 18 months of age (RR 0.76; 95% CI, 0.65–0.89). Notwithstanding the increase in the need for inotropic support and a significant increase in thrombocytopenia, the reviewers concluded that the benefits of cooling on survival and neurodevelopment outweighed the short-term adverse effects. Given that most of these studies have been small and none were conducted in low-income countries, further trials are needed to determine the effectiveness and appropriate method of providing therapeutic hypothermia. A large multicenter trial of total body cooling in the treatment of newborns with neonatal encephalopathy is currently underway [90]. While therapeutic hypothermia is a high technology intervention, modifications have been developed for application in low-resource settings, including use of water bottles and servo-controlled fans [91,92]. However, the effectiveness may not be equivalent given different methods and settings, and randomized controlled trials are required and presently being conducted [93].

4. Considerations for scaling up neonatal resuscitation in low- and middle-income countries

Table 3 summarizes the evidence and recommendations based on a Grades of Recommendation Assessment, Development and Evaluation (GRADE) approach for the components of neonatal resuscitation at each level of the health system: in the home; health post or maternity clinic with skilled attendant; health facility with Basic Emergency Obstetric Care (BEmOC) services; district hospital with Comprehensive Emergency Obstetric Care (CEmOC) services; and tertiary referral level facilities. To save the lives of newborns who do not breathe, birth attendants at all deliveries must be competent in neonatal resuscitation at a level appropriate to the setting.

Simple immediate newborn care should be provided to newborns in all settings as part of essential newborn care, including warming, drying, stimulation, hygiene and thermal care. These immediate steps are the first in neonatal resuscitation, and can even be performed by family members. The most rational program approach at all levels is to ensure training in essential newborn care, either before or concurrent with training in basic and advanced neonatal resuscitation. Basic neonatal resuscitation training can be effectively performed by a wide range of health providers (from traditional birth attendants, CHWs, nurses, and midwives to physicians) resulting in reductions in intrapartum-related mortality in both the facility and home settings [11,35]. Advanced neonatal resuscitation, including intubation and medications, is typically only feasible in district or referral level facilities in most low-income settings.

4.1. Training, competency, and maintenance of resuscitation skills

Training courses in neonatal resuscitation can effectively increase the competency of health workers in conducting neonatal resuscitation and reduce potentially harmful practices [93]. Several training tools and materials are available to assist training courses (Fig. 6). Active monitoring of competency must be emphasized. In a cross-sectional evaluation of approximately 1500 skilled birth attendants in 5 countries, only half were competent to perform neonatal resuscitation with a bag-and-mask device [94]. Maintaining resuscitation knowledge and skills is a major challenge, particularly in settings where providers attend few deliveries and infrequently resuscitate newborns. In rural settings, TBAs, who may attend 30 or fewer births a year, would be expected to resuscitate with a bag-and-mask only once or twice a year, making maintenance of skills a challenge. Refresher training needs to be provided on a regular basis, as frequently as every 6 months, to prevent loss of skills [95,96]. In Zambia, resuscitation knowledge and skills of midwives declined significantly 6 months after a neonatal resuscitation program training [96]. In Indonesia, PATH conducted routine refresher training every 3 months for midwives and distributed DVD movies demonstrating resuscitation skills and found no decline in the resuscitation knowledge and practice

Table 3
Summary of GRADE level of evidence and recommendations for low- and middle-income settings.

Intervention	Level of evidence (GRADE)	Recommendations and program implications by health system setting				
		Community with birth attendant	Health post or peripheral maternity clinic	Health facility (BEmOC)	District hospital (CEmOC)	Tertiary referral level hospital
Simple immediate newborn care						
Warming, drying, stimulation	Very low	Strong recommendation for all births.				
Neonatal resuscitation						
Routine nasal and oropharyngeal suction	Very low	No proven benefit. Clearing the airway is standard of care for neonatal resuscitation, however it may also induce bradycardia and cause airway trauma if inexpertly performed. Oropharyngeal suctioning is not indicated for a vigorous baby. In the light of studies showing absence of benefit of routine suction for babies born through meconium-stained liquor, routine suction of nonvigorous babies cannot be recommended; although, based on practice norms, suction should be provided if there is any evidence of airway obstruction with suction to a level below the hypopharynx, performed only by providers skilled in airway management.				
Nasal and oropharyngeal suction on perineum to prevent meconium aspiration syndrome	Moderate against (including against endotracheal suctioning for vigorous baby)	Given evidence of lack of benefit and potential for harm, would not recommend suctioning for meconium at low-level health facilities.			At referral or tertiary level, for non-vigorous babies, endotracheal suctioning by skilled personnel is appropriate.	
1) Positive pressure ventilation and 2) Type of resuscitator (bag-and-mask vs tube-and-mask)	1) Moderate 2) Low	Feasible for nonmedical cadres, requires practice and supervision. Bag-and-mask preferred.		Strongly recommended with appropriate supervision, retraining. Self-inflating bag-and-mask resuscitator preferred.		
Ventilation with room air vs oxygen	Moderate–high	Initiate resuscitation with room air.		Initiate resuscitation with room air, may have oxygen if available and poor response to resuscitation		
Chest compressions when persistent bradycardia despite adequate ventilation	Low	Not recommended.		Requires 2 personnel at delivery, may not be feasible for most deliveries.	If 2 providers present at delivery, may consider in cases of bradycardia not responsive to effective ventilation.	
Sodium bicarbonate	Moderate against use	Of no benefit and potential for harm – not recommended.				
Adrenaline	Low	Evidence insufficient to show benefit; not feasible in this setting, not recommended.		Evidence insufficient to show benefit; requires at least 2 providers and skills, risk for incorrect dosing; not feasible in this setting and not recommended.	Evidence insufficient to show benefit; requires at least 3 providers present during resuscitation and skills. Consider administration after poor response to adequate ventilation and chest compressions for at least 90 seconds.	
Dextrose routinely	Very low	Lack of evidence; not recommended.				
Post resuscitation management						
Prevention of hypoglycemia	Low	No proven benefit and not feasible in this setting; recommend routine immediate and frequent breastfeeding.		No proven benefit, however routine immediate and frequent breastfeeding should be encouraged.	No proven benefit, however consider monitoring for hypoglycemia with neonatal encephalopathy and providing parenteral glucose if feasible, taking care to avoid hyperglycaemia.	
Prophylactic anticonvulsants	Low	Lack of evidence of benefit; not recommended.				
Fluid restriction	Low	Lack of evidence of benefit; not feasible in this setting, not recommended.		Lack of evidence of benefit, not presently recommended.		
Thermal care	Low–moderate	Moderate evidence to support recommending avoiding hyperthermia.				
Hypothermia: selective or whole body	High for high-income settings	Evidence of benefit in HIC, however not feasible in this setting, not recommended.			Evidence of benefit in HIC, however of uncertain benefit in LIC/MIC. Difficult to monitor with limited human resources, not recommended until further data available.	

Abbreviations: HIC, high-income countries; MIC, middle-income countries; LIC, low-income countries.

scores of community midwives at 3, 6 and 9 months after training [34]. In the Basic Support for Institutionalizing Child Survival (BASICS) program in Madagascar, group supervision and practice drills were instrumental in maintaining competency. Supervisory visits were conducted in group sessions every 3 months when staff were retrained using the mannequin and examined for competency with checklists [97]. At 6 months, 88% of providers remained competent to perform neonatal resuscitation [97].

There are no clear guidelines regarding the number of resuscitations per year required to maintain skills and few data to guide programs on the frequency and method of refresher training. Countries and training institutions need to plan for supervision and regular refresher training when primary training is instituted. Major initiatives that only provide training without this ongoing support and supervision should not be promoted. Most high-income country programs require full recertification

Current technology	Advancing the technology
Ventilation devices	
Self-inflating bag-and-mask (US$12–30) [34]  Volume 500 mL preferred (range available , 240–750 mL) Pressure release valve (30 mm Hg) Soft face masks in sizes for term and small babies Tube-and-mask device (US $9–15) [34] (no longer recommended as the device of choice)	Development of self-inflating bag-and-mask that is: • durable, but easy to disinfect (auto-clave) • low cost and ideally produced locally Development of a "T-piece" resuscitator linked to compressed air/oxygen • easy to use and can vary pressure and flow • durable, but easy to disinfect (auto-clave) • low cost and ideally produced locally
Suction devices	
Bulb suction (US $1–3 per bulb)  Mucus extractors with a one-way valve (ideally single use) Mechanical suction not to exceed 100 mm Hg (13.3 kPa) (operated electrically or by foot pump) Limited to a depth of 5 cm from lips 	Development of low-cost production of mucus extractors with a one-way valve Advance or increase availability for reusable sterilizable bulb suction devices • durable, but easy to subject to high level disinfection or sterilization (auto-clave) eg "penguin" device • low cost and ideally produced locally 
Resuscitation training materials	
Training mannequin (approx US $300 for basic resuscitation, $800 or more for advanced resuscitation)  Training manuals: • WHO Basic Newborn Resuscitation guide [3] • American Academy of Pediatrics' Neonatal Resuscitation Program[108] • UK Resuscitation Council Newborn Life Support [109] • Helping Babies Breathe [20] (Note: some essential newborn guides by organizations, also include neonatal resuscitation such as Save the Children, BASICS, and JHPIEGO)	Advance or increase availability for training mannequins:  • low cost (eg Laerdal NeoNatalie approx $50) • allows assessment of key competencies, especially ability of trainee to ventilate adequately, position airway etc • durable, easy to take apart/reassemble/transport and easy to disinfect • culturally sensitive e.g. dark skinned versions
Post resuscitation management	
Oxygen supply, piped or condensor Pulse oximeter Continuous Positive Airways Pressure (CPAP) ventilation Syringe drivers for controlled fluid and drug administration	Lower cost, robust oxygen condensers, including portable options Advance existing prototypes of lower cost, robust pulse oximeters with alternative power options (eg Freeplay/PET), develop finger tip versions Lower cost, robust CPAP equipment Lower cost, robust syringe drivers able to take a range of syringes

Fig. 6. Neonatal resuscitation and post-resuscitation care, equipment, and innovations required [107,108]. *Note reference to specific devices or use of images does not constitute endorsement. Bag-and-mask image reprinted with permission granted by from Programme for Appropriate Technology in Health (PATH); Reusable sterilizable bulb suction device ("penguin") image and training mannequin images reprinted with permission granted by Laerdal.

every 2 years. There is a dearth of data on what works in terms of frequency of supervision or formal retraining in low-income country health systems. However, within the large scale programs showing impact, a 6-monthly process of supervision appears to be the minimum. This remains a key area for health systems implementation research.

4.2. Availability of equipment and supplies

Before birth, the necessary resuscitation equipment needs to be available, functioning, and clean. Essential equipment for basic neonatal resuscitation and key considerations are highlighted in Fig. 6. Difficulty procuring equipment is a key challenge, especially in countries where the equipment is not included on essential supply lists. Even senior health workers may be unaware of what to order in terms of a correctly-sized self-inflating bag, valve pressure, and mask size for neonatal resuscitation. Procurement of equipment may be facilitated by identifying local manufacturers, and this has been instrumental in reducing equipment costs in Asia. Equipment should be designed to withstand autoclaving.

4.3. Cost of neonatal resuscitation: Training and equipment

4.3.1. Equipment

The prices of common resuscitation equipment are shown in Fig. 6. In Gadchiroli, India the cost of a tube-and-mask resuscitation device was US $10 and a bag-and-mask device was US $20; however, the utilization rate was low (approximately 1–2 uses per year) with a village health worker attending an average of 20 births per year and an incidence of 6% for a non-breathing baby [35]. Hence, the estimated cost of equipment alone was US $13 per averted death.

4.3.2. Training

The main cost, apart from some outlay on equipment, is training. A few studies that assessed the effect of broader training in perinatal care included cost data, and costs are often not easily comparable. A study from Brazil compared two strategies for in-service training in essential newborn care, one based on a conventional 5-day classroom teaching course and the other, a self-directed course using a manual [98]. There were no differences detected between the 2 training strategies, although the cost for the self-directed learning was US $6260 per course in contrast to US $8160 per course for the conventional training. While the course covered all aspects of essential newborn care with a small component on resuscitation, we can use these costs as an estimate for a neonatal training course, which is likely to take a similar time period and investment. A rough estimate of intrapartum-related early neonatal deaths in these hospitals is 236 per 1000 live births [56]. If 30% of these could be averted by resuscitation [11], the number of lives saved would be 71, giving a cost per life saved for a comprehensive essential newborn care course of US $88. In an analysis of management of the non-breathing baby in Cirebon, Indonesia, amortizing the cost of training and equipment over a 5-year period was US $0.25 per baby delivered, or US $42 per life saved [34]. Including the follow-up and refresher training into routine maternal/neonatal care, the cost was reduced to US $0.16 per baby delivered and US $28 per intrapartum-related neonatal death averted. In summary, although the data are limited, the cost per life saved appears to be well below the currently accepted benchmarks for cost-effectiveness of 3 times the national Gross National Income per capita per DALY averted, which is currently around US $900 in South Asia and Sub-Saharan Africa.

4.4. Monitoring outcomes

Monitoring the progress of neonatal resuscitation programs in low/middle-income settings is particularly challenging because of the lack of consistent case definitions and challenges to birth surveillance in community settings [21]. In a survey of program implementers, 35% did not collect routine data on intrapartum-related events, while those that did used vital registration, hospital records, population-based surveys, or CHW collected surveys [21]. A preferred indicator was the onset of convulsions in the first 24 hours of life, and death in the first week, of a baby weighing more than 2500 g; however, this may not be feasible in community settings where birth weight is not often measured. The proportion of babies requiring resuscitation may be a reasonable indicator, and was considered more feasible than Apgar scores [21].

4.5. Scaling up in referral and first-level (district hospital) facilities

National groups such as the National Neonatology Forum in India, the Perinatal Society of Malaysia, and the Ministry of Health/China (see Panel 1) have disseminated the American Academy of Pediatrics-American Heart Association Neonatal Resuscitation Program (NRP) at a national level via a train-the-trainer model [48,99,100]. Local programs that build a core of national master trainers and engage governments to incorporate neonatal resuscitation into national perinatal strategies have potential to reach a greater scale in that they promote local ownership, national policy changes to sustain and scale programs, and institutionalization of neonatal resuscitation into preservice training curricula, medical education, and licensure requirements [47,101].

4.6. Should neonatal resuscitation be scaled in the community?

There is evidence from India and Indonesia that community-based neonatal resuscitation may be both feasible and effective in reducing intrapartum-related mortality in settings with high rates of home birth and delivery attendance by community cadres, ranging from TBAs and CHWs to midwives. There are several forthcoming trials of community cadres providing home-based neonatal resuscitation that will add to this evidence base [102]. Whatever the results of these trials, training for community-level neonatal resuscitation should not occur in isolation without undertaking parallel efforts to strengthen health systems and the quality of, and linkages to, facility-based skilled emergency obstetric care. Only these efforts will avert the severe intrapartum insults that result in stillbirth and neonatal deaths.

In low-income countries, where the majority of births occur at home, if there are existing health cadres but skilled attendance is not achievable in the near future, then community-based resuscitation may be an option [103]. There are several key considerations required for an effective and sustainable program because community based-neonatal resuscitation may not be appropriate for every setting: (1) cadres must be present at birth, to recognize and assist the baby who does not breathe, and attend an adequate number of cases to maintain skills; (2) training should focus on essential newborn care first; (3) adequate systems should be in place for equipment procurement, cleaning/maintenance, resupply; (4) systems are required for supervision, refresher training, and monitoring of skills retention; and (5) functional referral systems should exist for post-resuscitation care and to follow-up resuscitated newborns. The Indonesian Ministry of Health took steps to scale neonatal resuscitation training nationally via district-level in-service training and incorporation of neonatal resuscitation training into the national curriculum. However, scaling up in a decentralized health system poses challenges because implementation requires district-level commitments and resources for training, equipment procurement, supervision, and monitoring.

A critical research question is how community-based resuscitation programs affect chronic disability among survivors. An evaluation of resuscitation training in India suggests that although intrapartum-related deaths were reduced, neonatal encephalopathy was unchanged, supporting the possibility of an increasing number of babies surviving with disability [8]; however, there are no follow-up data in community settings as yet.

5. Conclusion

Neonatal resuscitation, when implemented systematically by personnel using standard guidelines and competency-based training,

has the potential to avert an estimated 192 000 intrapartum-related neonatal deaths per year [11]. Furthermore, resuscitation may avert 5%–10% of deaths due to complications of preterm birth [11]. Neonatal resuscitation training should be incorporated into national neonatal strategies to complement the top priority of improved prevention of intrapartum-related deaths through obstetric care [6]. The dilemma is whether and how to apply this in settings where most of the babies who require resuscitation are born in the home, without skilled attendants. Possible strategies include training community cadres who already attend the majority of deliveries, ranging from skilled birth attendants to TBAs and CHWs, and linking them with the formal health system. A noteworthy concern is whether better resuscitation and improvements in care may increase the number of newborns who survive but are impaired; there is a dearth of follow-up data on newborns who required resuscitation in low- and middle-income countries, and particularly from community settings.

Many questions remain to be answered at all stages of the research pathway, from better description, through development of interventions, and particularly regarding delivery of this high impact intervention in the settings with highest burden yet weakest health systems [104]. The most effective strategy may vary by setting, and be strongly linked to which cadres are available to reach high coverage at the time of birth [104]. However, the fact remains that at the present time, a baby born in rural Africa or South Asia has a very small chance of being resuscitated at birth if they do not breathe, which is in stark contrast to the careful attention paid to avoiding injury at the time of birth for a baby born in a high-income country.

Conflict of interest

The authors have no conflicts of interest to declare.

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Panel 1. Freedom of Breath, Fountain of Life: A nationwide neonatal resuscitation program, China

Background: China has approximately 17 million births per year. The neonatal mortality rate is 18 per 1000 live births, with more than 20% of neonatal deaths estimated to be due to intrapartum-related events. Although the proportion of births in health facilities approaches 100% for urban areas, there are wide regional variations, with up to 60% home births in the rural western regions. Previous efforts to introduce a standardized neonatal resuscitation protocol were greeted with an enthusiastic reception within institutions or regions; however, dissemination did not spread beyond areas of individual effort.

Strategy: In 2004, the Chinese Neonatal Resuscitation Program (NRP), "Freedom of Breath, Fountain of Life" launched a 5-year partnership among the Chinese Ministry of Health, National Center for Women and Children's Health (NCWCH, China CDC), the Chinese Society of Perinatal Medicine, Chinese Nursing Association, Johnson and Johnson Pediatric Institute LLC, and the American Academy of Pediatrics (AAP). Twenty provinces were targeted with the goal to have at least one provider skilled in neonatal resuscitation at every hospital delivery. Training utilized the AAP-NRP in Mandarin translation from the provincial through the district hospital level and a condensed "guidelines" booklet at the township level in a train-the-trainer cascade. Instructor teams included a pediatrician, obstetrician, midwife, and administrator. The China Task Force for NRP carried out direct supervision of provincial and regional instructors and designated qualified instructors. Staff from the NCWCH evaluated program management.

Results: In the 20 target provinces, data collected from 80 hospitals demonstrated a decrease in Apgar scores of less than 7 from 4.26% in 2003 to 2.61% in 2007. Intrapartum-related deaths in the delivery room decreased from 3.3 to 2.2 per 10 000 from 2003 to 2006. By the end of 2007, NRP covered 100% of urban and large peri-urban areas, as well as 95% of counties, with more than 44 000 health professionals trained (54% obstetricians, 21% midwives, 19% pediatricians/neonatologists, 6% anesthetists and health administrators). Through 2008, 21 000 copies of the textbook and wall chart, 70 000 copies of the guidelines, and over 700 sets of training equipment had been distributed. An audit of equipment availability revealed 98% availability of ventilation bag, masks, and suction in the delivery room. Meconium aspiration devices were present in approximately half of the delivery rooms. However, only 65%–75% of operating rooms used for cesarean delivery were equipped with bag, mask, and suction. New skills may not be fully applied in daily practice, especially where instructors are not on site and/or where the frequency of resuscitation is low. From 234 candidates, 191 instructors have been certified during supervision visits to lead provincial teams. Of 238 randomly selected staff evaluated on their practical resuscitation skills, 72% passed, with midwives scoring significantly higher (82%) than pediatricians and obstetricians. Recent national regulations require updated neonatal resuscitation training as part of midwifery licensure or re-licensure. Provincial health departments are including hospital-based NRP as a criterion for licensure of obstetrical services.

Conclusion: Strong linkages from the central Ministry of Health to provincial Health Bureaus facilitate the dissemination of training, maintenance of quality, and implementation of policy changes. Training coverage has been achieved in urban and peri-urban areas, with evidence of a reduction in low Apgars scores and death in the delivery room. A model of hospital-based instructors will incorporate supervision, continuing education, and quality improvement (case audit). An enhanced website (www.nrp.chinawch.org.cn) will facilitate course tracking and reporting of outcomes as training extends to the township level and outside the target provinces.

[Source: See main reference list: 100,109]

Neonatal Resuscitation Program Training in Beijing, China. Photograph reprinted with permission granted by the American Academy of Pediatrics, 2004.

Panel 2. Village midwives for newborn resuscitation in Cirebon, Indonesia: The impact of training and supervision

Background: Indonesia has 4.4 million births a year, and while the neonatal mortality rate has fallen by around one-third in 15 years, it remains high at 22 per 1000 live births, with an estimated 27% of neonatal deaths due to "birth asphyxia". The village-based midwife programme in Indonesia was established in 1989 and rapidly trained 54 000 midwives ("Bidan di Desa") within 7 years—increasing midwife density by more than 10-fold. Most Bidan di Desa were placed in "birthing huts." In rural areas, skilled birth attendance increased from 22% to 55% between 1990 and 2003. However, the Bidan di Desa were not trained or equipped for neonatal resuscitation. In 2003, PATH and Save the Children, supported by Saving Newborn Lives conducted a research study in Cirebon district to examine the feasibility and impact of training Bidan di Desa for neonatal resuscitation.

Strategy: All Bidan di Desa in the study area, together with their supervisors and program coordinators, received competency-based training in basic neonatal resuscitation. The supervisory structure was reorganized and supervisory methods were modified to a more supportive, adult-learning style. Regular follow-up was conducted at 3, 6, and 9 months after training. Neonatal mortality survey and verbal autopsy were done before and after the project to measure the changes in neonatal mortality rate. Knowledge and skills tests were also done before training, directly after training, and every 3 months after training.

Results: The baseline neonatal mortality rate was estimated to be 15 per 1000 live births. The mortality rate for babies not breathing at birth was estimated at 5.1 per 1000 live births. One year after the training, the study results showed that 65% of the trained Bidan di Desa had resuscitated at least one baby who did not breathe at birth, and in 85% of these cases the baby survived. The majority of babies (70%) needed only tactile stimulation and/or appropriate positioning of the head and maintenance of warmth. Overall, NMR decreased by 40% from 15 per 1000 to 9 per 1000. A simple cost analysis with training and equipment costs amortized over a 5-year period showed that the cost per baby delivered was US $0.25 and the cost per "asphyxia death" averted was US $42. If follow-up refresher training was absorbed into routine supervision, the cost would drop to US $0.16 per baby delivered and US $28 per "asphyxia death" averted.

Conclusion: Village midwives offer the main opportunity to provide wide-scale coverage to improve maternal and neonatal survival in Indonesia. Provision of a resuscitation device, competency-based resuscitation training, and strengthened supervision were associated with a major reduction in neonatal deaths. National policy and training is now being adapted to include newborn resuscitation for all midwives.

[Source: See main reference list: 34,110]

Panel 3. Home-based management of birth asphyxia by village health workers in Gadchiroli, India

Background: In rural Gadchiroli, the baseline NMR in 1993–95 was 62 per 1000, with 10.5 per 1000 attributed to "birth asphyxia." Approximately 90% of babies were born in the home and the majority of home births were attended by traditional birth attendants (TBAs). The prevalence of "mild asphyxia" (not breathing at 1 minute) was 14%, while the prevalence of "severe asphyxia" was 5%. Given the high proportion of births attended by traditional birth attendants and community health workers (CHWs), there was the opportunity to train these providers in the recognition and management of the non-breathing baby.

Strategy: Since 1988, the SEARCH team has trained TBAs in community-based child and neonatal health. Interventions for intrapartum care were included in the package of Home-based Newborn Care interventions introduced in 1996. During 1996–2003, CHWs performed simple immediate newborn care including drying, tactile stimulation, and suctioning of the oropharynx. For ventilation, in the baseline period (1993–1995), trained TBAs used mouth-to-mouth resuscitation; in the first intervention phase (1996–1999), CHWs were trained to use a tube-and-mask device for ventilation; and in the final intervention phase (1999–2003), CHWs were trained to use a bag-and-mask device. Other concurrent interventions during 1996–2003 included essential newborn care and home-based management of neonatal sepsis.

Results: Before-and-after data are reported from 3 phases with different management strategies for birth asphyxia. TBAs attended 89%–95% of home deliveries and CHW attended 78%–84% over the study periods. In the intervention regions, the incidence of "mild asphyxia" significantly decreased by 60% (14.2 to 5.7) over the study period, while the incidence of "severe asphyxia" was unchanged. The "asphyxia specific" mortality rate was significantly reduced by 65% comparing periods before and after CHW training (with either tube-and-mask or bag-and-mask), and case fatality of "severe asphyxia" was reduced by 48%. When comparing periods that used different ventilation techniques, the "asphyxia" specific mortality rate was reduced equally with both types of ventilation; however, although the case fatality rate and fresh stillbirth rate were lower (39.2% and 32.6% respectively) with bag-and-mask compared with tube-and-mask ventilation, the reductions were not significant. In a separate subanalysis, the SEARCH team was able to compare the intervention to control arms during the early study period when CHWs used tube-and-mask ventilation (1996–1999), and found a significant 51% difference in "asphyxia specific" mortality in the intervention areas according to verbal autopsy. The cost of the bag-and-mask was US $13 per averted death.

Conclusion: The period of home-based neonatal resuscitation by CHWs with the capacity for bag-and-mask ventilation was associated with 65% lower rates of "asphyxia" mortality than the baseline period. High coverage of home births was achieved with TBA/CHW teams and they were able to successfully identify a non-breathing baby in the community. The bag-and-mask apparatus was preferred to the tube-and-mask. However, challenges to the feasibility of implementation included the cost of bag-and-mask (US $16) and the low utilization rate, because each CHW only used the bag-and-mask ventilator on average twice a year.

[Source: See main reference list: 35,111]

Photograph reprinted with permission granted by SEARCH, Gadchiroli, India.

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INTRAPARTUM-RELATED DEATHS: EVIDENCE FOR ACTION 4

Linking families and facilities for care at birth: What works to avert intrapartum-related deaths?

Anne CC Lee [a,b], Joy E. Lawn [b], Simon Cousens [c], Vishwajeet Kumar [a], David Osrin [d], Zulfiqar A. Bhutta [e], Steven N. Wall [b], Allyala K. Nandakumar [f], Uzma Syed [b], Gary L. Darmstadt [a,*,1]

[a] Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA
[b] Saving Newborn Lives/Save the Children-USA, Washington, DC, USA and Cape Town, South Africa
[c] London School of Hygiene and Tropical Medicine, London, UK
[d] UCL Centre for International Health and Development, Institute of Child Health, London, UK
[e] Division of Women and Child Health, the Aga Khan University, Karachi, Pakistan
[f] Heller School of Social Policy, Brandeis University, Waltham, MA, USA

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ABSTRACT

Background: Delays in receiving effective care during labor and at birth may be fatal for the mother and fetus, contributing to 2 million annual intrapartum stillbirths and intrapartum-related neonatal deaths each year. *Objective:* We present a systematic review of strategies to link families and facilities, including community mobilization, financial incentives, emergency referral and transport systems, prenatal risk screening, and maternity waiting homes. *Results:* There is moderate quality evidence that community mobilization with high levels of community engagement can increase institutional births and significantly reduce perinatal and early neonatal mortality. Meta-analysis showed a doubling of skilled birth attendance and a 36% reduction in early neonatal mortality. However, no data are available on intrapartum-specific outcomes. Evidence is limited, but promising, that financial incentive schemes and community referral/transport systems may increase rates of skilled birth attendance and emergency obstetric care utilization; however, impact on mortality is unknown. Current evidence for maternity waiting homes and risk screening is low quality. *Conclusions:* Empowering communities is an important strategy to reduce the large burden of intrapartum complications. Innovations are needed to bring the poor closer to obstetric care, such as financial incentives and cell phone technology. New questions need to be asked of "old" strategies such as risk screening and maternity waiting homes. The effect of all of these strategies on maternal and perinatal mortality, particularly intrapartum-related outcomes, requires further evaluation.
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1. Introduction

Each year there are around 136 million births, of which ~60 million occur outside facilities [1]. At the time of an obstetric emergency, every moment of delay in seeking and receiving skilled obstetric care increases the risks of stillbirth, neonatal or maternal death, or disability. For some emergencies such as antepartum hemorrhage, even hours can be the difference between life and death for mother and fetus. For the baby not breathing at birth, every minute counts. Many of the estimated 1.02 million intrapartum stillbirths and 904 000 intrapartum-related neonatal deaths could be avoided by access to skilled care at birth, timely emergency obstetric care, and immediate newborn care. Intrapartum-related neonatal deaths were previously loosely termed "birth asphyxia" [2], but in this Supplement we follow the recommended shift in terminology [1] based on a series of international consensus statements to use the terms "intrapartum-related deaths" for cause-of-death and "neonatal encephalopathy" for the acute complications manifesting soon after birth [3–5].

There are many real and perceived barriers to accessing care, particularly for women in rural areas of low-income countries. The delays in accessing care for women with obstetric emergencies, the fetus, and neonate are usually described in 3 groups [6–8]: (1) delay in the decision to seek care; (2) delay in reaching a health facility; and (3) delay in receiving quality care.

In an analysis of DHS data from 41 countries (Fig. 1), the most common obstacles to seeking obstetric care included financial barriers (>50%), challenges with transport (37%), and distance (37%). Furthermore, many social factors may influence the decision to seek care, such as lack of knowledge about seriousness of complications or where to receive services, requiring permission from family decision

* Corresponding author. Integrated Health Solutions Development, Global Health Program, Bill & Melinda Gates Foundation, PO Box 23350, Seattle, WA 98102, USA.
E-mail address: Gary.darmstadt@gatesfoundation.org (G.L. Darmstadt).
[1] Current address: Integrated Health Solutions Development, Global Health Program, Bill & Melinda Gates Foundation, Seattle, WA, USA.

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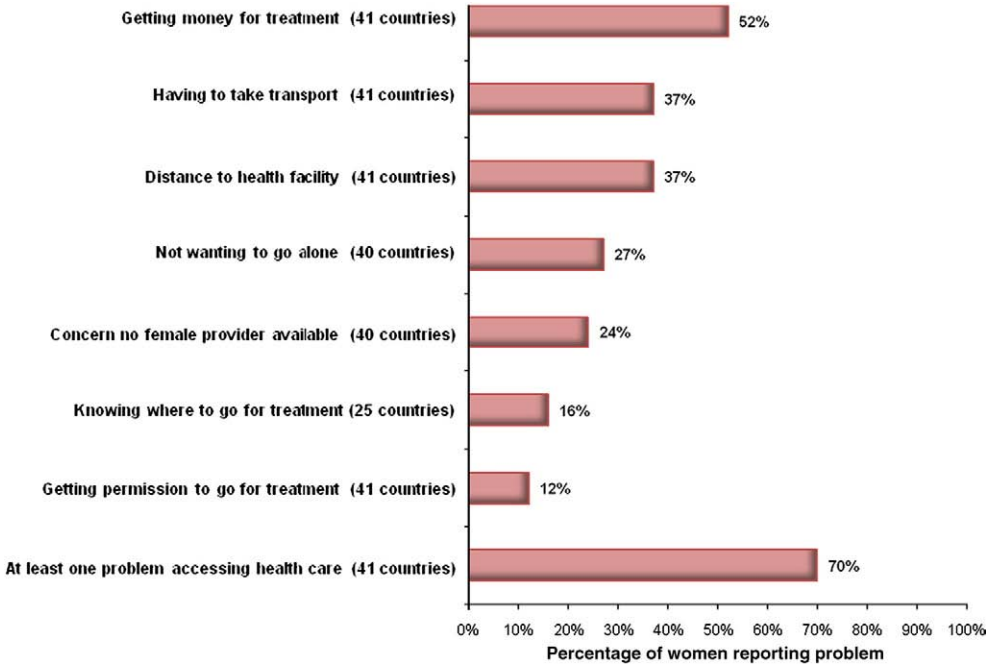

Fig. 1. Maternal perceptions of barriers to obstetric care based on analysis of large-scale household surveys (2000–2007). Source: Based on new analysis of DHS data (2000–2007) from Macro DHS Statcompilier, May 2009. Since the specific questions vary by country, the number of countries with data per question is given.

makers, and cultural beliefs that may prevent the removal of the mother or newborn from the home [9]. Unavailability and high costs of transportation, poor road conditions, and time to arrange transport may increase the time to reach a health facility. In rural Bangladesh, the use of skilled birth attendance decreased by half when the distance to a health center was beyond 1 kilometer [10]. The delay in receiving quality obstetric care may be caused by understaffing, lack of supplies and equipment, staff incompetence, and lack of trained personnel. In Indonesia, the requirement for prepayment for supplies and medications, lack of resuscitation equipment in the emergency room, and unavailability of staff trained in neonatal resuscitation led to delays in receiving prompt intervention for a newborn with "birth asphyxia" [9]. In an audit of perinatal deaths in a Tanzanian hospital, the first, second, and third delays contributed to 19%, 21%, and 73% of perinatal deaths, respectively [11].

A functioning continuum of care between home and hospital is required to minimize these potentially deadly delays and effectively link women and newborns with care [12]. Much of the literature on provision of effective care at birth focuses on the content of care or the provider. There has been limited attention to review of the evidence for linkages between home and hospital and between levels within the health system. While some of these issues may be context specific depending on local constraints such as distance, difficult terrain, or cultural seclusion practices [1], there are also shared constraints and possible strategies.

Strategies to build this household-to-hospital continuum and overcome the first and second delays are the focus of the present paper and may involve two main approaches. Firstly, delays can be reduced by "moving" the community toward facilities, for example through mobilizing and empowering families to seek health care with birth preparedness planning, transportation systems, as well as financing strategies to reduce the up-front costs of transport or hospital care. Further delays in transportation may occur between first level health facilities and the referral hospital, especially if emergency obstetric care is not available at the first level, and may be reduced by communication and referral systems. Secondly, the formal healthcare system can reduce delays by bringing the necessary care closer to the community; for example, providing community midwives or birthing centers in the community [13], or identifying women at highest risk to come to maternity waiting homes near a hospital with emergency obstetric care. Some interventions may be provided at community level by skilled attendants or community cadres, although this is typically not feasible for emergency obstetric care [13]. Strategies to address the third delay by improving the quality and supply of care in the facility are reviewed in the second (intrapartum care) [14], third (neonatal resuscitation), and sixth (perinatal audit) [15] papers in this Supplement.

1.1. Objectives

This paper is the fourth in a series that focuses on reduction of intrapartum-related deaths. The objectives of this paper are to describe the evidence for interventions to link mothers with skilled care during pregnancy, labor, and birth, and to summarize the implications for programs. We describe the content of the interventions, summarize the evidence using the modified GRADE system [16] (Grading of Recommendations Assessment, Development, and Evaluation system for rating strength of evidence and recommendations), and present data on effects, when available, on early neonatal mortality rate (ENMR), intrapartum-related neonatal mortality rate (IPR-NMR), stillbirth rate (SBR), intrapartum stillbirth rate (IP-SBR), and perinatal mortality rate (PMR) [17,18]. We also present evidence on the effects on intermediate outcomes such as care seeking, skilled birth attendance and facility delivery rates, cost and cost-effectiveness. The strategies reviewed in this paper are shown in Table 1.

2. Methods

Details of the searches undertaken and the selection criteria for inclusion are described in the first paper of this series [1]. Searches of the following databases of the medical literature were conducted:

Table 1
Strategies included in the present review.

Increasing community demand for obstetric care (Section 3 in this paper)
3.1 Community mobilization
3.2 Financing strategies
• Elimination of user fees
• Community-based health insurance
• Community loans
• Conditional cash transfers
• Voucher schemes
• Contracting out and pay for performance
Bringing pregnant women closer to the formal health system (Section 4 in this paper)
4.1 Community referral systems and transport approaches
4.2 Antenatal risk screening by health workers
4.3 Maternity waiting homes

PubMed, Popline, EMBASE, LILACS, IMEM, African Index Medicus, Cochrane, and World Health Organization (WHO) documents. The initial search was conducted during 2002 and was updated to May 2009. Keywords utilized in the searches included "birth asphyxia/asphyxia neonatorum," "hypoxic ischemic encephalopathy," "neonatal encephalopathy," or "neonatal-perinatal mortality" in various combinations with "emergency transport," "information communication technology," "community based insurance," "emergency loans," "emergency funds," "community mobilization," "community action cycle," "public private partnership," "maternity waiting homes," and "risk screening." Under each subheading we review the background of, the evidence of effectiveness, data on cost if available, and summarize the implications for programs. All effect sizes reported are relative percentage mortality rate reduction, as opposed to absolute percentage reduction. The level of evidence was assessed using the GRADE system [16] criteria to evaluate the quality of the evidence (strong, moderate, low, or very low) and given a recommendation for programmatic application (strong, weak, conditional). We use an adaptation of GRADE developed by the Child Health Epidemiology Reference Group (CHERG) specifically for low- and middle-income settings [19]. Our particular interest is in intrapartum-related ("birth asphyxia") outcomes, this is a particular constraint since cause-specific data are limited [1]. Costing data are from the actual year reported and not adjusted for inflation.

We also conducted a meta-analysis of community mobilization using the Mantel-Haenszel pooled relative risk (RR) and corresponding 95% confidence interval (CI). When significant heterogeneity was detected ($P<0.10$) a random effects model was used to estimate the RR and CIs. Studies were considered for inclusion if the study design was a randomized controlled trial or quasi-experimental study with replication of intervention and control units, reporting the outcomes of interest (skilled birth attendance, PMR, or ENMR). Meta-analysis of all-cause NMR was not conducted since most packages addressed multiple neonatal conditions, and in the absence of cause-specific mortality data, PMR and ENMR may more specifically reflect the burden of intrapartum-related events. Studies were excluded if they were observational before-and-after studies or did not report the desired outcomes. All analyses were conducted using STATA 10.0 statistical software (StataCorp, College Station, TX, USA).

3. Increasing demand for obstetric care

3.1. Community mobilization

3.1.1. Background

Community mobilization is a process of enabling people to organize themselves, recognize opportunities, identify their collective potential, and utilize available resources to realize a shared goal through unified action. Strategies to "mobilize" communities are diverse, and may entail differing levels of intensity of engagement, community involvement, and ownership (see Panel 1 at the end of the paper) [20,21]. Mobilization strategies for maternal-newborn care include approaches to:

1. *Change individual behaviors* to implement key preventative practices: for example, peer counseling and home visitation to promote healthy pregnancy and birth behaviors, immediate newborn care, and rapid care seeking [22].
2. *Increase collective knowledge* and practice of preventative behaviors, as well as recognition, identification, and care seeking for danger signs and symptoms: for example, women's groups and engaging key stakeholders to enhance individual behavior change and to shift community norms [23,24].
3. *Promote broader community action* to address major barriers to care: for example, engaging with village health committees to address transport and financial barriers to care.

Over the last decade, more focus has been placed on community approaches specifically designed for a given setting and purpose based on formative research to understand local culture, beliefs, and practices. [20,22]. Community mobilization may have the most power to change behaviors and enable access to care where neonatal deaths are seen as inevitable, and community norms, such as seclusion for pregnant women and new mothers, preclude care seeking in the formal health sector [1].

3.1.2. Evidence for community mobilization

There are an increasing number of studies of community mobilization to improve maternal, newborn, and child health (Table 2), predominantly from South Asia, with a few from Latin America or Africa [22,24–29]. Here we focus on studies that illustrate key mechanisms for mobilization or that report specific intrapartum-related or mortality outcomes.

The Warmi project in rural Bolivia was the originator of the "Community Action Cycle" methodology (Panel 1) and worked with women's organizations and community members in 50 rural communities to galvanize women around health issues [11]. At the end of the project period, there were improvements in prenatal care utilization and PMR was reduced from a baseline level of 117 per 1000 to 44 per 1000 from 1990 to 1993 (RR 0.37; 95% CI, 0.25–0.56), primarily due to a reduction in deaths on the first day of life, which probably included a reduction in intrapartum-related neonatal mortality (IPR-NMR). In 1994, the program was expanded into the Bolivian National Health plan to over 500 communities, and while no mortality data are available, rates of skilled birth attendance reportedly increased in the target communities [30].

The MIRA (Mother and Infant Research Activities) project in Nepal adapted the methodology of the Warmi project to link women with primary maternal-neonatal services [10]. A cluster randomized controlled trial (cRCT) was conducted in Makwanpur district, a mountainous region with 94% home births, in which 12 groups of villages convened monthly participatory women's groups led by a local female facilitator, using the community action cycle (Panel 1). In these intervention clusters there was a 30% reduction in neonatal mortality (OR 0.70; 95% CI, 0.53–0.94), and a 78% reduction in maternal mortality (OR 0.22; 95% CI, 0.05–0.90) compared with the control clusters. Women in the intervention areas had significantly improved care-seeking behaviors, including increased prenatal care visits, visits to health facilities for acute illness of the mother or infant, institutional delivery, and skilled birth attendance (Table 2). Although improvements in the early identification of pregnancy complications and access to prenatal

Table 2
Evidence for community mobilization: Mortality effect and intermediate outcomes.

Intervention/study (date order)	Setting	Percent skilled attendance	Baseline mortality rate	Mortality Effect: Percentage relative reduction in mortality rate *(number of deaths in intervention or end line group)*; RR or OR (95% CI)					Intermediate outcomes	Investigator and year
				SBR	ENMR	PMR	NMR	MMR		
Before-and-after comparison of community empowerment specifically through women's groups.	Rural Bolivia	23%	PMR 117	47% *(21)* RR 0.53 (0.31– 0.89)	-	62% *(31)* RR 0.37 (0.25–0.56)	76% *(10)* RR 0.24 (0.12– 0.47)		Pre vs Post Comparison • Received prenatal care 49% to 64% ($P=0.009$) for control subjects • Breastfeeding on first day of life 25% vs 50% ($P<0.001$)	O'Rourke et al. [23] 1998
Cluster RCT of community mobilization through participatory women's groups using action-learning cycle to identify perinatal problems and create community strategies to address. Upgrading of health services in both intervention and control arms.	Rural Makwanpur District, Nepal Populations 170 000 Intervention area (14 884 households) Control area (14 047 households)	<13%	NMR 25.4 (intervention) NMR 25.1 (control) MMR 539	Nonsignificant change aOR 1.06 (0.76–1.47)			30% *(76)* aOR 0.70 (0.53–0.94)	78% *(2)* aOR 0.22 (0.05–0.90)	Intervention vs Control • Any prenatal care 55% vs 30% (OR 2.82; 1.41–5.62) • Iron-folate 49% vs 27% (OR 1.99; 1.14–3.46) • Institutional delivery 7% vs 2% (OR 3.55; 1.56–8.05) • Birth attended by skilled provider 7% vs 2% (RR 3.53; 1.54–8.10)	Manandhar et al. [24] 2004
Before-and-after comparison of community mobilization with formation of village health committees, establishment of emergency loan/transport funds, and training of Home-based Life Saving Skills.	Rural Uttar Pradesh, India Population 20 000	20%	NMR 42	Nonsignificant change[a]			17%[b] *(21)*	60%[c] *(3)*	Pre vs Post Comparison • Birth preparedness index, any of 3 indicators 15% vs 82% ($P<0.001$)	Fullerton et al. [27] 2005
Cluster randomized trial of package of birth and newborn care preparedness (BNCP) interventions in Home vs Community care. In Home-care group CHWs provided prenatal visit, promoted BNCP, postnatal visits in first week of life, referred sick newborns, and treated sepsis at home with injectable antibiotics. In Community care arm, community mobilizers promoted BNCP in group sessions. In comparison and intervention arms, promoted improvement of government health facilities.	Rural Sylhet district, Bangladesh Population 200 000 Home care: (14 880 pregnancies) Community care: (16 449 pregnancies) Comparison: (15 779 pregnancies)	CHWs attended 5% of births	NMR 48				Community Care 5% aRR 0.95 (0.69–1.31) Home Care arm[d] 34% aRR 0.66 (0.47–0.93)		Community Care vs Control • Any prenatal care 62% vs 49% ($P=0.13$) • Iron-folate 45% vs 25% ($P<0.001$)	Baqui et al. [29] 2008
Pilot study training of Lady health workers (LHW, CHW) and Dais (TBAs) in home-based newborn care (including basic resuscitation), improvement of linkages between LHWs and Dais, and community mobilization with group educational sessions and establishment of health committees and emergency transport funds. Strengthening of health facilities in intervention/control areas with training and upgrading equipment.	Hala and Matiari sub districts, rural Sindh province, Pakistan Intervention: 2672 Control: 2462	Baseline skilled attendance 18% LHWs attended 5% of births in intervention areas	Baseline stillbirth 65.9 (intervention) Baseline NMR 57.3 (intervention)	35%[e] *(132)*	36.2%[e] *(90)*	34.6%[e] *(222)*	28%[e] *(121)*		Intervention areas Before vs After • Home births 79% vs 65% ($P=0.01$) • Skilled birth attendant 18% vs 30% ($P=0.03$)	Bhutta et al. [25] 2008

Cluster randomized trial of essential newborn care package delivered by CHWs via collective meetings, prenatal and postnatal visits. Participatory social mapping and formative research conducted in local community to develop behavior-change strategies for intervention package. Intervention clusters received either essential newborn care (ENC) package or ENC plus use of a hypothermia indicator (Thermospot).	Shivgarh, rural Uttar Pradesh, India Total population of study area 104 123	Baseline skilled attendance in all groups <5%	Baseline stillbirth 24.4 (ENC) 27.2 (control) Baseline NMR 64.1 (ENC) 54.2 (control)	ENC: 28% *(59)* RR 0.72 (0.52–1.00) ENC + TS: 15% *(48)* RR 0.85 (0.56–1.29)	ENC: 44% *(51)* ENC + TS: 47% *(36)*	ENC: 41% *(113)* aRR 0.59 (0.47–0.74) ENC + TS: 38% *(96)* aRR 0.62 (0.47–0.81)	ENC: 54% *(64)* aRR 0.46 (0.35–0.60) ENC + TS: 52% *(48)* aRR 0.48 (035–0.66)		Intervention vs Control • Any prenatal care 26% vs 14% (RR 1.84; 1.08–3.14) • Birth Preparedness Identification facility 14% vs 4% (RR 3.43; 2.12–5.14) Identification attendant 22% vs 5% (RR 4.94; 3.19–7.63) Arrange money 25% vs 15% (RR 1.55; 1.15–2.09) • Institutional Delivery 19.7% vs 14% (RR 1.41; 0.93–2.13)	Kumar et al. [22] 2008
Quasi-experimental study of Skilled Care Initiative including health systems strengthening and community mobilization interventions including advocacy, social marketing, behavior change communication and capacity strengthening. Including analysis and prioritization of community problems, birth preparedness activities and promotion of emergency funds.	Rural Ouargaye district Burkino Faso	Baseline institutional births 30%–35%	PMR 33			28% aOR 0.72 (0.68–0.77)		31.5% [f]	Institutional births increased significantly in intervention areas OR 1.23 per yr (95% CI, 1.018–1.28) more than in comparison area 1.08 per yr (95% CI, 1.05–1.12). Significant difference in trend ($P<0.001$)	Hounton et al. [33] 2009
Community mobilization activities for birth planning. Development of Community Support System with emergency funds for transport, hospital fees, volunteer for support or blood donation. Improvement in quality of care in health facilities through community input and hospital audit. Health facilities were upgraded in comparison and intervention regions.	Dinajpur, Northewestern Bangladesh Pop: 200,000	16%	NS						• Proportion of facility-based births in intervention area increased from 2% to 21%; comparison area (facility upgrade only) from 7% to 13%; with no change in control area • Skilled attendance at delivery 19% in intervention areas, 5% in control area • Met need for EmOC services increased 24% in intervention area, 13% in comparison, and 1% in control areas • 15 Community groups purchased riskshaw-van for transport and 13 established loan funds. 52 women used money from emergency funds, 23 were transported and accompanied to health facility	Hossain et al., 2006

Abbreviations: SBR, Stillbirth Rate; ENMR, Early Neonatal Mortality rate; PMR, Perinatal Mortality Rate; NMR, Neonatal Mortality Rate; IPR-NMR, Intrapartum-related Neonatal Mortality Rate.
[a] Nonsignificant change in stillbirth rate (baseline rate 2.7 per 1000 vs end line 4.4 per 1000, $P=0.095$). [b] Nonsignificant reduction in NMR (baseline rate 4.2 per 1000 vs end line 3.5 per 1000, $P=0.56$). [c] Significant reduction in MMR (baseline rate 1.5 per 100 000 vs end line 0.4 per 100 000, $P=0.053$). [d] Community care arm includes mobilization; home care arm includes mobilization and home management of sepsis. [e] Before-and-after comparison in intervention clusters. [f] In intervention district MMR decreased from 446 to 305 per 100 000 vs control district decreased from 562 to 473 per 100 000.

and intrapartum care may have reduced the burden of intrapartum events [31,32], preliminary analysis has failed to show a reduction in intrapartum-related mortality, possibly due to the low rates of skilled birth attendance even after the intervention (7%) (Personal communication, D. Osrin, June 2009).

In the Saksham (Hindi for empowerment) Study in Shivgarh, India [22], formative research regarding childbirth and newborn care practices was conducted, risk factors for mortality were identified, behavior change messages targeting key risk factors were developed, home-based counseling on newborn care was conducted by Community Health Workers (CHWs), and a variety of community stakeholders were engaged in group meetings to stimulate behavior change tailored to be compatible with local customs and childbirth practices (Panel 1). In the intervention areas, mothers were more prepared for birth, with significantly higher rates of identification of health facility and birth attendant, arrangement of money in case of emergency prior to delivery, and care seeking from a qualified practitioner for signs of maternal illness. Neonatal mortality was reduced in the intervention arms (combined) versus comparison arm (adjusted RR 0.47; 95% CI, 0.37–0.59). The reduction in stillbirths (adjusted RR 0.77; 95% CI, 0.62–1.23) and in early neonatal deaths (adjusted RR 0.53; 95% CI, 0.42–0.65) indicates that primary prevention through birth preparedness may have been effective in reducing adverse intrapartum events; cause-specific mortality data will help elucidate this effect.

The Skilled Care Initiative in Ouargaye district, Burkina Faso, utilized community mobilization strategies to generate higher demand for skilled obstetric care in parallel with supply-side quality improvement [33,34]. Behavior change communication was a key component of community workshops in addition to social marketing and stakeholder engagement. PMR was 25% lower in the intervention versus comparison district (OR 0.75; 95% CI, 0.70–0.80), and rates of institutional delivery increased in the intervention district (OR 1.23 per year; 95% CI, 1.18–1.28) more quickly than in the comparison district (OR 1.08; 95% CI, 1.05–1.12). There was no difference in cesarean delivery rates between districts (0.34% vs 0.46% in intervention vs control).

The creation of village health committees was a key strategy to increase demand for skilled birth care in a pilot study in Hala and Matiari subdistricts of rural Sindh province [25]. Lady Health Workers from within the government health system, along with community volunteers, established village health committees and led 3-monthly group educational sessions. Most villages (86%) in intervention clusters established community health committees, of which 31% established emergency funds for transport and hospital fees. In the intervention clusters there was an increase in the proportion of births taking place in public sector facilities (from 18% to 30%), a reduction in home-births (from 79% to 65%), and reductions in stillbirth (65.9 to 43.1 per 1000) and neonatal mortality (57.3 to 41.3 per 1000) rates following the intervention in the absence of major changes in the concurrent control areas. Although data on intrapartum-related neonatal mortality rates are not yet available, the substantial reductions in early neonatal mortality and stillbirths may reflect the impact of these interventions on intrapartum-related hypoxia via improved intrapartum management, and emphasize the potential effectiveness of a public sector program approach.

Program experience with village health committees in Bangladesh and India has also demonstrated significant improvements in birth preparedness, improved rates of institutional delivery, and met need for emergency obstetric care services (Table 2) [27,132].

Community education sessions of lower intensity or without active solution-making processes may not mobilize communities as effectively. In Sylhet, Bangladesh, group education meetings alone did not appear to improve neonatal outcomes or care-seeking behaviors [29]. The interactions were of relatively low intensity (meetings once every 4 months with a mobilizer:population ratio of 1:18 000) and the mobilization activities did not utilize an action-oriented approach, which may have contributed to the lack of effect. In Siraha, Nepal, monthly community education sessions resulted in improvements in knowledge of birth preparedness and prenatal, postnatal, and essential newborn care, but no improvements in intrapartum care seeking [26].

Meta-analysis of 4 studies of community mobilization was conducted [22,24,25,29]. The Skilled Care Initiative and Dinjapur Safe Motherhood Initiative studies were excluded as there were 2 districts compared, which had large pre-existing differences between the areas at the beginning of the study; it is thus impossible to properly account for the uncertainty associated with between-area variation [33,34]. The Projahnmo study community care arm was used to evaluate the effect of isolated mobilization on facility delivery; the home-care arm was not included as this also involved the home-based management of sepsis with antibiotics. The meta-analysis indicated evidence of increase in demand for skilled obstetric care, as the proportion of institutional births increased by 71% (RR 1.71; 95% CI 1.10–2.64) (Fig. 2A); however, the mobilization strategies were heterogeneous between studies, and in a sensitivity analysis that included only the more intensive and participatory mobilization strategies [22,24,25], the proportion of institutional births doubled (RR 2.08; 95% CI 1.23–3.49) (Fig. 2B). For these studies there was also evidence of a reduction in PMR (RR 0.75; 95% CI, 0.59–0.96) and ENMR (RR 0.64; 95% CI, 0.48–0.85). These studies did not differentiate cause-specific fetal or neonatal mortality due to intrapartum-related events; however, approximately one-third of stillbirths [2] and 30% of early neonatal deaths are estimated to be intrapartum-related in settings with low skilled attendance at birth [1,35]. As community mobilization could prevent intrapartum-related deaths by reducing delays in receiving obstetric care and increasing facility delivery rates, it is plausible that reductions in perinatal and early neonatal deaths reflect some level of reduction in intrapartum-related mortality.

3.1.3. Cost-effectiveness of community mobilization

Cost data for community mobilization packages are limited and variable depending on the specific components implemented and the economic methods used. In the initial Warmi Project covering 50 communities (population 15 000), the cost of training materials, women's group facilitators, and related program expenses was about US $100 000 per year, with an average cost of US $6 per population, and about US $1923 per perinatal death averted. When the program was scaled to the national level, the budget was US $1.25 million per year. In the Makwanpur trial, Nepal, the total cost of the women's group interventions including training, equipment, transportation, and upgrading the local health services was US $77 765 per year, with an average cost of US $0.90 per person (population 86 704), US $5.22 per married woman of reproductive age, US $6912 per neonatal death averted, and US $251 per life year saved [36].

3.1.4. Implications regarding community mobilization

Three cRCTs, 2 quasi-experimental studies, and 1 before-and-after study gave moderate-quality evidence that community mobilization programs can reduce early neonatal and perinatal mortality and increase skilled birth attendance. Our meta-analysis showed a 71% increase in institutional deliveries, with a two-fold increase for high intensity mobilization strategies. While none of these indicators is a direct measure of intrapartum-related mortality, it is plausible that skilled birth attendance is an important pathway to reduce intrapartum stillbirths and intrapartum-related neonatal deaths. Programs demonstrating mortality reduction had high levels of active community participation, contextualized newborn problems in the local customs and culture, involved a broad range of key community

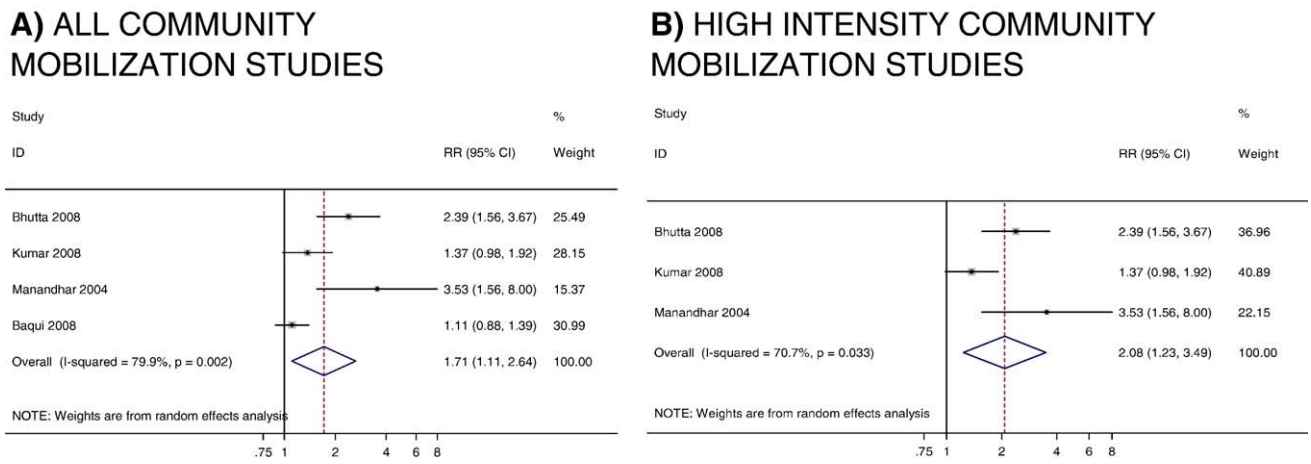

Fig. 2. Estimates of the effect of community mobilization on institutional delivery. (A) All community mobilization studies meeting inclusion criteria. (B) High-intensity community mobilization studies.

stakeholders, and included home visitation and peer counseling. Programs with passive community involvement, low frequency contacts, or which provided education without addressing problems generally failed to demonstrate effectiveness. The GRADE recommendation for implementation of intensive, participatory community mobilization is strong, however, additional research is needed to determine the effect of community mobilization on cause-specific mortality, cost-effectiveness, and effectiveness in different settings, particularly Africa. While the quality of evidence for an effect of community mobilization on perinatal and neonatal mortality is moderate, there are no data on intrapartum-related mortality, and limited data from Africa, and hence, the GRADE quality of evidence for interventions affecting this specific outcome is not available (Table 3).

3.2. Financial strategies

3.2.1. Background

For the poor, the costs of transportation and obstetric care are frequently prohibitive [37–39]. In the regions with the lowest rates of skilled birth attendance, Sub-Saharan Africa and South Asia, 40%–54% of all health expenses are paid directly out-of-pocket by families who are already in the lowest income countries of the world (Fig. 3). In low-income settings, a normal hospital delivery may cost 3%–26% of annual gross domestic product per capita and the cost of a cesarean delivery may exceed a family's annual income [40]. Having adequate funds available at the time of need is a challenge for the poor. In Bangladesh, 74% of mothers who had a cesarean delivery did not have the money to pay for it at the point of care [37].

In this section we will briefly review several promising financial strategies to increase community demand for obstetric care: elimination of user fees, community-based insurance schemes, community loan funds, conditional cash transfers, vouchers schemes, contracting out and pay for performance (Table 4). Some examples of supply-side interventions will also be discussed. Borghi et al. [40] comprehensively review financial strategies for improving maternal health in the fourth paper of *The Lancet* Maternal Survival series.

3.2.2. Evidence for financial strategies

We identified many reports of small-scale programs implementing community emergency loan funds and community-based health insurance schemes, primarily from Africa and one from South Asia and Latin America (Table 5) [41–52]. There were fewer reports of conditional cash transfers and voucher schemes, mainly from South Asia and Latin America [53–57]. While some of these reports present data on utilization of obstetric care, we did not identify any that reported on maternal or neonatal health outcomes, long-term sustainability, or cost-effectiveness.

3.2.2.1. Elimination of user fees. The removal of user fees for maternal health services has been piloted in several African countries (Ghana, South Africa, Burundi) [58] and several districts in Nepal. In South Africa, user fees for pregnant women were removed in 1994 and resulted in increases in prenatal care attendance (14.9%) and booked facility births (4.6%) [59]. However, the increase in care for acute services also resulted in reductions in preventative medical care [60], and concerns about the quality of care provided have arisen [59].

In Ghana, exemptions for childbirth fees were instituted in 2004 and resulted in higher proportions of births supervised by skilled birth attendants (14%–17%) and births in public institutions (19%) [58,61]. The proportion of catastrophic out-of-pocket payments was reduced for the poorest quintile, but the proportionate decrease in out-of-pocket payments was even greater for the rich [58]. Furthermore, with increasing utilization, Ghana faces many challenges including that of overworked public midwives and doctors, who increased their working hours by 27% and deterioration in quality of services [58].

In the poorest districts in Nepal, free institutional delivery has been offered along with cash payments to cover transport costs for all pregnant women. However, this policy has been implemented in only a few districts and no formal evaluation has yet been published [36].

3.2.2.2. Community-based health insurance schemes. Community-based health insurance programs have been implemented in several African settings [45–49,51,52]. These have been successful in increasing institutional delivery rates when obstetric care was included in the insurance package [52]. While the financial viability of small-scale programs may be tenuous because of fluctuating membership levels and low recuperation of operating costs with membership fees (as low as 2%) [46], the incorporation into national health financing strategies has been more sustainable [45–49,52]. In the Gambia [62], Rwanda [47], Senegal [52] and Mali [52] community insurance schemes were associated with 12%–45% increases in facility delivery, and in the Democratic Republic of Congo, a 7-fold

Table 3
Interventions reviewed: Evidence GRADE, feasibility, and recommendations.

Intervention	GRADE evidence level for perinatal mortality outcomes	GRADE recommendations	Feasibility in low- and middle-income settings
Increasing community demand for obstetric care			
Community mobilization	**MODERATE:** Two cRCTs, 2 quasi-experimental trials, and 1 before-and-after study have shown benefits of community mobilization in increasing institutional delivery and reducing perinatal mortality. The data is consistent for programs of higher intensity mobilization; one RCT failed to show impact. The evidence is generalizable to low- and middle-income settings, although indirect, as intrapartum-related mortality was not available.	**STRONG:** Several moderate-high quality studies have shown benefit of high intensity community mobilization strategies, with the likely indirect effects on intrapartum-events. Given the benefit on all cause perinatal mortality, lack of harm, and low cost, the strategy is strongly recommended.	Successful program experience has been demonstrated in South Asia, Latin America, particularly with increasing levels of community participation-ownership. Programs may be started with low cost; more evaluation is needed on cost-effectiveness, sustainability, and scalability.
Financing Strategies • Elimination of user fees • Community-based health insurance loans • Conditional cash transfers • Vouchers • Community loans	**VERY LOW:** There are several low-quality before-and-after program reports showing that different financial strategies may be associated with greater obstetric care seeking. The data is generalizable to low- and middle-income settings, and is primarily from Africa and South Asia. There are no direct data on the impact on perinatal health outcomes or on intrapartum-related events.	**CONDITIONAL**: There is promise for these strategies to increase institutional delivery and access to emergency obstetric care for the poor, but more rigorous evaluation of the impact on health outcomes, cost-effectiveness, and sustainability is needed before recommendations for implementation can be made.	Program experience in several low- and middle-income country settings, primarily Africa and South Asia. Challenges include sustainability, high administrative costs, repayment-defaults of loans. Insurance premiums and loan systems may still marginalize the poor. Most programs may require government support to ensure sustainability. All of the demand-side strategies need to be accompanied by increasing supply of obstetric services maintaining quality of care.
Communication and transport systems	**LOW:** There are several low-quality before-and-after program reports showing that communication and transport systems may increase obstetric care seeking. Few studies report reduced transport time and maternal case fatality. The data is generalizable to low- and middle-income settings, though most studies were from Africa. There is only 1 program report on perinatal outcomes, with no reports of intrapartum-specific mortality.	**CONDITIONAL:** There is promise for communications and transport systems to reduce transport time and increase receipt of obstetric care. However, impact on health outcomes, cost-effectiveness, and sustainability need to be assessed before recommendations for wide-scale implementation can be made.	Challenging in rural settings with poor road transport and communication infrastructure; high costs of vehicles and maintenance, and 24-7 on call coverage. Potentially sustainable, lower-cost models use existing infrastructure, drivers or transport systems (transport union, taxis, flagging system).
Bringing pregnant women closer to the formal health system			
Prenatal risk screening by community-based workers	**VERY LOW:** There are several low-quality validation studies of risk screening using observational data, demonstrating poor predictive value. There was one before-and-after observational study demonstrating a reduction in perinatal and intrapartum-related mortality in a program including risk screening, and risk-screening for admission to maternity waiting homes has been associated with lower perinatal mortality in 3 low-quality observational studies.	**CONDITIONAL:** While early risk screening algorithms used maternal characteristics, there may be a role for testing risk screening algorithms using early pregnancy complications with higher predictive value and low prevalence. Further evaluation of the effects of such algorithms need to be evaluated.	Simple algorithms to identify high-risk women can be followed by non-professional health workers. However, algorithms or checklists using pregnancy complications (such as breech, multiple pregnancy, late pregnancy, vaginal bleeding, or high blood pressure) need to be evaluated in a program-intervention context considering risk of over referral and overloading health facilities with limited supply.
Maternity waiting homes	**LOW:** Four low-quality observational cross-sectional studies associated lower perinatal-neonatal mortality with babies of mothers who stayed in maternity waiting homes. However, only 1 study adjusted for the difference in baseline obstetric risk between mothers of intervention and comparison groups. The majority of studies were from Africa and generalizable to low- and middle-income settings. No data on intrapartum-related mortality were available.	**WEAK:** There is potential for this strategy in rural settings, however there is a lack of convincing evidence of effectiveness and a need for rigorous evaluation of the impact on maternal and perinatal outcomes, as well as cost-effectiveness.	Pilot tested in several African settings. Challenges include acceptance and utilization in different cultures, costs of stay, and cost-effectiveness of strategy. Services need to be coordinated and linked with hospital facility with CEmOC.

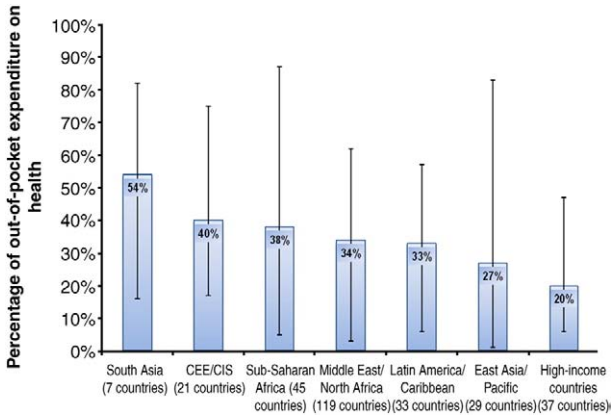

Fig. 3. Out-of-pocket expenditure as a percentage of total expenditure on health. Source: New analysis using data from National Health accounts available from WHO Statistical Information System, June 2009. The range lines demonstrate the minimum and maximum for each region. Percentages are unweighted regional averages for countries with data on out-of-pocket expenditure as a percentage of total of expenditure on health. Currently, there is no comparable national data on out-of-pocket expenditure specific to maternal, newborn and child health expenditure because National Health Accounts do not routinely split out and report this figure.

increase in obstetric hospital admissions was found [49]. In West Africa, over 600 community-based insurance schemes had been established by 2004, including at least 5 national health insurance strategies.

In Nouakchott, Mauritania, the Ministry of Health implemented an Obstetric Risk Insurance Plan that achieved high coverage and financial viability [48]. Membership covered prenatal care, emergency transportation, basic care at birth, and cesarean delivery, and the fee was waived for the poorest. Membership coverage achieved 95% in the urban catchment area. From 2003–2005, the number of births in participating hospitals increased by 31% and the number of cesarean deliveries increased by 60% (2.8% to 3.5% of births). The program generated positive revenue, doubling that of user fees, and covered all recurring costs other than health worker salaries.

3.2.2.3. Community loans. Community loans for emergency transport and obstetric care have been established in several safe motherhood initiatives in Nigeria; however, the long-term sustainability and impact on maternal and newborn outcomes remains unclear. In two small pilot projects in Nigeria [41,63], emergency loan funds were successfully established, providing loans that were repaid with low interest rates charged to families (0%–2%). However, in Cross River State, while a majority of villages had established community loan funds, fewer than half had been accessed during the study, and in many villages there were insufficient funds [64].

In Makwanpur, Nepal, community maternal and child funds helped to enable care seeking for some mothers, but there is some evidence that they did not reach the poorest and most marginalized community members [38]. Most women's groups established funds with voluntary monthly donations (US $0.15) and charged 1%–2% interest on loans. Three years into the program, the funds had an average of US $31 per group, and across all funds US $6764 had been distributed with approximately half repaid. Loan funds were, however, a disincentive to joining women's groups for the poorest women, who saw mandatory contribution as an obstacle to participation. In some cases, the poorest women were not allowed to take loans because of a perceived risk of default. While community funds may have contributed to improved maternal and neonatal outcomes, it is impossible to determine their role in the overall effect.

3.2.2.4. Conditional cash transfers. Conditional cash transfers have been effective in increasing utilization of prenatal care services and rates of institutional delivery [53–55]. A cRCT was conducted in 70 cities in Honduras, in which intervention households were given monthly cash vouchers in exchange for attending routine prenatal and well-child clinics. Compared with the control households, those receiving cash transfers in intervention areas utilized prenatal care 18%–20% more often [53]. In a retrospective case report from rural Mexico, women participating in a conditional cash transfer program were 12% more likely than nonparticipants to receive prenatal screening or case management procedures [54]. In India, the National Rural Health Mission established the "Janini Suraksha Yojna" (JSY) program in 2001 to pay poor, marginalized women for institutional delivery. In this national-level scheme, pregnant women in rural areas are given cash incentives at the time of institutional delivery, with additional payments for emergency transport, cesarean delivery, and postdelivery expenses [55]. Nationally, institutional births increased from an estimated 10.9 million in 2005–6 to 13.6 million in 2007–8, although this cannot be attributed directly to the program. No evaluation of impact of the JSY program on health outcomes is

Table 4
Financial strategies to increase access to obstetric care.

Strategy	Definition
Elimination of user fees	Out-of-pocket expenses for hospital fees for maternal-newborn health care have been abolished in several settings, in an attempt to reduce inequities in access to care for the poor. Families may incur other charges during hospitalization, however, and cost of transport is not typically covered [40].
Community-based insurance schemes	Insurance plans at the community level aim to reduce out-of-pocket expenses by risk pooling; members typically pre-pay a fixed fee to join a program at the beginning of pregnancy and qualify for free or reduced rate obstetrical services at the time of childbirth. However, fees are often unaffordable for the poor and in programs with small membership, a high frequency of expensive procedures may exceed the gross income, and therefore be unsustainable. Some plans exclude more expensive costs, such as childbirth care [40].
Community loans funds	Funds are generated from contributions of community members and permit families to borrow sums to pay up front for emergency transportation and hospital costs. They are typically managed by appointed community members, and may have varying procedures for repayment and interest; however, repayment is required for fund replenishment and sustainability [38,40,64].
Conditional cash transfers	Conditional cash transfers provide cash payments to pre-selected mothers or families, typically from poor or marginalized groups, on the condition that they use specified services [40]. However, families must locate and afford transport and hospital fees in order to receive care, since conditional cash transfers are not given until after its receipt.
Vouchers	Vouchers are given to pre-identified, poor or marginalized mothers and can be redeemed for free health services at specified facilities. These may be advantageous as mothers do not need to pre-pay for services, and thus for a costly procedure such as a cesarean section, the family would not need to come up with a large sum of money before accessing care [40,72,121].
Contracting out and pay for performance	Contracting and providing financial incentives to private practitioners or organizations to provide obstetric health services for the poor may improve their access to childbirth care. Penalties for non-performance have also been attempted to improve quality of care provided.

Table 5
Effect of financing strategies to increase demand for obstetric care.

Intervention/study (date order)	Setting	Care seeking/demand	Other intermediate outcomes	Investigator and year
Elimination of user fees				
Removal of user fees for pregnant women in 1994.	South Africa	• Increase in prenatal care by 14.9% • Increase in booked facility births by 4.6%		Schneider et al. [59] 1999
Exemption for delivery fees in 2004.	Ghana	• 19% increase in births in public institutions • 14%–17% increase in skilled birth attendance	• Cost US $22 per delivery • Reduction in incidence of catastrophic out-of-pocket payments from 55% to 46% for poorest quintile • No significant effect on maternal mortality	Witter et al. [58] 2009
Community loan funds				
Establishment of community loan and transport systems.	Rural Makarfi District, Nigeria	• 18 women transported to hospital for emergency	• Raised US $20 500 • 18 loans approved in 9 months • Transport system of 23 permanent, 58 part-time drivers • Skilled attendance increased from <20% to 59% at end program	Essien et al. [41] 1997
Establishment of community loan fund managed by village health committee.	Sierra Leone		• Increase in utilization in coverage areas compared with non-covered areas	Fofana et al. [42] 1997
Educational campaign regarding use of obstetric services. Community mobilization though loan and transport programs.	Semi-urban Ikot Omin and rural Ikot Ene, Nigeria	• Trend of increasing referrals to university hospital for obstetric complications • Decline in utilization of obstetric services; however, parallel inflation, increasing transport costs, and user fees in study areas during period	• Awareness of obstetric complications increased 5%–63% • 14/39 communities established new loan programs • Loans granted and transport systems established in 9 communities	Olaniran et al. [64] 1997
Government funding of NGOs to provide basic health services to reach poor, rural, indigenous populations.	Guatemala	• Substantial increase in coverage an quality of Emergency Obstetric Care • Increase in Hospital Based delivery rates • Increase in met need		Nieves et al. [43] 2000
Participatory women's groups established community funds for maternal health care.	Nepal	• Increased institutional delivery in women's group areas 7% vs 2%; (RR 3.55; 1.56–8.05) • Increased birth attended by skilled provider in women's group areas 7% vs 2%; (RR 3.53; 1.54–8.10)	• Majority of women's groups had established funds • Half of funds repaid • Charge 1%–2% interest	Morrison et al. [44] 2008
Community-level insurance schemes				
Insurance for prenatal care and pregnancy care.	Gambia		• High uptake of insurance 90% joining	Fox-Rushby et al. [45] 1996
District-based insurance scheme to cover majority of hospital fees with co-payment.	Democratic Republic of Congo	• Rate of obstetric admission for insured vs non-insured (7:1)		Criel et al. [49] 1999
Community-financing scheme to partially cover costs of health delivery. Insurance providing vehicle and nurse for emergency referrals.	Rural Samburu district, Kenya	• Referral of 655 patients for emergencies (all cause) in 8 years, average 6 patients per month transported from clinics to higher-level care	• Average enrollment 324 members per year (25% of households) • Average cost US $16 per year, sliding scale fees	MacIntyre et al. [46] 1999
Development of community health fund for basic reproductive health and other services at rural health centers.	Tanzania		• Expansion to 4 districts	Krasovec et al. [50] 2000

Development of pre-payment schemes in 3 districts.	3 districts, Rwanda	• Increase of facility births in pilot districts increased 14%–49% in pilot districts • Prenatal visits increased 5%–27%		Schneider et al. [47] 2001
Creation of Obstetric Risk Insurance to cover EmOC, hospital care, postnatal care. Poorest enrolled at no charge.	Nouakchott, Mauritania	• Maternal case fatality 2.8% • Rate increased from 2.6% to 3.5% • Increase of births in Obstetric Risk Insurance facilities from 29% to 48%	• 95% coverage • Membership premium US $21 vs fee for basic delivery and for non-members $13 and $163 • Generation US $382 320 in revenue, twice of current user fees • Decrease in partograph use (80% to 47%)	Renaudin et al. [48] 2008
Community-based health insurance schemes established in Senegal, Mali, and Ghana.	Mali, Ghana, Senegal	• In Senegal, insurance members with maternal health service coverage had 93% facility delivery compared with 71% of nonmembers. No increase in those belonging to insurance without coverage of maternal services • In Mali, members had 94% facility delivery compared with 65% in nonmembers.		Smith et al. [52] 2008
National maternity referral system: communication systems established between primary and referral level facilities, ambulance transport, and cost sharing scheme.	Mali	• Institutional births increased from 19% to 39% from 2003–2006	• Obstetric emergencies treated increased from 0.9% to 1.9% • Obstructed labor management increased from 22% to 38% • Number of cesarean deliveries tripled over 3 years • Maternal mortality reduced by 50%	Fournier et al. [51] 2009
Conditional cash transfers				
cRCT of monthly cash transfers for making routine prenatal visits.	Honduras	• Prenatal care utilization 18%–20% higher in intervention clusters		Morris et al. [53] 2004
Retrospective case report of users of conditional cash transfer program vs nonusers.	Mexico	• Conditional cash transfer participants 12% more likely to use prenatal screening		Barber et al. [54] 2009
Janini Suraksha Yojna program to pay for impoverished women for institutional delivery, transport expenses.	India	Increase in number of annual institutional births from 10.9 to 13.6 million over 2 years		Lahariya [55] 2009
Vouchers				
Maternal Health Voucher Scheme piloted in 21 upazillas for impoverished residents.	Bangladesh	• Increase in prenatal care, at least 1 visit from 30% to 60% in 1 year • Increase in health facility delivery from <10% to 40% and end of first year		Helal S [56]
Public-private partnership providing free delivery care to impoverished families via private sector.	India	• Institutional births for the poor increased from 27% to 48%	• Contracted 852 doctors, subsidized 165 278 births	Unicef [57]
Contracting out and pay for performance				
Ministry of health contracted out health service network in El Alto city to an NGO, providing incentives for meeting process and outcomes indicators.		• Institutional births by 41% and births at primary care centers increased from 5% to 9% in study district		Lavadenz F [71] 2001
Ministry of health contracted out services to NGOs to delivery health services as alternative to conventional government provision. Contractors have full responsibility of services in district and management control.	Cambodia	• Greater increase in prenatal care use in contracted districts vs. control (402% vs 160% increase in contract out vs control areas) • Greater increase in facility births (142% vs 0% increase in contract out vs control areas)		Bushahan [69] 2002

available. Cash transfer programs are also being implemented in Bangladesh and Nepal to increase maternal healthcare utilization [36,65,66].

3.2.2.5. Voucher schemes. Many countries have adopted fee waiver programs to increase utilization of services. A variant of this is voucher programs, which not only reduce financial barriers to access but also permit the beneficiary to purchase care from a provider of their choice. As vouchers are targeted at the poor, they improve equity. Voucher schemes are being piloted in India, Bangladesh, Tanzania, Cambodia, Uganda, and Kenya [56,67]. However, there are limited data from long-term evaluations. In Bangladesh, the Maternal Health Voucher Scheme, piloted in 21 subdistricts, targets poor residents without a regular source of income and covers the costs of prenatal care and care at birth, including care for obstetric complications, and transport. In the preliminary first year evaluation, 73% of targeted beneficiaries had utilized services covered by the scheme, the proportion of mothers receiving at least one prenatal visit had increased from 30% to 60%, and their use of public facilities for delivery had increased from less than 10% to 40%. Challenges identified included ensuring the quality of care and access to EmOC at the subdistrict level, and retention of specialists (obstetricians and anesthesiologists).

In Gujarat, India, a public-private partnership, "Chiranjeevi Yojana," was initiated in 2005 that provides free obstetric care for impoverished families via the private sector [68]. The government compensates participating private obstetricians for providing maternal healthcare services free to women below the poverty line, and provides a small stipend to mothers to cover transport and lost wages for her accompanying partner. By 2008, the program had expanded from 5 to all 25 districts of Gujarat, enlisting 852 private doctors, subsidizing 165 278 births, with an increase in institutional births for the poor from 27% to 48% [57]. Since its inception in 2005, there were 599 neonatal deaths and 32 maternal deaths reported among the beneficiaries, for an estimated NMR of 3.4 per 1000 and an MMR of 19 per 100 000 among the enrolled. However, while the estimated baseline preprogram NMR was 40 per 1000 and the MMR was 400 per 100 000, there are no population-based data against which to evaluate the program's effectiveness.

3.2.2.6. Contracting out and pay for performance. Changes in how providers are compensated can be a powerful tool to change their behaviors and align their incentives with those of the payor or government. The "Chiranjeevi Yojana" discussed above is an example of a program that pays providers a capitated or per beneficiary amount for a bundle of services. In Cambodia, NGOs were contracted to provide maternal and child health services. In addition to a capitation rate per person, there was a penalty for nonperformance. The outcomes from this were compared with the government delivery system as well as one in which the emphasis was on strengthening management. Assessments [69,70] showed that the contractual model worked better than the other two, resulting in an increase in prenatal care use (402% vs 106% increase in contracted-out vs control areas) and facility births (142% vs 0% increase in contracted-out vs control areas). In Bolivia, achievement of process and outcome indicators was used as an incentive to pay providers for delivering maternal and child health services, which led to increased institutional births by 41% and births in primary care centers increased from 5% to 9% [71].

3.2.3. Costs of financial strategies to increase demand for obstetric care

There are limited costing data on financial strategies for maternal and newborn health, and given the lack of data on mortality effects, cost-effectiveness cannot be reliably estimated. In Markafi District, Nigeria, the establishment of a loan fund cost US $3409 and a transport fund cost US $2272, with 60% covered by the community and 40% by the Prevention of Maternal Mortality project. In Mauritania, the starting costs of the Obstetric Risk Insurance Plan was US $60 000 to serve a population of 200 000, and within the first year the income generated was sufficient to cover annual operating costs, excluding health worker salaries. By 3 years US $382 320 had been generated.

Preliminary costing analysis of conditional cash transfer programs indicates substantial operating and administrative costs, emphasizing the urgent need for data on cost-effectiveness [54,72]. In Mexico the conditional cash transfer program covered 5 million beneficiaries (20% of households) and was 4% of the total health budget, with an average cost of US $560 per family beneficiary and US $20 transferred to each household, indicating substantial overhead and administrative costs. In Honduras, the program served 411 000 beneficiaries (about 35% of households) comprising 28% of the total national health budget, with an average cost per household of US $60.83, and a mean transfer of US $17 to the household.

The cost of the Chiranjeevi voucher scheme for the entire state of Gujarat, India was US $12.6 million per year, which was approximately 3.6% of the annual health budget. Since its inception in 2005, the program has cost US $18.1 million, and has been roughly estimated to have saved about 6000 newborns and 610 mothers, although this is not based on a rigorous evaluation [68]. However, using this rough estimate, the cost per newborn and mother saved was approximately US $3000 and US $30 000, respectively.

3.2.4. Implications for financial strategies

While the available data suggest that financial strategies may increase obstetric services utilization, evidence on health outcomes for the mother and newborn is lacking. Hence, the quality of evidence is graded very low. Community-based insurance schemes have been piloted in several, primarily African, settings, and while small-scale programs may have limited financial viability, national programs partnering with governments have been successful in increasing rates of facility-based delivery and access to emergency obstetric care. The elimination of user fees has been piloted in Africa and parts of Nepal, and initial evaluations indicate increased coverage rates of skilled birth attendance. However, strategies to increase demand for services need to be accompanied by actions to ensure the supply side can cope with the increased demand, as illustrated in Mauritania, where the rapid increase in hospital births met with insufficient capacity and resulted in deterioration in quality of care [48].

There is limited evidence available currently to support community-based emergency loan funds, conditional cash transfers, and voucher schemes. While community-based loan funds have been successfully initiated in many settings, they are often difficult to sustain, infrequently utilized, and may not reach the poorest families. Conditional cash transfers and voucher schemes can increase utilization of services and, furthermore, preliminary data from the Chiranjeevi program suggest lower neonatal mortality among beneficiaries. However, further studies are needed to evaluate the impact of these programs on maternal and perinatal health outcomes and their cost-effectiveness to determine the sustainability and affordability for scale up of these programs. Provider payment reforms show promise, but once again the evidence is sparse and rigorous impact evaluations are needed. Where both demand and supply-side interventions are used, it is difficult to estimate their relative impacts.

4. Bringing pregnant women closer to the formal health system

4.1. Community referral and transport systems

4.1.1. Background

Delays in transportation are associated with low utilization of skilled obstetric care and increased risk of maternal-neonatal

morbidity and mortality [11,39,73,74]. In an assessment of 10 low- and middle-income countries, over 80% of the population did not live within 5 km of a hospital [75]. Lack of transportation was the primary preventable cause of death in 28% of maternal deaths in rural Zimbabwe [39], and 21% of perinatal deaths in Tanzania [11].

Reducing transport time to emergency obstetric care is challenging in rural settings, where roads, public transportation, and communication infrastructure are poor, and the terrain may be formidable. Improving communication between a home birth attendant and trained staff via two-way radios or mobile phone technology may reduce delays in recognizing the need for referral and arranging timely transport to a first level facility [76]; and communication between peripheral and Comprehensive Emergency Obstetric Care (CEmOC) hospitals may reduce delays in receiving cesarean delivery [51]. Innovative transportation approaches are required in remote and resource-limited settings and may involve adaptation of low-cost vehicles, use of all terrain vehicles, optimizing existing transport mechanisms, and arrangement of on-call driver coverage (Panel 2).

4.1.2. Evidence for community referral and transport systems

We identified numerous program reports of community referral and transport systems from Safe Motherhood programs from Africa and South Asia (Table 6). A wide range of strategies for communication and transportation were identified and are shown in Panel 2. In this section, we highlight studies reporting intrapartum-related or mortality outcomes, or that underline key program experiences and challenges.

4.1.2.1. Improved communication systems. Enhanced communication between community-based workers and medical professionals, as well as between primary and referral health centers, may reduce transport delays and improve referral rates. In the Ugandan program, Rural Extended Services and Care for Ultimate Emergency Relief (RESCUER), Traditional Birth Attendants (TBAs) attending home births were given mobile walkie-talkies to call medical staff in the event of labor complications to triage problems and call for emergency transport to the home; TBA referral rates increased over the project period. In Bo District, Sierra Leone [77], messengers from primary health centers were sent by motorbike to summon referral vehicles but often encountered difficulties with curfews or vehicle malfunction; the establishment of solar-powered radio communications reduced the referral time to the district hospital by 2 hours from the most peripheral centers. In Malawi, repeater-based VHF radio communication systems were established in district health centers to assist in the dispatching of ambulances to health centers [78]. After establishment of the system, the number of

Table 6
Effect of transport referral systems on care seeking and intermediate outcomes.

Intervention/study (date order)	Setting	Care seeking/demand	Other intermediate outcomes	Investigator and year
Faisalabad Obstetric Flying Squad provided free ambulance services staffed by skilled obstetric personnel for women in rural areas, free maternity services.	Pakistan		• 394 transports from 1989–1992 • Common indications: labor pains, abortion, eclampsia, postpartum hemorrhage • Referrals comprised 2%–5% of hospital admissions • Challenges to contacting the service	Andina et al. [122] 1995
Establishment of communications system, emergency transport, and 24-hr driver to bring mothers with obstetric emergency to referral hospital.	Rural Bo District, Sierra Leone	Transports increased from 0.9 to 2.6 per month	• Maternal case fatality from obstetric complications reduced from 20% (3/15) to 10% (2/21)	Samai [77] 1997
Two villages provided bicycle ambulances and community transport plans.	Nsanje District, Malawi	Home delivery rates in case villages decreased from 37% to 18%	• Time of transport was 90 minutes for all transport used, no change in ambulance villages • Cultural beliefs deterred most pregnant women from using bicycle ambulances, used primarily for nonobstetric transport	Lungu et al. [82] 2001
Community Capacity Building and Empowerment Imitative developed community-level transport systems, ranging from canoes, ox carts or loan of truck.	Rural Tanzania	Obstetric complications attended at district hospitals increased from 4% to 15%	• Most of 52 villages had a written action plan for transport with varying methods • At 2-year follow-up only 12 (27%) villages had put the plan into action and the transport system was only used in 10 villages (23%) in previous 3 months	Schmid et al. [123] 2001 Ahluwalia et al. [124,125] 1999, 2003
TBAs used wireless telecom systems to call for and arrange ambulance transport to hospital.	Balochistan, Pakistan		• NMR 48 (intervention area) to 32.4 (control) • PMR 49 (intervention) vs 85 (control)	Midhet [84] 2006
National maternity referral system: communication systems established between primary and referral level facilities, ambulance transport, and cost-sharing scheme.	Mali	Institutional births increased from 19% to 39% from 2003–2006	• Obstetric emergencies treated increased from 0.9% to 1.9% • Obstructed labor management increased from 22% to 38% • Number of cesarean delivereis tripled over 3 years • Maternal mortality reduced by 50%	Fournier et al. [51] 2008
Motorcycle ambulances to transfer mother from primary health facility to referral hospital for EmOC.	Rural Malawi		• Reduction in median delay to referral hospital 2–4.5 hours (35%–76%) • Price of motorcycle 19 times cheaper than car ambulance • Annual operating costs 24 times cheaper than car ambulance	Hofman et al. [83] 2008
Establishment of emergency obstetric transport service, with emergency obstetric supplies, radios.	Rural Brong Ahafo, Ghana		• Transfer of 364 mothers and 2 babies in 15 months • 30% of mothers transferred required medical interventions	MaterCare International [126]
Referral system developed in rural district including walkie-talkies, ambulance transport via 4-wheel drive vehicles, 24-hour drivers.	Rural Iganga district, Uganda	Supervised births increased from 15% to 27%	• Hospital-based maternal case fatality reduced 50% • Increased coverage to 56 districts, however difficult to sustain maintenance costs	UNFPA [76]

monthly obstetric admissions, referral rates, and referrals within one hour of decision all increased, with a reduction in median time of transport from three to two hours. However, for many mothers the transport time was still too long, due to the paucity of available ambulances.

4.1.2.2. Private-public partnerships. Existing transportation mechanisms may be modified to create solutions for transport of mothers. In West Africa, a local truck drivers' union volunteered to provide emergency transport for pregnant women. Families placed a yellow flag along regular truck routes to notify truck drivers of the need for transportation [79]. In Nigeria, a local transport union of bus drivers negotiated to provide free transport for women with obstetric emergencies on market days [80]. In Pakistan, the largest private ambulance service is run by philanthropic donations and contributions of community members. The Edhi foundation has established an extensive communication network and a fleet of over 400 ambulances, a helicopter, and 2 airplanes that provide emergency transport for the whole country and serve the most remote areas, where government services do not reach [81].

4.1.2.3. Community-based emergency transport systems. Alternative means to transport pregnant women have been piloted in remote regions with varied success. In Malawi, the introduction of bicycle ambulances did not reduce transport time and they were infrequently used because of cultural beliefs that publicizing labor resulted in summoning evil spirits [82]. However, motorcycle ambulances were found to be both effective and culturally acceptable in another district in Malawi and this experience is highlighted in Panel 2 [83].

In the Balochistan Safe Motherhood Initiative, Pakistan, TBAs played a central role in strengthening the referral-transport chain for obstetric emergencies that resulted in significant reductions in neonatal and perinatal mortality. TBA were trained to recognize, stabilize, and refer for obstetric emergency and were given wireless telecom systems to call for and organize ambulance transportation. In the intervention areas the perinatal mortality rate was 49.4 per 1000 compared with 85.2 per 1000 in the comparison areas, and the neonatal mortality was 32.4 per 1000 compared with 48 per 1000 in the comparison area [84].

In the Sierra Leone and Ugandan RESCUER programs, enhanced communication systems coupled with emergency transport via 4-wheel drive ambulances significantly increased obstetric referrals, and reduced maternal case fatality. In Sierra Leone [77], the number of successful referrals increased from 0.9 to 2.6 per month, and the case fatality of mothers with obstetric complications was reduced from 20% to 10%. In the Ugandan RESCUER program, from 1995 to 1998, the proportion of supervised births increased from 15% to 27% and hospital-based maternal case fatality was reduced by 50%. However, by 2005, when the program was scaled up to 56 districts, the high demand and cost of vehicle maintenance were difficult to sustain and there were insufficient funds [76].

The Government of Mali launched a national maternity referral system in 2002 to improve access to and quality of comprehensive obstetric care [51]. The maternity referral program established radio communications between primary health centers and district hospitals, an ambulance system, and community cost-sharing schemes to cover the majority of health costs. An evaluation of the program was conducted in Kayes, a rural region with poor roads where 56% of the population lived more than 5 km from a primary health center. Within 2 years of implementation (2003–2006), the proportion of institutional births increased from 19% to 39%, and the proportion of obstetric emergencies treated increased from 0.9% to 1.9% of births; with a higher absolute number and proportion of cases of obstructed labor managed, from 107 (22.5% of obstetric emergencies) to 351 (38.4%). The number of cesarean deliveries increased from 112 (24% of obstetric emergencies) to 383 (42%). The overall case fatality among facility births was reduced by half (OR 0.48; 95% CI, 0.30–0.76); however, neonatal outcomes were not reported.

4.1.3. Costs of community referral and transport systems

Several programs report running costs of communications and transport systems, which may be substantial and often prohibitive in low-resource settings. The Uganda RESCUER program cost US $236 700 in the first pilot district and the annual maintenance was US $6000 per year [76], after scale up to the entire district, the maintenance costs were unsustainable. In Sierra Leone, the cost of start up in Bo District (population 53 000) was US $74 836, with annual operating and maintenance costs of US $5486. In Niger, an emergency referral system in a rural district included a 4-wheel drive ambulance and a solar-powered radio communication system for health centers (serving 66 500 rural inhabitants). The annual cost for replacement and recurrent costs was US $21 799 ($9120 for communication, $11675 for ambulance with $7625 generated by user fees), costing US $49 per successful transport [64,85].

4.1.4. Implications for community referral and transport systems

Community referral and transport schemes may increase rates of facility delivery, reduce referral time, improve access to emergency obstetric care for women with obstetric complications, and reduce maternal morbidity and case fatality. However, there was only 1 program report perinatal outcomes, and thus the overall GRADE level of evidence for intrapartum-related mortality is low (Table 3). Effective communication systems are key components of transport systems. Challenges include the high cost of vehicles and maintenance, establishing effective communication systems in remote settings, maintaining driver coverage, and sustainability within a resource-constrained health system. Recent data from Mali's National Maternity Referral System demonstrate that the key components of program success were the integration of the communication and transport system into the existing government health system and parallel efforts to reduce point of care costs. The evaluation of the impact of community and referral transport systems on perinatal outcomes should be prioritized in addition to evaluation of long-term program sustainability and cost-effectiveness. Additionally, new technologies, such as alternative transportation vehicles or mobile phones, are becoming available in low-income settings and need to be evaluated in the context of maternal-newborn health referral systems.

4.2. Prenatal risk screening

4.2.1. Background

A key recommendation of the 1987 Nairobi Safe Motherhood Conference was that women at "high obstetric risk" (defined as age younger than 20 years or older than 35 years, height less than 145 cm, parity 0 or more than 4, and poor obstetric history such as prior cesarean delivery, complication, or perinatal loss), deliver in a health facility [86]. In settings where the majority of births occur unassisted at home, the early identification of mothers at high risk for developing childbirth complications could help to ensure that they receive skilled care during delivery, to book for delivery at hospitals with CEmOC capacity, or to bring them closer to facilities before anticipated delivery via a maternity waiting home. However, several studies that demonstrated the poor predictive value of this risk-based approach led to the rejection of this strategy at the 1997 Sri Lanka Safe Motherhood Conference, to advocate for skilled birth attendance at all births.

In this section, we revisit the strategy of prenatal risk screening, to assess whether there may be a role for focused risk

screening using more predictive risk factors of lower prevalence. In a review of risk factors and complications, Lawn et al. [1] showed that intrapartum conditions are more predictive of perinatal mortality (risk range, 2–85) than prenatal conditions such as anemia (risk range, 2–14), which in turn are more predictive than conditions present before pregnancy such as age, height, etc (risk range, 1–5) [1]. The role of the community provider in triaging and identifying complications during labor is discussed by Darmstadt et al. [13]. Here, we focus on the strategy of risk screening by community-based workers that may be detected before the time of labor, including both maternal risk factors and pregnancy complications to bring high-risk mothers and babies closer to skilled birth care.

4.2.2. Evidence for prenatal risk screening

4.2.2.1. Predictive accuracy of prenatal risk screening. Studies have examined the predictive value of prenatal "risk scoring" for intrapartum stillbirths and first-day neonatal deaths. Bartlett et al. [87] found that for 342 births in rural Guatemala, identification of antepartum maternal characteristics (defined as primigravida, or multipara with previous obstetric problem, short birth interval or mortality of more than half of previous infants) predicted 100% of intrapartum stillbirths and first day neonatal deaths. However, 70% of all women were categorized as "at risk," with a positive predictive value of 9%, which was infeasible to address in a setting with limited obstetric care [87]. Different prenatal risk screening algorithms including maternal age, parity, height and/or obstetric history have been evaluated in Kasongo, Zaire [88], Zimbabwe[89], and Tanzania [90] with relatively low positive predictive values reported ranging from 42%–53%, largely because of low risk and high prevalence of these conditions. An analysis from Matlab, Bangladesh showed that while some prenatal risk factors may have a moderately high associated risk, many were very prevalent resulting in a low positive predictive value (e.g. 33% of the women were primigravida giving a positive predictive value of 33%). Furthermore, many newborns requiring resuscitation may not have any predicable risk factors [91,92].

However, early prenatal identification and management of low prevalence but high-risk pregnancy complications holds more promise and should not be discarded in the rush to leave risk screening behind. In Matlab, twin pregnancy, vaginal bleeding, and diastolic blood pressure greater than 90 mm Hg had a positive predictive value of 56%–67% for labor complications and each condition was present in only 1% of pregnancies [93]. In the MOMA study (Morbidite Maternelle en Afrique de l'Ouest)—a 7-center prospective population-based study in West Africa—noncephalic presentation, eclampsia, and vaginal bleeding after the eighth month of pregnancy were highly predictive and of low prevalence, and accounted for a significant attributable risk percentage for potentially viable late-term stillbirths (which were more likely to be intrapartum-related) [94].

4.2.2.2. Prenatal risk screening: Mortality impact. In a rural district in Shunyi, China [95], village midwives assigned risk scores to pregnant women during prenatal care, and those with a "high risk" score were prebooked at the county hospital for delivery; those with zero risk were required to deliver at home or in primary health facilities. The specifics of the risk scoring system are not described in detail. Physicians at the primary health facilities were taught to recognize early pregnancy complications (such as breech presentation) and manage or refer complicated cases (eclampsia) to the county hospital. Over the 4 years of the program, PMR was reduced 34% from 25.9 to 17.1 (RR 0.65; 95% CI, 0.44–0.98), intrapartum-related perinatal mortality was reduced from 4.1 per 1000 births in 1984 to 3.0 per 1000 births in 1986, and mortality associated with breech presentation from 3.6 per 1000 in 1982 to 1.7 per 1000 in 1986 (confidence intervals not provided). Furthermore, several maternity waiting homes have used risk stratification to determine eligibility for admission and these results are reported in the next section.

4.2.3. Implications for prenatal risk screening

In several early studies, risk screening algorithms had low positive predictive value, often including very prevalent conditions, thus resulting in frequent referrals of uncomplicated pregnancies. Few rigorous evaluations were undertaken and the overall quality of evidence for risk screening is very low (Table 3). In settings with limited resources, efficient allocation of available personnel requires screening tools that have a positive predictive value for complications and are easy to use [87,93]. Screening may be warranted for a few identifiable conditions that are of lower prevalence and associated with substantially elevated risk for perinatal and maternal death (OR >3). Candidate maternal risk factors include primiparous mothers under the age of 16 years [96], multiple pregnancy and malpresentation [94], and pregnancy complications for inclusion in an algorithmic approach would include vaginal bleeding in late pregnancy, hypertensive disorders, and severe anemia [94]. There is limited evidence, from low-quality observational studies, that triaging mothers with high obstetric risk for hospital delivery or to a maternity waiting home (see below) may be associated with improved perinatal outcomes. Additional research is needed to develop and validate improved focused risk screening algorithms or checklists for women in different settings and to evaluate the tool as an intervention in combination with access to obstetric care.

4.3. Maternity waiting homes

4.3.1. Background

A maternity waiting home is defined as a "residential facility located near a qualified medical facility where women defined as "high risk" can await their delivery and be transferred… shortly before delivery or earlier should a complication arise" [97]. As one part of a system of care, the maternity waiting home may provide a "geographical bridge," bringing the woman and her baby closer to emergency care. Although maternity waiting homes seem a simple, attractive, low-cost intervention, it must be emphasized that they are only a "link in a larger chain of comprehensive maternity care, all the components of which must be available… of sufficient quality... and linked with the (maternity) home" [97]. The key links in this chain are selection criteria for women and determination of gestation at referral; a system for identification and referral of women; skilled obstetric and newborn care available; and support of the community, especially to encourage women to use the home (adapted from WHO 1996) [97].

4.3.2. Evidence for maternity waiting homes

There are 6 cross-sectional studies that report perinatal outcomes among women admitted to maternity waiting homes, primarily from Africa. However, there are no population-based studies and few controlling for confounding risk factors affecting admission, therefore results are difficult to interpret. We also identified historical data from Cuba, and program reports from Mongolia, Bangladesh, and Peru, but perinatal outcome data were not available. Table 7 displays evidence from studies of waiting homes with impact data, and Panel 3 highlights further programmatic considerations.

Three studies from rural hospitals in Zimbabwe report perinatal mortality among infants of mothers admitted to maternity waiting homes. Chandramohan et al. [98] reported on a hospital-based cohort study in rural eastern Zimbabwe. The maternity waiting

Table 7
Evidence for the impact of maternity waiting homes (MWHs): Mortality effect.

Intervention/study (date order)	Setting	Percentage skilled attendance	Baseline mortality rates	Mortality Effect: Percentage relative reduction in mortality rate *(number of deaths in intervention or end line group)*; RR or OR (95% CI)					Investigator and year
				SBR	ENMR	PMR	NMR	MMR	
Evaluation of outcome for 151 women admitted to the MWH in 1987 compared with women admitted from home. No adjustment for baseline differences in maternal risk.	Ethiopia Rural central Nearest hospital about 2 days walk	NS	SBR 253 (direct admission group)	90% *(4)* RR 0.10 (0.04–0.28)	-	-	-	-	Poovan et al. [102] 1990
Evaluation of 822 singleton and 32 twin births at a rural hospital in 1987. 502 women stayed at the MWH, remainder admitted in labor from home. No adjustment for baseline differences in maternal risk.	Zimbabwe Rural	NS	PMR 24 (direct admission group)	56% *(9)* RR 0.44 (0.19-1.01)		51% *(17)* RR 0.49 (0.27–0.90)	46% *(8)* RR 0.54 (0.22–1.35)	-	Millard et al. [101] 1991
Evaluation of pre-existing MWH attached to rural district hospital. 1573 mothers using the MWH compared with 2915 women delivering at the hospital without using the MWH (twins, and preterm births excluded). Risk adjusted for maternal risk factors.	Zimbabwe Rural eastern district Population 208 000 Nearest hospital up to 140 km away	NS	PMR 32 (overall)		-	33% *(30)* aRR 0.66 (0.40–1.05) 40%[a] *(20)* aRR 0.53 (0.29–0.91)		-	Chandramohan et al. [98] 1995
Evaluation of MWH established in a comprehensive Maternal and Child Programme including improvement of prenatal care, increasing quality and utilization of hospital facilities (63% to 99%) from 1962–1989. 148 MWHs established, with 30% of all births admitted through MWH. Pregnant women admitted from rural areas or urban areas with risk factors.	Cuba	Cuba: 63% in 1962	MMR 118 PMR 15.7					75%[b]	Figa-Talamanca [103] 1996, Riveron et al. [105] 1989
Comparison of 280 women using MWHs with 790 women admitted from home. No adjustment for baseline differences in maternal risk.	Zimbabwe Rural	NS	PMR 29.8 (direct admission group)	48% *(3)* RR 0.52 (0.15–1.76)	NS *(4)* RR 1.56 (0.46–5.29)	16% *(7)* RR 0.84 (0.36–1.94)	-	-	Tumwine et al. [100] 1996
Comparison of risk status and pregnancy outcomes of all high-risk pregnant women admitted to MWHs vs those directly admitted to hospital during study period[c].	Rural eastern Zambia, Population about 60 000. Nearest hospital about 80 km	NS	PMR: 0.53 at MWH			No significant difference[d]		No significant difference[d]	Lonkhuijzen et al. [104] 2003
Six satellite maternity homes attached to tertiary care hospital in India. Comparison of pregnancy outcomes in mothers cared for in MWHs vs national average.	India		PMR 70 national			PMR 21 in MWH vs 90 national average			Guruvare [107] 2007

Abbreviations: SBR, Stillbirth Rate; ENMR, Early Neonatal Mortality rate; PMR, Perinatal Mortality Rate; NMR, Neonatal Mortality Rate; IPR-NMR, Intrapartum-related Neonatal Mortality Rate; NS, not significant.

[a] Adjusted RR for mothers with at least 1 prenatal risk factor.

[b] Historical reduction in MMR from 118 to 29 per 100 000 from 1962 to 1989.

[c] Women admitted to MWH were more likely to have prenatal risk factors, experience labor complications, and have assisted delivery (cesarean or vacuum). No significant difference in mean birth weight or proportion of low birth weight.

[d] PMR in waiting group 53 per 1000 vs 54 per 1000 in non-waiting group. Study may not have been adequately powered to detect mortality difference. Mothers in maternity waiting were at higher obstetric risk (nulliparity, history of cesarean delivery, breech or transverse position, or hypertension) than "non-waiters."

home provided free self-catering accommodation beside the hospital, and preferentially admitted women starting from 36 weeks of pregnancy with the following risk factors: parity 0 or more than 6; history of perinatal death or of previous operative delivery; medical risk factors; height less than 150 cm; noncephalic presentation; and multiple pregnancy. After adjusting for confounding risk factors, among women with antepartum risk factors, the PMR for women who were admitted from the maternity waiting home was half that of the nonwaiting mothers (21 vs 43 per 1000; RR of non-waiters vs waiters 1.9; 95% CI, 1.1–3.4); however, this was not significant for all mothers admitted. Although the cesarean delivery rate was the same for the women in the maternity waiting home as for those coming from home, the delay to cesarean delivery may be the key factor for reducing intrapartum-related stillbirths and neonatal deaths. A parallel paper from the same hospital assessed the screening criteria used and found a 78% sensitivity, 51% specificity, and 25% positive predictive value for dystocia [99], concluding that these screening criteria (Zimbabwean MOH policy) were of use in this setting. The remaining studies report perinatal outcomes of admissions to maternity waiting home versus direct admissions and are shown in Table 7, but none adjust for baseline characteristics of the mothers [98,100–107].

4.3.3. Cost of maternity waiting homes

Only one study, from Ethiopia, reported cost data [102]. The maternity waiting home was built in the style of a local house at a cost of US $1000 in 1976. The community supplied all the labor and most of

the materials. Annual overheads were estimated in 1990 at US $500 per year to cover maintenance, laundry, and a watchman. In Cuba, the Ministry of Health reported that the average cost of maternity waiting homes in 1988 was about US $10 per day for each pregnant woman [103]. The average user admission fee for a maternity waiting home in Nyanje, Zambia was 1000 Kwacha (US $3), including the cost of hospital birth [104].

4.3.4. Implications regarding maternity waiting homes

In certain settings, maternity waiting homes may have been associated with lower neonatal mortality and a similar if not greater effect on stillbirths (Table 7). However, the majority of evidence is based on low-quality observational studies from Africa that do not control for differences in mothers' underlying baseline risk and thus the quality of evidence is low (Table 3). For example, if maternity waiting homes admit higher-risk women, then the effectiveness may be underestimated, whereas if direct admissions to hospitals are at higher obstetric risk, then the effectiveness may be overestimated. Panel 3 highlights additional programmatic experiences with maternity waiting homes. There is a need to assess the impact and cost-effectiveness of maternity waiting homes, ideally in a randomized trial design and in various settings. Asian data on acceptability as well as effectiveness is a key gap.

5. Considerations

The present paper highlights several promising strategies to improve links between homes, communities, and health facilities by generating community demand for institutional obstetric care, and by extending the reach of health systems to bring pregnant women closer to skilled care.

Community mobilization interventions educate, motivate, and empower mothers and families to practice preventive care and to seek care for complications, and those with high stakeholder participation and ownership have resulted in significant positive effects on health outcomes. There is promising evidence that community mobilization, when successfully implemented, increases institutional births (2-fold for high intensity strategies in our meta-analysis) and is associated with a 36% reduction in early neonatal mortality, which is likely to reflect a reduction also in intrapartum-related neonatal deaths. In addition, behavior change interventions may reduce the risk of maternal infections during pregnancy and, hence, minimize the potential synergistic effect of infections with intrapartum hypoxia [108,109]. While cause-specific mortality data are required to better understand the mechanisms whereby community mobilization results in the reduction of perinatal deaths, the 2-fold increase in facility births is a probable pathway to mortality reduction. Community mobilization should be prioritized as a key strategy to link women in poor, rural communities with skilled obstetric care.

How can community mobilization be implemented and brought to scale? Not all methods of mobilization are equal or applicable in every context. Programs with increasing community participation and ownership have had greater impact particularly with one-on-one peer counseling through home visits [22,24,25]. Modifying behaviors may vary substantially across cultures and settings, and requires local formative research [22]. Program considerations are shown in Table 8. The community action cycle methodology may empower communities and be a mobilization tool that can be readily adapted for different cultures, as participatory groups are led by facilitators from within the community, and it has been successfully implemented in Latin America and South Asia [21,24]. Engaging a wide range of key newborn stakeholders, from fathers to faith healers, was instrumental in invoking behavior change in Shivgarh [22]. Furthermore, mobilization activities can be integrated into national newborn health strategies and NGOs may partner with governments to deliver these interventions, particularly in poor, remote areas. NGOs were instrumental in the national scale up of the Warmi project in Bolivia [30], as well as the national ReproSalud program in Peru [110,111].

There is low-quality evidence that community-level financing, financial incentives, and referral transport systems may increase rates of facility delivery, access to CEmOC, and reduce maternal case fatality; however, data on perinatal outcomes are lacking. Arranging for transport and hospital fees are essential components of birth planning packages, and the impact of the individual components is reflected to some degree in the mortality reduction observed in mobilization packages. Furthermore, there are preliminary data from Gujarat that voucher programs may be associated with reductions in neonatal and maternal mortality among beneficiaries. Additional research is needed to determine the impact of these programs on perinatal and intrapartum-related mortality, and access to emergency obstetric care, in addition to operational research on sustainability and cost-effectiveness, before recommending wide-scale implementation. Specific considerations for financing programs are highlighted in Table 8. To bring these programs to scale, ensure sustainability and broader impact, government support is key, particularly for transportation and health finance infrastructure.

Since 1997, the "Risk Approach" to care during pregnancy has been widely criticized and abandoned by the Safe Motherhood Programs [86,112,113]. Several early prenatal risk screening algorithms utilized prevalent, low-risk characteristics, with poor positive predictive value resulting in high rates of referral. However, certain risk factors and pregnancy complications that were not previously used in these checklists, such as multiple pregnancy, malpresentation, hypertensive disease, and late vaginal bleeding are associated with substantially increased risk of intrapartum-related hypoxia in addition to maternal mortality; have a high positive predictive value; are relatively infrequent; and could be identified during routine prenatal care. Risk screening linked with facility births in rural China or with maternity waiting homes has been associated with reductions of intrapartum-related and perinatal mortality [95,98,101]. The quality of the evidence is low, and thus, insufficient to recommend the implementation of risk screening. However, evaluating risk screening algorithms that incorporate risk factors with high attributable risk and lower prevalence deserves further attention.

While maternity waiting homes have been a cornerstone of many, particularly African, safe motherhood programs, the limited observational data are presently insufficient to recommend their widespread use. While it is plausible that this intervention, particularly in regions with low access to facilities, would reduce the burden of intrapartum-related hypoxic events, further evaluation is needed to assess the impact, cost-effectiveness, and cultural acceptability of maternity waiting homes in other regions of the world.

The ultimate success of demand-based strategies requires parallel supply-side efforts to reduce intrapartum-related mortality. Health system strengthening and improving the quality and quantity of obstetric care must accompany or even precede demand-side strategies [114]. Supply-side strategies are discussed further in the second (intrapartum care) and sixth (perinatal audit) papers in this Supplement [14,15]. In Mauritania, implementation of the national high-risk obstetric insurance scheme and maternal transport system resulted in a substantial increase in institutional births, but also in a subsequent deterioration in the quality of obstetric care [48]. Skilled birth attendants, without timely access to CEmOC, may not directly improve maternal-perinatal outcomes [115], and conversely, in certain settings, unskilled birth attendants may safely assist domiciliary births with the proper recognition and referral for CEmOC within the health system [114,116]. In Pakistan, this model of strengthening primary health care through a community-based

Table 8
Implementation considerations for programs.

Increasing community demand for obstetric care	
Community mobilization	• Formative research to identify key newborn stakeholders, opinion leaders (both traditional, formal, and informal sector), excluded/marginalized groups (usually at most risk), resources, map barriers, co-set goals and determine plan of action and measures of success. • Identify community institutions/community-based organizations to institutionalize/integrate the community mobilization processes and ensure sustainability. • Determining level of responsibilities, supervision, and funding from different stakeholders: community, NGOs, local and national government. • Careful selection of community mobilizers and application of human resource management including training, supportive supervision, evidence-based appraisal, and coordination with other cadre of workers. • Encourage greater level of community ownership, facilitated by community mobilizers. • Appropriate mix of community mobilization methods for optimal impact. • Alignment and integration between communication strategies and targeted home visitation. • Identify inter-sectoral opportunities for synergizing health mobilization activities (agriculture extension worker, self-help groups).
Financial strategies to increase demand for obstetric care	• Source of funds (government, donor agency) and implications for long-term sustainability, cost-effectiveness. • Purpose of funds eg transport costs and emergency obstetric or neonatal care. • Groups targeted to receive conditional cash transfers or vouchers. • Determining level of insurance premium, affordability to poor, or if loan then level of interest charged, terms of repayment and estimated success of repayment. • Determining size of the conditional cash transfer needed to stimulate demand. • Monitoring of fund use and administrative costs of funds, risk for black market selling of vouchers.
Bringing pregnant women closer to the formal health system	
Communication and transport systems	• Existing road and transportation infrastructure. • Cultural beliefs regarding transport in labor. • Use of information communication technology for rapid communication notification of need of emergency transport (cell phone, text message, walkie-talkies, two way radio). • High expense of vehicle and parts for all-terrain, 4-wheel drive vehicles, difficulty obtaining parts for repair. • How to modify vehicles to transport reclining women in labor, +/- family member. • Drivers: how to cover 24-7 (on call), cost of drivers, willingness to transport women with obstetric emergency. • Recurrent costs of fuel and repair. • Monitoring costs.
Risk screening	• Capacity of health system: Are facilities staffed and equipped to handle a substantial increase in referrals, particularly if risk screening algorithms may have poor positive predictive value? • Which lower prevalence prenatal risk factors accurately predict intrapartum complications, and can these be detected before birth (e.g. twins, breech)? • Level of provider with skills to conduct risk screening, likelihood that family will comply.
Maternity waiting homes	• Determining criteria for admission – risk factors, distance from health facility. • Community-cultural beliefs regarding place of birth, participants involved, and need for confinement; formative research on acceptability in different settings and cultures. • Strategies to promote community development and involvement in maternity waiting homes. • Costs of staffing and overhead. • Determining appropriate costs charged to “waiters” that is affordable and not barrier to use.

approach with obstetric service availability at first and second level health facilities has been estimated to be capable of averting 20% of intrapartum-related neonatal deaths at an achievable coverage level [117].

5.1. Data tracking, challenges, and research gaps

The effectiveness of community mobilization in increasing skilled care and reducing perinatal mortality is promising, however the impact on intrapartum-related mortality, while plausible, remains to be established. While cause-specific mortality may soon be available from several trials, verbal autopsy ascertainment of intrapartum-related neonatal deaths in community settings may be nonspecific, particularly with multiple comorbidities, and results vary substantially depending on case definitions and hierarchies used to assign cause of death [118–120]. Improved and validated methods are required to determine the burden of intrapartum-related mortality, including intrapartum stillbirths, in community settings to evaluate the impact of interventions and track the progress of programs.

Furthermore, when measuring the effectiveness of programs to link pregnant mothers and skilled obstetric care, the health outcomes of the mother and infant are inextricably linked and there need to be conscious efforts among researchers and programmers to monitor and report both. For many of the studies of maternal transport and referral, perinatal outcomes were not reported, and may be more responsive to reductions in transport time and statistically easier to detect. For evaluating community mobilization, met obstetric need would be a valuable indicator of care reaching those at high risk for intrapartum hypoxia. Furthermore, process indicators to track program effectiveness are inconsistently reported by investigators (for example time to reach referral hospital) [83]. Finally, perinatal audit has been used in Tanzania to determine the contribution of the 3 delays to perinatal death, and may be an indirect method to track program progress [11].

6. Conclusion

There is increasing evidence that strategies to link mothers to skilled facility-based obstetric care may reduce perinatal mortality, and presumably affect intrapartum-related deaths. Our meta-analysis shows that high intensity, participatory community mobilization programs resulted in a 2-fold increase in institutional births and prevented 1 out of 3 early neonatal deaths. There is limited program experience that financial strategies, community referral and transport systems, and cell phone technologies increase use of skilled obstetric care and may reduce maternal case fatality. These strategies are promising and require further evaluation of their impact on perinatal outcomes, cost-effectiveness, and sustainability. Maternity waiting homes may also have potential, although well-designed evaluations are needed to evaluate their effect on perinatal-maternal outcomes and acceptability in different regions. Risk screening, while previously

rejected, deserves re-evaluation to determine the potential validity and impact of refined algorithms. New questions need to be asked of these "old" strategies.

Creative demand-side strategies appear to increase use of skilled childbirth care for the poor, and have the potential to contribute to reducing the 2 million intrapartum-related stillbirths and neonatal deaths each year. Increasing investment in the supply side of obstetric care should be partnered with investment and more rigorous evaluation of demand-side strategies to ensure mothers and newborns can and do link with the care they need, especially at the time of birth.

7. Conflict of interest

All authors declare that they have no conflicts of interest to disclose.

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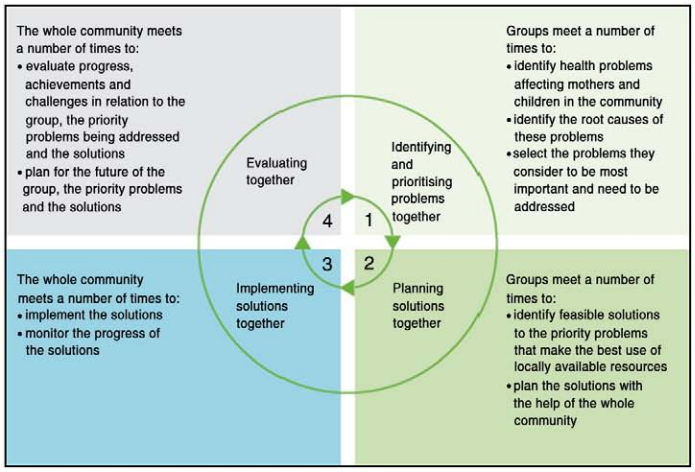
Panel 1. Strategies to mobilize communities to seek skilled birth care

Women's Groups with Community Action Cycle

The community action cycle was originally developed in the Warmi project and involves 4 main processes [23]: (1) identification and prioritization of key maternal and newborn health problems in the local community; (2) developing a formal action plan; (3) implementation of solutions as a community; and (4) evaluation of the progress of the program, assessing challenges and solutions.

In the Warmi [23] and Makwanpur projects [24,114,127], the community-designed interventions included a wide range of activities from creation of community funds for transport, acquisition of stretchers, and education regarding danger signs in pregnancy with interactive picture card games and role playing.



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· Community Action Cycle: Figure reprinted with permission granted by Lancet.
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Community groups with socio-contextualized behavior change messages

The Saksham study conducted extensive formative research regarding childbirth practices and engaged stakeholders at multiple levels, from household members, village leaders, priests, teachers, traditional birth attendants, other practitioners, and community volunteers [22]. Newborn care interventions were tailored to the local traditions and customs at birth, and disseminated at community group meetings and one-on-one community health worker visits. The Skilled Care Initiative in Burkino Faso also used community groups to map local health beliefs, engage local traditional and religious leaders, and implement activities using existing social platforms [33].

Community education meetings

Many programs use community group meetings to educate women and families about prenatal care, danger signs during pregnancy, signs and symptoms to refer, essential newborn care, and postnatal care. Educational strategies may include lecturing, flip charts, role playing, and video. Group leaders may include CHWs, TBAs, key community members, or program staff.

Village health committees

Village health committees may organize community members to develop actions to address key issues, such as the development and administration of emergency funds and transport driver systems. Members may include key stakeholders, and those with specific expertise, such as members of the local bank to assist administration of local funds [38]l.

Community campaigns

Social marketing campaigns have been used to generate awareness of maternal and newborn health issues, including a wide range of activities from public concerts, radio campaigns, video, and TV commercials. The Prevention of Maternal Mortality Group in Nigeria has promoted childbirth health awareness, particularly focusing on male decision makers and used a range of media such as puppets and a video drama of a maternal death [28,64,128].

Photograph from Shivgarh, Uttar Pradesh, India, reprinted with permission granted by Bill & Melinda Gates Foundation/Jeffrey Spector.

Panel 2. Community referral, transport schemes, and communication technologies

For the 60 million women who deliver at home each year, distance and transport are major barriers to seeking skilled obstetric care. In certain regions of the world, such as Nepal, almost 85% of the population does not live within 2 km of an all-weather road.

Communication Strategies

The use of one-way or two-way radios, telephones, cell phones, flagging mechanisms along common travel routes, computers-internet, satellite phones, and global positioning systems may help families notify drivers of the need for transportation, and improve the communication across all levels of care, from the community birth attendant, to first level and referral facilities.

Vehicles

Innovative strategies have been developed to transport women in labor in low-resource settings and rugged terrain. The capacity to accommodate the recumbent patient is preferred, and methods have included stretcher schemes, tractors, ox carts, bicycle or motor cycle ambulances, motor boats or canoes, trucks, 4-wheel drive vehicles, and formal ambulances [24,83,124,129,130].

Driver coverage

24-7 coverage is needed as obstetric emergencies may occur at any time of day. Solutions have included on-call rotations for village drivers; pre-negotiated agreements with existing bus, truck, or taxi services; use of transport unions; and flagging systems along ordinary trucking and travel routes [50].

A Case Study: Motorcycle ambulances in Malawi [83]

In the rural district of Mangochi, Malawi, motorcycle ambulances were stationed at 3 primary health centers to facilitate transfer of patients with obstetric emergencies to the district hospital. The health centers were on average 70 km from the referral hospital, and connected by dirt roads difficult to handle during the rainy season. The use of a motorcycle ambulance was estimated to reduce the referral time by 2–4.5 hours (35%–76%). The purchase price of the motorcycle ambulance was US $1965, approximately 19 times cheaper than an automobile ambulance, and the annual operating costs were US $508 annually, approximately 24 times cheaper than a car ambulance.

Challenges to implementation, sustainability, and scale up

- High costs of all-terrain vehicles.
- Frequent breakdown and high maintenance costs of repairs, parts, fuel; require fund for recurring costs.
- Challenge to provide in low population density.
- Need for improvement in basic road infrastructure.
- Require communication from family in need to transport mechanisms.

Panel 3. Maternity waiting homes

Brief history

Since the beginning of the 20th century, waiting homes have existed in Europe, Canada, and the USA to serve women from remote communities. Maternity waiting homes (MWHs) may be instigated from within healthcare facilities or from the community, such as Casa Materna [98], the result of an initiative by the Nicaraguan Women's Organization [97]. Others result from governmental initiatives such as in Cuba.

Range of services

Maternity waiting homes may provide prenatal care and birth preparedness counseling for the waiting women, informing them about danger signs for themselves and their newborn, and preparing them to breastfeed and provide other aspects of basic newborn care. Other homes include care for "high-risk" women and newborns for several days after delivery, helping to establish breastfeeding and identify early complications [97].

Considerations for program implementation

Selection of women for admission: Medical risk factors may be considerations for admission (nulliparity, multiple pregnancy) or a broader social definition including poverty and distance from a facility. Such criteria for selection, including gestation at referral (eg 2–4 weeks before), must be set locally, depending on transport systems and cultural acceptability, as well as medical risk. The role of TBAs in referring women to maternity waiting homes and their continued involvement within the home is not reported in the literature, but would be a consideration in settings where TBAs conduct significant numbers of births.

Cultural acceptability is crucial to the utilization of maternity waiting homes. One maternity waiting home in Ghana was built next to the hospital mortuary and was virtually unused [131]. MWHs have been piloted in Africa and Latin America, whereas there is little experience in South Asia, where traditions of privacy and confinement during pregnancy and labor may affect use.

Challenges to implementation:

- Length of waiting time may be associated with substantial opportunity costs as this is often 3–4 weeks. Mothers require caretakers and food for other children and family members. There are case reports of mothers attempting to induce labor with herbal teas to reduce waiting time [97].
- Mothers must bring a relative to attend to her during her stay because of staffing shortages.
- MHWs often lack kitchens and it is difficult to support a mother's normal diet.

· Boat picture: photograph reprinted with permission granted by Indu Alhuwhalia.
· Bike picture: photograph reprinted with permission granted by Save the Children/Michael Bisceglie. Mozambique.
· Stretcher picture: photograph reprinted with permission granted by Luwei Pearson.

- Lack basic supplies and materials, such as sheets and blankets.
- Need for strong government support: In Mongolia and Mozambique, the lack of political and financial support were key contributors to the deterioration and underutilization of maternity waiting homes.

Case example: Cuba

In 1989, 30% of Cuban women who delivered had stayed in a waiting home [97]. While in the home, women rested, were given special food, and community groups helped to take care of other children. Twice-weekly prenatal clinics were carried out and 24-hour care was available for emergencies. Building and maintenance of the homes were community tasks, and agricultural cooperatives donated food. Careful evaluation of the impact of these homes has not been carried out, but the government credits maternity waiting homes as an important factor in reducing MMR from 118 to 29 per 100 000 between 1962 and 1989, as well as in facilitating transition to facility-based delivery. Now, 99% of births occur in hospital and 30% follow admission to a maternity waiting home [103]. In Cuba, successful expansion of the maternity waiting home program may have been aided by effective partnership with communities, as community-based organizations contributed to maintenance, food, and care [97].

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INTRAPARTUM-RELATED DEATHS: EVIDENCE FOR ACTION 5

60 million non-facility births: Who can deliver in community settings to reduce intrapartum-related deaths?

Gary L. Darmstadt [a,b,*], Anne CC Lee [a], Simon Cousens [c], Lynn Sibley [d], Zulfiqar A. Bhutta [e], France Donnay [b], Dave Osrin [f], Abhay Bang [g], Vishwajeet Kumar [a], Steven N. Wall [h], Abdullah Baqui [a], Joy E. Lawn [h]

[a] Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA
[b] Current address: Integrated Health Solutions Development, Global Health Program, Bill & Melinda Gates Foundation, Seattle, WA, USA
[c] London School of Hygiene and Tropical Medicine, London, UK
[d] Department of Family and Community Nursing, Nell Hodgson Woodruff School of Nursing; Hubert Department of Global Health, Rollins School of Public Health, Emory University, Atlanta, GA, USA
[e] Division of Women and Child Health, The Aga Khan University, Karachi, Pakistan
[f] UCL Centre for International Health and Development, Institute for Child Health, London, UK
[g] Society for Education, Action and Research in Community Health, Gadchiroli, Maharashtra, India
[h] Saving Newborn Lives/Save the Children-US, Washington, DC, USA and Capetown, South Africa

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ABSTRACT

Background: For the world's 60 million non-facility births, addressing who is currently attending these births and what effect they have on birth outcomes is a key starting point toward improving care during childbirth. *Objective:* We present a systematic review of evidence for the effect of community-based cadres—community-based skilled birth attendants (SBAs), trained traditional birth attendants (TBAs), and community health workers (CHWs)—in improving perinatal and intrapartum-related outcomes. *Results:* The evidence for providing skilled birth attendance in the community is low quality, consisting of primarily before-and-after and quasi-experimental studies, with a pooled 12% reduction in all cause perinatal mortality (PMR) and a 22%–47% reduction in intrapartum-related neonatal mortality (IPR-NMR). Low/moderate quality evidence suggests that TBA training may improve linkages with facilities and improve perinatal outcomes. A randomized controlled trial (RCT) of TBA training showed a 30% reduction in PMR, and a meta-analysis demonstrated an 11% reduction in IPR-NMR. There is moderate evidence that CHWs have a positive impact on perinatal-neonatal outcomes. Meta-analysis of CHW packages (2 cluster randomized controlled trials, 2 quasi-experimental studies) showed a 28% reduction in PMR and a 36% reduction in early neonatal mortality rate; one quasi-experimental study showed a 42% reduction in IPR-NMR. *Conclusion:* Skilled childbirth care is recommended for all pregnant women, and community strategies need to be linked to prompt, high-quality emergency obstetric care. CHWs may play a promising role in providing pregnancy and childbirth care, mobilizing communities, and improving perinatal outcomes in low-income settings. While the role of the TBA is still controversial, strategies emphasizing partnerships with the health system should be further considered. Innovative community-based strategies combined with health systems strengthening may improve childbirth care for the rural poor, help reduce gross inequities in maternal and newborn survival and stillbirth rates, and provide an effective transition to higher coverage for facility births.
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1. Introduction

Every year an estimated 60 million women give birth outside health facilities, mainly at home, and 52 million births occur without a skilled birth attendant (SBA) [1]. Access to skilled care at birth and especially to emergency obstetric care (EmOC) is lowest for the poor, who carry the burden of maternal and neonatal morbidity and mortality related to complications of childbirth. Globally, the lowest rates of skilled birth attendance are in South Asia and Sub-Saharan Africa, and progress to achieving universal skilled attendance is staggeringly slow, particularly in Sub-Saharan Africa, where the average increase in skilled birth attendance is rising by only about 0.2% per year [2]. At this rate, by the Millennium Development Goal (MDG) target date of 2015, still fewer than half of births in the region will occur with an SBA [3]. The long-term strategy to reduce mortality and morbidity related to intrapartum hypoxia (previously loosely termed "birth asphyxia") requires strengthening of weak health systems to provide universal skilled birth attendance and improving the quality and equity of skilled obstetric care, as discussed in prior papers in this Supplement [4–6]. In this series we follow the

* Corresponding author. Integrated Health Solutions Development, Global Health Program, Bill & Melinda Gates Foundation, PO Box 23350, Seattle, WA 98102, USA.
E-mail address: Gary.darmstadt@gatesfoundation.org (G.L. Darmstadt).

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recommended shift in terminology based on a series of international consensus statements to use the terms "intrapartum-related deaths" for cause of death and "neonatal encephalopathy" for the acute complications manifesting soon after birth [2,7,8]. One-hundred newborns die every hour from intrapartum-related events, however, many of which are preventable. Thus, there is an urgent need for effective solutions that will overcome implementation bottlenecks to reach those most in need and build toward long-term solutions.

For the 60 million non-facility births, a key starting point is identifying who is currently attending these births and the competence, confidence, and connectedness to the health system that they possess. In fact, many home births occur without any attendant or with a family member; for example, in Sub-Saharan Africa approximately 30% of births are unattended or only attended by family members (Fig. 1). For settings where home births are attended by community members, the existing cadres vary by region, mortality setting, culture, and existing health system infrastructure [3,9]. They may also differ widely in their characteristics, training, and skill set to intervene for intrapartum-related outcomes (Table 1). Their principal role in the prevention of intrapartum injury to the fetus and newborn is in primary and secondary prevention, and there may additionally be a role for referral in tertiary prevention [2]. Community-based SBAs, including midwives, auxiliary nurse midwives, or physicians may be common in intermediate mortality settings where there are increased human resources and capacity for training, such as in Indonesia where the government systematically scaled up community midwives [10], or where private providers have a relatively strong presence in the provision of primary care in peripheral health clinics, as in South Asia (Fig. 1). In higher mortality settings, home births are frequently attended by traditional birth attendants (TBAs) who lack formal medical training, but have been care-givers for generations of pregnant women. In Sub-Saharan Africa and South Asia, an average of 23%–40% of births are attended by TBAs [1] (Fig. 1), and approximately half of the TBAs were formally trained in modern medical childbirth techniques with a focus on clean delivery. Community health workers (CHWs) and government extension workers are a final cadre of providers who may have a higher level of education than TBAs, provide prenatal care, health promotion, attend births, and interface with the formal health system.

Engaging community-based cadres to advocate for and/or directly provide essential obstetric-newborn care is controversial [11,12], but may have both advantages and disadvantages that need to be considered. Community-based health providers live ideally within the community in which they work, understand local culture and customs surrounding pregnancy and childbirth, and are likely to be well respected by community-members, thus increasing the acceptability and uptake of interventions and galvanizing behavior change [13]. On the other hand, community-based providers may be firmly entrenched in traditional customs that may either be potentially harmful to the newborn or the mother, or delay the receipt of appropriate care [14].

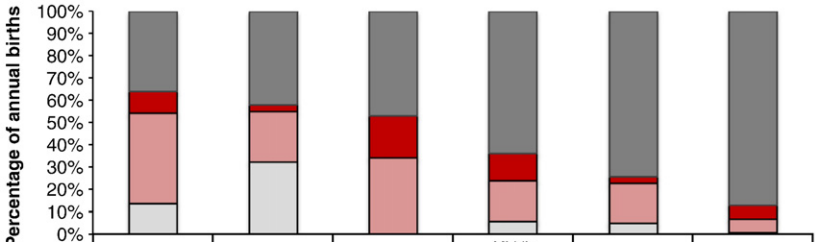
1.1. Objectives

The present paper is the fifth in a series on intrapartum-related deaths. The main objective of this paper is to review the evidence for the effect of care by different community cadres during pregnancy and childbirth. In a previous paper in this series, we evaluated community-based strategies to increase demand for skilled childbirth care at health facilities [6] and neonatal resuscitation provided by community-providers [5]. In the present paper, we focus on the effectiveness of each cadre for the primary and secondary prevention of intrapartum-hypoxic injury. As described in the first paper in this series [2], we use GRADE criteria to assess the quality of evidence for the mortality-effect of these community-based providers on outcomes related to acute intrapartum hypoxia, including stillbirth rate (SBR), perinatal mortality rate (PMR), intrapartum-related neonatal mortality rate (IPR-NMR), early neonatal mortality rate (ENMR), and neonatal mortality rate (NMR). We also sought evidence on intermediate outcomes such as care seeking, skilled birth attendance, facility-based delivery rates, and cost and cost-effectiveness.

2. Methods

Details of the searches undertaken and the selection criteria for inclusion are described in the first paper in this series [2]. Searches of the following databases of the medical literature were conducted: PubMed, Popline, EMBASE, LILACS, IMEM, African Index Medicus, Cochrane, and World Health Organization (WHO) documents. The initial search was conducted in November 2002, and was updated May 2009. Keyword searches relevant for this paper included "birth asphyxia/asphyxia neonatorum," "hypoxic ischaemic encephalopathy/hypoxic ischemic encephalopathy," "neonatal encephalopathy," or "neonatal mortality," and a combination of "TBA/trained TBA/traditional birth attendant," "community health worker/village health workers/community health aides," "birthing center," "skilled birth attendant/skilled attendant," or "community midwives OR midwifery."

Modified GRADE criteria were used to evaluate the quality of the evidence [15] (strong, moderate, low, or very low) and give a



	South Asia (5 countries)	Sub-Saharan Africa (36 countries)	East Asia/Pacific* (3 countries)	Middle East/North Africa* (3 countries)	Latin America/the Caribbean* (6 countries)	CEE/CIS* (2 countries)
Facility births	36%	42%	47%	64%	74%	87%
Skilled Birth Attendant	10%	3%	19%	12%	3%	6%
Traditional Birth Attendant**	40%	23%	34%	18%	18%	6%
Other or no assistance	14%	32%	0%	6%	5%	1%

Fig. 1. Coverage of care for facility and home births according to birth attendant. Source: New analysis based on data from UNICEF [1] 2009 and Demographic Health Surveys (2000–2007). Percentages are the weighted averages for countries with data on facility birth, skilled birth attendance, and TBA attendance at deliveries. Facility births presume skilled attendant at birth. Coverage of skilled birth attendance outside of facility is the difference between skilled attendant and facility birth coverage. * The regional data shown is higher than actual regional averages for home births because we are using weighted averages for countries with information by country from DHS, which are not administered in all countries. Thus, this information is not representative of these regions. ** Traditional birth attendant includes both trained and untrained TBAs for 4 countries that have DHS data on trained TBAs: Ghana, Niger, Tanzania, and Zimbabwe.

Table 1
Cadres of workers attending births in domiciliary settings.

Type of provider	Characteristics	Training	Skills
Skilled birth attendant (SBA)	An accredited health professional - such as a midwife, doctor or nurse. Live in and part of community served.	Midwifery skills with classroom and labor ward experience and competency-based examinations.	Manage normal labor and delivery, perform essential interventions, start treatment and supervise the referral for interventions that are beyond their competence [101] Skills for SBAs undertaking home births (WHO-SEARO) [102] • Active management of third stage of labor • IV infusion (antibiotics, anticonvulsants, oxytocics) • Management of postpartum hemorrhage • Manage convulsions in pre-eclampsia or eclampsia • Basic neonatal resuscitation • Recognize incomplete evacuation of placenta, cervical tears, uterine rupture, bleeding, obstructed labor – stabilize and refer
Trained traditional birth attendant (TBA)	Community members who provide childbirth care; may range from family member attending only occasional births to women with considerable expertise attending 20+ births/year. Not usually salaried, often paid in-kind. Typically not civil servants or employed by Ministry of Health.	Community-acquired skills, and variable add-on training usually limited in time. Training may vary from a few days of non-focused didactic teaching to a carefully planned and targeted training scheme employing a competency-based approach and ongoing supervision and support. Factors likely to lead to success in training TBAs [58,82,83] include: careful selection criteria TBAs (for example, a consistent work load such as ≥20 births per year) and of trainers; careful design of training to address local practices and include practical procedures; incorporation of ongoing supervision; attention to relations with formal health system providers; and systematic approach to sustainable remuneration and social rewards.	• Social and cultural support • Clean delivery if trained • Not trained to manage obstetric complications but some evidence for recognition and referral for obstetric complications (highly debated)
Community health worker (CHW) (*Village health worker, Village health guide, Health extension worker, Community health volunteer*)	CHWs are selected, trained and work in the communities from which they come. May or may not be formally employed; health extension workers are government cadres.	Varies between countries. Initial training may vary from 12 days to 1 month, with ongoing refreshers and supervision.	• Link between community and health system • Preventive health measures • Birth preparedness • Clean delivery • Identification and treatment of minor illnesses (including IM injection with antibiotics, basic neonatal resuscitation with bag and mask)

recommendation for programmatic application (strong, weak, conditional), as detailed in an earlier paper in this series [2]. We use an adaptation of GRADE developed by the Child Health Epidemiology Reference Group (CHERG) specifically for low- and middle-income settings [16]. As our specific interest is for intrapartum-related ("birth asphyxia") outcomes, this is a particular constraint as cause-specific data are limited.

Mortality reduction is reported as relative reduction unless otherwise reported. We conducted meta-analyses of studies evaluating packages of interventions provided by SBAs and CHWs using the Mantel-Haenszel (MH) pooled relative risk (RR) and corresponding 95% confidence interval (CI). When significant heterogeneity was detected ($P<0.10$), a random effects model was used to estimate the RR and CI. Studies were included if they reported the outcomes of interest (IPR-NMR, PMR, or ENMR). Meta-analysis of all-cause NMR was not conducted as most packages addressed multiple neonatal conditions, and the other mortality indicators may more specifically reflect the burden of intrapartum-related events in the absence of cause-specific mortality data. Higher quality studies were included and considered for pooling risk estimates if the study design was a randomized controlled trial (RCT) or quasi-experimental study. In the absence of high-quality studies, observational studies of lower quality were considered for meta-analysis if the intervention, study design, and the outcomes of interest were comparable. However, historic or ecologic data were excluded. All analyses were conducted using STATA 10.0 statistical software (StataCorp, College Station, TX, USA).

3. Results for community-based strategies

3.1. Increasing skilled childbirth care in the community

3.1.1. Background

SBAs are defined by the United Nations as "medically qualified providers with midwifery skills (midwife, nurse or doctor) who have been trained to proficiency in the skills necessary to manage normal deliveries and diagnose, manage, or refer obstetric complications, ideally who live in, and are part of, the community they serve. They must be able to manage normal labor and delivery, perform essential interventions, start treatment and supervise the referral of mother and baby for interventions that are beyond their competence or not possible in a particular setting" [17] (Table 1). The core skills of the SBA include monitoring the progress of labor, augmenting labor, conducting normal delivery with aseptic technique, actively managing the third stage of labor, and newborn resuscitation [12]. Furthermore, WHO recommends that in remote areas with poor access to a health facility with capacity for surgical intervention, the SBA should be able to perform vacuum or forceps extraction, vacuum aspiration for incomplete abortion, and symphysiotomy for obstructed labor [12].

SBAs may provide domiciliary childbirth care in the home or in community birthing centers. Community birthing centers may range from a simple "maternity home" to a rural hospital that is staffed 24 hours a day by an SBA who provides basic emergency obstetric care (includes BEmOC, caesarean delivery and blood transfusion). This

strategy may or may not provide transport to comprehensive EmOC (CEmOC) (including cesarean delivery and blood transfusion) [18].

3.1.2. Evidence for skilled childbirth care in the community

Given that the SBA directly provides clinical care at the time of labor and delivery, s/he by definition performs procedures for both primary prevention (management of intrapartum care and monitoring or use of the partograph, capacity to perform basic interventions in the home, and referral of complicated cases to EmOC) and secondary prevention (assessment and management of the non-breathing baby, e.g. neonatal resuscitation). Table 2 summarizes the evidence for the effect of SBAs on intermediate outcomes and Table 3 outlines the effect on mortality.

3.1.2.1. Training, skills, and competency of community-based SBAs. While there is a core skill set for SBAs defined by WHO, the training and competency of SBAs in using these core skills varies substantially between settings and countries [19]. In Nepal and Bangladesh, SBAs were trained for as little as 6 months, yet have been found to have acceptable knowledge and competency [20,21] (Table 2). Studies in Zambia, Indonesia, and Vietnam have demonstrated improvements in knowledge and skills of midwives trained in essential newborn care and obstetric life-saving skills [22–25]. However, an assessment of SBAs in Benin, Rwanda, Kenya, Ecuador, and Jamaica demonstrated poor retention of knowledge and skill competency; only half of SBAs displayed competency to deal with specific obstetric and neonatal complications [19]. Competency and skill retention of providers are major concerns for SBAs, particularly those practicing independently in the community and conducting advanced procedures, emphasizing the need for adequate supervision and monitoring of competency.

Monitoring the progress of labor is a core skill for SBAs, and the partogram has been used effectively by midwives in community settings and birthing centers [26]. In North Sumatera Province, Indonesia [27], training midwives in use of the revised WHO partograph resulted in a lower proportion of labor augmentation (adjusted odds ratio [aOR] 0.21; 95% CI, 0.12–0.36), obstructed labor (aOR 0.38; 95% CI, 0.15–0.96), higher rates of referral for crossing the partograph alert line (aOR 4.23; 95% CI, 2.1–8.1), and lower proportions of infants with Apgar scores of less than 7 at 1 minute (aOR 0.45; 95% CI, 0.26–0.79). However, there was no significant improvement in 5-minute Apgar scores or need for neonatal resuscitation. The use of the partograph in facility settings is discussed further in paper 2 of this series [4].

3.1.2.2. Community midwives: Intrapartum-related mortality effect. In Matlab, Bangladesh, a community-based maternity care program was instituted in 1987 in an intervention area, to increase coverage of skilled midwives for home births to monitor the progress of labor, administer medications for pre-eclampsia, and manage malpresentation (Table 3) [28,29]. The intervention area also had a basic obstetric care facility, and referral-transport mechanisms (speedboat and ambulance) to transfer mothers with labor complications. The comparison area received routine government services. Obstetric mortality was reported to be 65% lower in the intervention area compared with the government-serviced comparison area [28]. However, subsequent re-examination of the data revealed that the maternity mortality rate (MMR) had declined to a similar level without the intervention in the southern comparison area of Matlab, possibly due to increasing access to EmOC through other sources, and better family planning [30]. During the period of SBA-assisted home births (1987–1996), in the intervention areas, 27% of women gave birth with a SBA compared with 4% in the comparison area [29], and the crude SBR and IPR-NMR were significantly lower in the community midwife-served versus comparison areas (crude OR for SBR 0.85; 95% CI, 0.76–0.94; crude OR for IPR-NMR 0.78; 95% CI, 0.64–0.95). Beginning in 1996, there was a gradual shift from skilled home births to facility-based care in all of Matlab [31].

Indonesia is a well-known example of a nationwide scale up of community-based midwifery services since the late 1980s. The national MMR declined from 400 (in 1989) to 300 per 100 000 births by 2003, and all-cause neonatal mortality was reduced from 32 to 20 per 1000 live births [10]. However, an analysis of Demographic Health Services (DHS) data reported that, while ENMR decreased 3.2% annually over the time period, there was no significant change in the rate of decline after the village midwife program was initiated. Furthermore, the adjusted risk of first-day and early neonatal deaths was not significantly different between midwife-attended versus unattended births [32]. Rapid recruitment of midwives may have resulted in acceptance of candidates with lower qualifications and less clinical training than expected for SBAs [10]. Furthermore, there was limited mentorship, ongoing training, or incentives for retention, as well as inadequate linkages to effective EmOC. In 2003, in a pilot program, midwives in the Cirebon district were additionally trained in the identification and resuscitation of newborns using a tube-and-mask apparatus [33]. The specifics of neonatal resuscitation training and content are described in the third paper in this series [5]. Over the study period, midwives successfully managed 85% of cases of non-breathing babies and there was an approximate reduction in IPR-NMR of 47% based on estimated crude birth rates (IPR-NMR 5.1 per 1000 before training to 2.7 per 1000 after training).

In Khartoum, Sudan, community-based midwives were trained to conduct pregnancy surveillance and pregnancy monitoring (blood pressure, presence of edema, weight gain), birth planning for newborn care, and to refer to the central hospital for obstetric emergencies. A key component was linking the village midwife to the primary healthcare system and mobilizing pregnant women to seek pregnancy care. Over the 3-year period, the PMR was significantly reduced by 25% [34]. In Ghana, community midwives were trained in the use of the partograph and emergency obstetric skills and partnered with TBAs for referrals of obstetric emergencies; however, while there was a trend in reduction of PMR, the change was not statistically significant [35].

3.1.2.3. Birthing centers: Intrapartum-related mortality effect. In West Java, Indonesia, Alisjahbana et al. [36] evaluated the effect of village birthing centers or "polinades" as part of a comprehensive maternal healthcare program from 1992–1993 (Table 3). Given the local cultural belief that the home provides a "life force" to save the mother in labor, birthing homes/centers were established in the community and promoted through social marketing to enable the provision of prenatal, childbirth, and postpartum services by resident SBAs. Emergency transport and communication systems with a district hospital were also implemented. The 1-year evaluation found that prenatal care with a skilled provider was significantly higher for the intervention than for the comparison areas and a significantly higher proportion of women who had prenatal complications delivered in a health facility (31% versus 11%). The proportion delivered by an SBA remained low (<15%), although the proportion with intrapartum complications who were delivered by a midwife or doctor was significantly higher in the intervention area (14% versus 3%). There was no difference in PMR between the intervention and comparison areas; however, the baseline PMR in the control area was lower than the intervention area and the study was inadequately powered. Within the intervention area the PMR fell from 50 to 37 per 1000 over the study period.

In China in the early 1980 s, birthing centers (maternal-child health centers) in rural Shunyi province [36] were staffed by village doctors or midwives who monitored and managed hypertensive disorders and conducted external cephalic version for breech, and referral of high-risk women to deliver at the county hospital. Over a 4-year period, PMR was reduced from 26.7 per 1000 births (1983) to 17.6 per 1000 births (1986) (relative risk [RR] 0.65; 95% CI, 0.44–0.98) and perinatal deaths attributed to an intrapartum hypoxic event were reduced from 4.1 to 3.0 per 1000 births.

Malaysia made universal skilled birth attendance a national priority from the time of independence (1957), and achieved this by making the

gradual transition to skilled care at home with community midwives and then to birthing homes and institutions by using TBAs as partners. Benefits of the birthing center included shorter travel distance, the presence of female staff, and companionship/support from husbands, relatives, and/or TBAs [37]. Historical data suggest an 80% reduction in NMR over two decades when birthing homes and community availability of skilled childbirth care were introduced [38,39]; however, many other interventions (e.g. economic growth) and social changes may have contributed.

3.1.2.4. Effect of community skilled birth attendance on intrapartum-related mortality: Meta-analysis. We did not identify any high quality RCTs of SBAs in the community. There were 2 quasi-experimental studies with a non-randomized comparison group; however, in these studies the comparison group had either different baseline characteristics [40] or contamination by the intervention in comparison areas [30]. Thus, we used the before-and-after data from intervention areas for these trials. We found 4 studies with observational before-and-after data on training community SBAs for which we conducted a meta-analysis, and showed a 12% reduction in PMR (RR 0.88; 95% CI, 0.83–0.95) (Fig. 2A) and a 13% reduction in ENMR (RR 0.87; 95% CI, 0.79–0.97) (Fig. 2B). Excluded studies were the Matthews study [35] because of the large component of TBA training and the PATH study [33] that focused primarily on additional neonatal resuscitation training and estimated the number of births based on crude birth rates. Three studies reported IPR-NMR; however, the definitions of "birth asphyxia" varied across studies and the study designs and interventions were heterogeneous and thus the results were not pooled.

3.1.3. Cost of care by SBAs

An economic evaluation of the community-based midwifery training component of the South Kalimantan MotherCare project in Indonesia in the 1990s estimated training costs of between US $1214 and US $1694 per trainee (including life-saving skills training, continuing education, and internship), who performed an average of 3.3–5.5 births per month; 68% of costs were attributed to technical assistance and central administration [41]. The incremental cost was US $5651.5 per 1% increase in the number of competent midwives.

Training of community midwives in Cirebon, Indonesia in postnatal care and neonatal resuscitation cost Rp 2375 (US $0.25) per baby delivered over a 5-year period, with a cost of US $42 per intrapartum-related neonatal death averted [33]. One possible lower cost model is the South African Perinatal Education program, which, through long distance self-education, has been shown to increase knowledge and skills at a direct cost of US $5 per trainee, although running costs are not reported [42–44].

3.1.4. Implications

The quality of evidence that skilled birth attendance in the community may improve perinatal outcomes is low by GRADE criteria, primarily from observational, before-and-after or historical studies (Table 4). A meta-analysis of observational before-and-after data from 4 studies of SBA training showed a 12% reduction in PMR and a 13% reduction in ENMR. However, this effect size should be interpreted with caution as it may underestimate the potential impact of community-based SBAs, since some of these studies reflect the effect of "additional" training, none of the studies clearly included neonatal resuscitation with bag and mask and, moreover, in these community settings it is often the more complicated cases who seek skilled care, reflecting a higher-risk population. The quality of data on intrapartum-related outcomes was heterogeneous and could not be combined; however, there was a reported range of 22%–47% reduction in mortality of the "non-breathing baby" in three studies. Despite the low-quality evidence, skilled childbirth care is strongly recommended for all pregnant women, and providing skilled birth attendance in the community may improve perinatal outcomes if properly linked with quality and expedient EmOC (Table 4). Thus, bringing SBAs into and retaining them in the community is a potentially important strategy to reduce inequities in access to skilled childbirth care. Considerable program experience of birthing centers exists; the advantages include easy access for women and the possibility to maximize coordination between the SBA and alternative cadres.

There is a need to better delineate and evaluate what procedures may be competently performed by a skilled provider in the home versus facility setting. For example, while improved monitoring, referral for obstetric emergencies, and provision of neonatal resuscitation may be reasonably conducted in the community, few data exist regarding complex procedures such as vacuum extraction or symphysiotomy. Some experience with community-based BEmOC in Burma [45] is further discussed in the second paper in this series. In many cases of obstructed labor, surgical delivery is required to save the lives of the mother and infant, and requires a functioning continuum of care from the community to facilities [6]. Thus, if community-based SBA training is undertaken, it should occur in parallel with and be linked to improvements in the quality and supply of facility-based intrapartum CEmOC; and outcomes should be carefully monitored. Important issues to be considered in community-based SBA programs include how to retain SBAs in rural communities, and how to maintain their skills with sufficient workload. In certain settings, particularly isolated communities with clusters of more densely populated villages, allowing the placement of several midwives in a birthing center may be a feasible and cost-effective approach to reducing fetal, neonatal and maternal deaths from complications in labor provided training costs are controlled. More research, including outcome evaluation and economic analysis, and the effect of financial incentives on care seeking for skilled community-based childbirth care, is urgently needed.

3.2. Training TBAs for providing labor and childbirth care

3.2.1. Background

TBAs have attended births for women delivering at home since time immemorial [46], and following the Alma Ata Declaration in 1978, WHO actively promoted the legalization and training of TBAs. By 2000, 85% of low-income countries had a TBA training program. During the 1990s, however, WHO policy moved to emphasize the importance of skilled birth attendance, and TBAs were to be "integrated into the system." In 2004, TBAs were excluded from the category of providers identified by "skilled birth attendance" [47].

The role, skills and training of TBAs vary widely between settings (Table 1). Here we focus on trained TBAs, given the lack of evidence evaluating the effect of family members and untrained TBAs on maternal and neonatal outcomes. The focus of early training programs was on clean delivery and maternal health outcomes, and one authority stated that a TBA's "status in the community depends on her ability to manage complicated cases without endangering the mother's life, the baby being considered less important" [14]. If the mother lives and the baby dies, the community may express gratitude for saving the mother's life while minimizing any blame for the newborn's death [48]. However, in the 1980s there was increased interest in specialized training for neonatal resuscitation and the focus has shifted more recently to include newborn outcomes, South Asia, since attention given to both mother and baby is more cost-effective [49–51].

3.2.2. Evidence for the effectiveness of training TBAs

While the majority of the early published literature with regard to TBAs was descriptive, more recent studies have addressed changes in knowledge and attitudes following training, and several have assessed changes in behaviors, including referrals [52–56]. There are few studies, however, of the effect of training on maternal or perinatal mortality or serious morbidity [50,56–61]. Lack of evidence for the effect of TBAs on maternal and perinatal mortality has perpetuated the debate on their

Table 2
Evidence for community midwives and birthing centers: Intermediate outcomes 2005-2008.

Intervention/study	Setting	% skilled attendance	Changes in knowledge/attitudes	Changes in care seeking/ demand	Other intermediate outcomes	Investigator and year
Non-randomized comparison of delivery procedures and outcomes at Patan Hospital Birth Center(BC) staffed by mid-wives vs consultant led-maternity unit (CMU).	Patan Hospital, referral hospital for urban Lalitpur, (Kathmandu valley) Nepal	87%		• Mothers attending BC were more likely to attend postnatal care clinics (33%) and access family planning services	• Mothers attending BC had significantly lower risk of cesarean (63%), episiotomy (36%), meconium (38%), and oxytocin augmentation (73%) • BC deliveries had higher likelihood of artificial rupture of membranes (26%) • No significant differences in delivery complications, birth weight, Apgar score, or special care unit between BC and CMU	Rana et al. [26] 2003
Quasi-experimental study assessing impact of Life-Saving Skills (LSS) training and strengthening of maternity facilities on labor management in clinics and hospitals	Lam Dong Province, South central Vietnam	Not stated			• Increased detection of obstetric emergencies in LSS trained hospital and clinic settings • Substantially improved management of obstetrical emergencies in LSS trained hospital facilities, but not in LSS trained clinics	Sloan et al. [25] 2005
Training of Bidan di Desa (village midwives) in neonatal care, including management of the non-breathing baby with neonatal resuscitation using tube-and-mask resuscitators. Refresher 5 minute video distributed with tube-and-mask devices. Before and after comparison of midwife knowledge, observed skills and neonatal mortality rates.	Rural Cirebon, West Java Indonesia	20% deliver in health facilities Skilled attendance rate not reported	• Increase in midwife knowledge post training • No significant reduction in knowledge or skills 9 months post training		• Increase in observed skills performing resuscitation • In 1 year, 466 cases of BA managed by 274 (65%) of midwives trained; 377 (85%) of asphyxiated infants were resuscitated and survived (70% with basic resuscitation 26% with positive-pressure ventilation	Ariawan [33] PATH 2006
Retrospective observational study of neonatal outcomes before and after Obstetrics Emergency Training of midwives and obstetricians in tertiary care hospital, including cardiotocograph. Training included cardiotocograph tracings, electronic fetal monitoring, obstetric emergencies, and neonatal resuscitation.	Tertiary Care Hospital in Southmeade, England	100%			• Statistically significant reduction in hypoxic ischemic encephalopathy (RR 0.50) and 5 minute Apgar <6 (RR 0.51) • Significant increase in rate of emergency cesarean delivery (9.35% pre, 11.4% post) • No change in stillbirth rates	Draycott et al. [103] 2006
Evaluation of training of midwives in low risk clinics in WHO Essential Newborn care course, including newborn resuscitation training. Pre-post training written and performance testing.	Urban Lusaka and Ndola, Zambia	43%	• Significant improvement in mean written knowledge test (pre-course 65, post-course 77) • Resuscitation was an area of greatest improvement; Knowledge of indications for resuscitation doubled post training (27 vs 54%)		• Significant improvement in observed performance evaluations after course (65 vs 84)	McClure et al. [23] 2007

Evaluation of knowledge, skills and competency of village mid-wives attending in service training program, internship program vs those receiving no training. Training program included the American College of Nursing-Midwifery Life Saving Skills for Midwives, partograph use, and neonatal resuscitation	Rural South Kalimantan province, Indonesia	Not stated	• Significantly improved knowledge in trained midwives regarding antepartum and intrapartum care		• Significantly improved sores for neonatal resuscitation (67 vs 32% skills; 61 vs 4% competency) and use of partograph (76 vs 66% skills; 82 vs 57% competency) in trained vs untrained mid-wives	McDermott et al. [22] 2001
Evaluation of Skilled Birth Attendant (SBA) training program piloted by Bangladesh MOH in 2003 (90 female health assistants trained). Focus groups, knowledge and competency tests conducted pre-post, and 6 months after training.	6 rural sub-districts Bangladesh Pop: 72,240	13%	• 55% of SBA retained knowledge of content topics of training	• SBAs attended 33% of home births, provided 52% of prentatal care visits, 44% of postnatal care visits • Each SBA performed 9–10 prenatal care visits, attended 2–4 births, and 3–5 postnatal care visits/month. • SBAs made an average 137 referrals/month comprising 55% of hospital referrals	• Scored average of 75% on 9 essential skills of delivery/newborn care • Scores on use and referral with partograph were high (80%–90%) • 68% of SBAs could correctly demonstrate newborn resuscitation • Skill retention during observed births was high [2nd stage 89%; 3rd stage 76%] • Women treated by SBAs experienced lower rates of problems/complications during pregnancy compared to those by TBAs (14% vs 34%) • 84%–90% of beneficiaries were satisfied by their service, and 60% planning for their next pregnancy would prefer SBA	Bhuiyan et al. [20] 2005
Assessment of knowledge and skills of 166 skilled birth attendants from Benin, Ecuador, Jamaica, and Rwanda (Phase 1); and 1358 from Nicaragua (Phase 2). Competence guidelines developed from WHO Integrated Management of Pregnancy and Childbirth (IMPAC).	Phase I: Benin, Ecuador, Jamaica, Rwanda Phase II: Nicaragua	31%–96%	• Overall knowledge of SBAs ranged from 48%–62%. • Active management of 3rd stage of labor knowledge scores ranged from 7.4%–74% • Knowledge of immediate newborn care ranged 44%–66%		• Competence to correctly use partograph ranged from 50%–66% • Competence in neonatal resuscitation skills using ambu-bag ranged from 40-68%	Harvey et al. [19] 2007

Table 3
Evidence for impact of community midwives and birthing centers: Mortality effect.

Intervention/study	Setting	% skilled attendance	Baseline mortality rates	Mortality effect: % Relative Reduction in Mortality Rate *(number of deaths in intervention or end-line group)*; RR or OR (95% CI)						Investigator and year
				SBR	ENMR	PMR	NMR	IPR-NMR	MMR	
Before-and-after study of training village midwives and doctors at rural maternal primary health centers. Trained to manage-monitor pregnancy-delivery (blood pressure monitoring, external cephalic version), refer high risk mothers to county hospital. High risk pregnancies screened and booked at county hospital.	Shunyi, China	NS	PMR 26.7		23% OR 0.77 (0.43–1.36)	34% OR 0.66 (0.44–0.98)		27% [a] *(7)*		Yan et al. [36] 1989
Before-after study of training and upgrading of skills of village midwives (antenatal care, monitoring in labor, referral of high risk births, post natal care). Also established referral-transport system.	Khartoum, Sudan	1985–1988 9% in health facility, 91% of home births attended by midwives	SBR 23 PMR 44 NMR 27	15% *(48)* RR 0.85 (0.60–1.19)	22% *(34)* RR 0.78 (0.61–1.01)		32% *(44)* RR 0.68 (0.48–0.97)			Ibrahim et al. [34] 1992
Quasi-experimental comparison of comprehensive package of tradtitional birth attendant (TBA) training, village birthing homes with skilled attendants, capacity building in facilities and strengthening facility-community transport links in intervention vs a comparison district.	Indonesia Sub-district rural West Java Intervention (90 000) area Control (40 000) area	< 15%	PMR 50			25% [b] (44) RR 0.75 (0.51-1.10)		-	-	Alisjahbana et al. [40] 1995
Quasi-experimental non-randomized comparison of maternal mortality for two control areas (north and south) and one intervention area (north) in Matlab after institution of a community-based maternity care program (two health centers, four midwives and a speedboat).	Bangladesh, rural (Matlab)	Intervention area (MCH-FP) Control area	SBR 39.8 ENMR 39 NMR	15% [c] *(622)* OR 0.85 (0.76–0.94)	17% [c] *(542)* OR 0.83 (0.75–0.93)			22% [d] OR 0.78 (0.64–0.95)	50% [e]	Fauveau et al. [28] 1991 Ronsmans et al. [104] 1997 Ronsmans et al. [29] 2008
Historical data of national prioritization of the reduction of maternal mortality ratio (MMR) with inter-sectoral approaches including birthing centers and increased skilled attendance.	Malaysia	1970 'majority at home with TBA' 1980 'majority at home with skilled attendant'	1957 NMR 75.5	-	-		80% (1957 to 1980 [f]			MOH Malaysia 1998 Koblinsky [38] 1999
Historical data of training midwives in home based delivery including use of forceps in 1829 in Sweden.	Sweden	Sweden 1829 73% home delivery	PMR 42			29% [g] 0.71 (0.62–0.82)				Andersson et al. [105] 2000

Quasi-experimental non-randomized comparison of a total of 4169 women in 3 randomly selected communities one with no trained TBAs, one with trained TBAs and one with good access to functioning maternities (nurses and midwives).	Mozambique rural	Varied by community from ~40% to 77%	NMR 12–15 SBR 15–22	No difference [h] detected OR 1.43 (0.69-2.93)		No difference detected OR 1.24 (0.52-2.89)		-	Gloyd et al. [106] 2001
Before-after study of training rural midwives in use of partograph and emergency obstetric skills. Also training of TBAs to recognize and refer danger signs. Emergency obstetric transport service established.	Rural Brong Ahafo, Ghana	~30%	PMR 26		No diff detected OR 0.69 (0.33–1.45)				Matthews et al. [66] 2004
Before-after study of training of Bidan di Desa (village midwives) in neonatal care, including management of birth asphyxia with neonatal resuscitation using tube mask resuscitators. Refresher 5 minute video distributed with tube mask devices. Observation of midwife knowledge, skills and mortality rates.	Rural Cirebon, West Java Indonesia Pop: 2 million	20% deliver in health facilities Skilled attendance rate not reported	NMR 15 SBR 8 PMR 21 IPR-NMR 5.1	No significant change Baseline 8/1000 End-line 6/1000	29% [i]	40% [i]	47% [i]		Ariawan, PATH [33] 2006
Historical data on national Ministry of Health training program of village midwives starting in 1989. Training of 54,000 village-based midwives with 96% of population with access.	Indonesia, national level	22% at baseline	NMR 32 MMR 400			37% [j]			Shankar et al. [10] 2008
Historical evaluation of Demographic Health Services (DHS) data during Village midwife training program started in 1989, by 1995 50,000 trained. In 1996 competency based training program including neonatal resuscitation.	Indonesia, national level	12% midwife attended in 1986					No difference detected RR 0.98 (0.95–1.02) per year reduction		Hatt [32] 2009

Abbreviations: SBR, Stillbirth Rate; ENMR, Early Neonatal Mortality rate; PMR, Perinatal Mortality Rate; NMR, Neonatal Mortality Rate; IPR-NMR, Intrapartum-related Neonatal Mortality Rate. [a] Authors report perinatal mortality attributed to "asphyxia," but not clearly defined. 95% CI not given. [b] Baseline PMR in control area lower than intervention area and no significant change with time so intervention/control results not used. Before-after data used. Non-significant comparison between first 6 months and second 6 months in intervention area. [c] Comparison of ICDDRB vs Government service areas in years 1989–1995, crude non-adjusted rate comparison. [d] Effect was not not significant versus southern control area where EmOC access increased. [e] Comparison of ICDDRB vs Government service areas in years 1987-1999. [f] Historical data and should be interpreted with caution as many other factors may have influenced the reduction, 95% CI not given. [g] Historical comparison (1891–1899) of midwife attended vs non-attended births controlling for some confounding factors. [h] Comparison of skilled birth attendant in midwife served area vs trained TBA served area, non-random allocation. [i] Reported significant change ($P<0.05$), no CIs given; number of births estimated based on crude birth rate that was not measured. [j] Historical data and should be interpreted with caution as many other factors may have influenced the reduction, 95% CI not given.

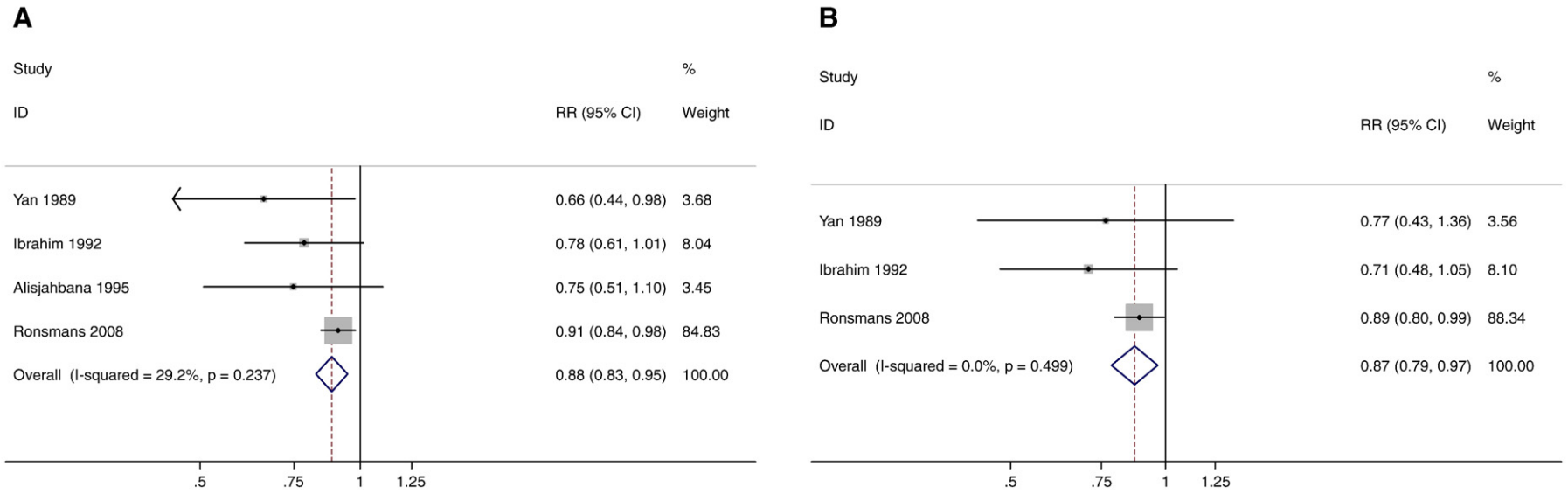


Fig. 2. Meta-analysis of mortality effect with before/after evaluations of community-based skilled birth attendants. (A) Perinatal mortality. (B) Early neonatal mortality rate.

Table 4
Interventions reviewed: Evidence grade, feasibility, and recommendations.

Intervention	GRADE Evidence Level	GRADE Recommendation	Feasibility in LIC-MIC
Skilled Birth Care in the Community: Skilled Birth Attendants (SBAs) or in Birthing Centers	**LOW:** We identified 3 quasi-experimental, 4 observational before-after, and 4 historical studies of skilled birth care at the community level. The data is inconsistent, as not all studies demonstrated a benefit. In a meta-analysis of before-and-after data from 4 low-quality studies of community midwife training there was a 12% reduction in all cause perinatal mortality. There is limited poor-quality data on effect on intrapartum-related neonatal mortality rate (IPR-NMR), as different definitions are used and likely include preterm mortality; the reported effect ranged from 22%–47% reduction in IPR-NMR. Most studies were set in low- and middle-income settings, primarily Asia, and may be generalizable to similar settings.	**STRONG**: Skilled childbirth care is recommended for all pregnant women, and there is low quality evidence that providing skilled birth attendance in the community may improve perinatal outcomes, if properly linked with quality and expedient emergency obstetric care. It would be unethical to conduct randomized controlled trials (RCTs) for skilled birth attendance. However, the quality of evidence is low, primarily observational before-after or historical studies; better monitoring and evaluation of the impact of SBA training programs is urgently needed.	Successful program experience and national scale-up in Indonesia, Bangladesh, Malaysia. In many settings, may not be feasible where there are human resource shortages. Large-scale national initiative on auxiliary nurse midwives failed to ensure SBA availability at delivery in India. Need to evaluate competency and capability of SBAs to perform basic emergency obstetric care (BEmOC) procedures in home settings vs facility. Requires close monitoring, evaluation, and need for frequent retraining.
Trained Traditional Birth Attendants (TBAs) partnering with the health system	**LOW:** There is one cluster RCT that TBA training may improve linkages with facilities and improve perinatal outcomes, although intrapartum-specific data is not available. There is evidence from a meta-analysis that TBA training may reduce perinatal-neonatal mortality by 6% and intrapartum-related mortality by 11%, from primarily low-quality studies The data is generalizable to low-middle income settings.	**CONDITIONAL:** The role of the TBA is still controversial, but there is some evidence that the TBA may partner with the health system, detect obstetric complications, refer to skilled obstetric care and positively impact stillbirths and neonatal outcomes. TBAs still attend up to 40% of home births in certain regions where skilled attendants are inaccessible, and their potential role as a facilitator with the health system should be further refined and rigorously evaluated.	Mixed program experience in the past, and history of controversy. While TBA does not equal a SBA, recent experiences have effectively used TBAs to link pregnant women with the formal health system, and may be feasible to include in collaborative partnership. Need to understand local culture, customs and practices surrounding childbirth.
Integrated Community Health Worker (CHW) Packages	**MODERATE:** There are 2 cRCTs and 2 quasi-experimental studies that have demonstrated the positive impact of CHW packages on perinatal-neonatal outcomes. A meta-analysis of these studies show a 36% reduction in early neonatal mortality. One quasi-experimental study showed a 42% reduction in IPR-NMR over time.	**STRONG:** The evidence is growing that CHW packages may be effective in improving perinatal outcomes, and this is a relatively low cost mechanism of providing care for the poor and marginalized in community settings in LMIC. There is a need for the evaluation of the impact of CHW packages on intrapartum-specific mortality and long term outcomes, and to also for further implementation research.	Feasible in several small-scale trials, need to be tested for sustainability and scalability, as well cost-effectiveness. Programs may be started with relatively low cost.

Table 5
Evidence for traditional birth attendant (TBA) training: Intermediate outcomes 2005–2008.

Intervention/study	Setting	% skilled attendance	Baseline mortality rates	Changes in knowledge/attitudes	Changes in care seeking/demand	Other intermediate outcomes	Investigator and year
Meta-analysis on relationship of TBA training (health promotion, disease prevention, clean birth practices) and use of professional antenatal care (ANC). Lack of adequate information about TBA training program characteristics.	15 studies from 8 countries, Africa and Asia	–	–	• TBA knowledge about ANC significantly increased by 157% in trained vs untrained TBAs (baseline 28%)	• Significant increase in maternal compliance and ANC attendance rates by 38% (baseline 42%)	• TBA behaviors (advice and assistance) supporting ANC use significantly increased 47% in trained vs untrained TBAs (baseline 41%)	Sibley et al. [63] 2004
Meta-analysis of effectiveness of TBA training and access to skilled birth attendance. Overall poor quality of studies, TBA training was often a component of intervention packages in several studies.	16 studies from 12 countries in Asia, Africa and Latin America	–	–	• No statistically significant effect of TBA training on TBA knowledge related to referral	• Small, positive significant 22% increase in maternal compliance with TBA referral or maternal use of health facility. [Small subsample 2 studies]	• Small, positive, significant 36% increase in TBA behavior related to referral vs baseline	Sibley et at. [64] 2004
Home-based Lifesaving Skills (HBLSS) Program (obstetric first aid skills) training for TBAs. Evaluation of second phase of training.	Rural Liben Woreda, Ethiopia ~33 000	10%				• HBLSS trained TBAs attended 24-26% of births • Estimated exposure of 54% of pregnant women to HBLSS • 78% increase in TBA performance scores for "first actions" for neonate including basic resuscitation, with 9% reduction after 1 year • Management of "first actions" by women and families was significantly higher in births attended by HBLSS guide (55% vs 32%)	Sibley et al. [68] 2006

role [46,62] and also reflects the methodological and logistic challenges of systematic outcome assessment in such settings, particularly of measuring maternal mortality. There are several published systematic reviews of TBA effectiveness [63,64]. In this section we present data on intermediate outcomes of relevance (Table 5) and evidence for effect on mortality, particularly intrapartum-related outcomes (Table 6).

3.2.2.1. Trained TBAs for the primary prevention of intrapartum-related mortality. Evidence for benefit of TBAs in primary prevention of intrapartum-related hypoxia fits into two main categories: their role in augmenting use of routine prenatal pregnancy care, and intrapartum recognition and referral for obstetric complications.

A meta-analysis by Sibley et al. [63] included 10 studies (4919 and 3368 women in pooled treatment and comparison groups, respectively) and found that TBA training was associated with a significant 38% increase in use of prenatal services (Table 5). In Ethiopia, a before-after study demonstrated that TBA training was associated with increases in the receipt of prenatal care (49% pre to 61% post), reduction in unsafe practices during delivery, and a significant decrease in the proportion of babies born requiring neonatal resuscitation (11% before vs 7% after) [65]. The reduction in the need for resuscitation indicates the effectiveness of primary prevention, although it is unclear whether this was mediated through improved prenatal or intrapartum care in this study.

Several programs have demonstrated the capacity of trained TBAs to recognize and refer for obstetric complications, but success may vary with TBA educational level or literacy, training program content, relationships with the formal health system, as well as accessibility and perceived quality of referral facility care. Illiterate TBAs have used pictographs in Ghana to identify danger signs in pregnancy and refer pregnant women with risk factors for skilled childbirth care with trends of increased referral post-training [35]. In another study in India, however, there was no significant difference in TBA referrals of mothers for health center delivery based on identification of 1 or more pictorially-represented complications [66]. In Ethiopia, TBAs were trained in the Home-based Lifesaving Skills (HBLSS) program [67], including recognition of prolonged labor for purposes of primary prevention. Eighty-five TBAs participated in training on "birth delay" and displayed a 108% increase in post-training scores over the pretraining values ($P<.001$) [68] (Table 5).

Little data exists on the effect of TBA training on timing to referral and receipt of referral-level care in case of complications. In rural Fortaleza, Brazil, where a TBA training program was begun in the mid-1970s [58], TBAs conducted 55% of births and were able to recognize labor complications and effectively refer mothers with high obstetric risk (antepartum factors or intrapartum complications) for hospital delivery. There was a significant increase in referrals after training [58]; almost 50% of women at hospitals with complications during delivery had been referred by TBAs, and TBAs referred an average of 12% of pregnant women for hospital delivery, primarily for obstructed labor (40%), primiparity (12%), abnormal presentation (9%), and maternal hemorrhage (7%). The program has not been replicated, however. In Ghana, in a random survey of 1961 TBAs, training was associated with significant reductions in intrapartum fever, which has been linked to neonatal encephalopathy [69].

A program in Guatemala used a controlled, before-and-after design to examine the effect of a 3-month hospital-based training program for TBAs on rapid recognition and referral of complications [56]. TBA training was part of a comprehensive program including referral and facility improvements. There was a significant increase in overall referrals in both intervention and control areas, and no differences between the areas. In the intervention communities, there were 16 perinatal deaths (n = 72 births) versus 24 deaths (n = 203 births) before-and-after the intervention, respectively, corresponding to a significant decrease in death rate from 22% to 12% (OR 0.47; $P = 0.032$). However, there were no significant differences for identification and referral of conditions plausibly related to PMR or NMR (e.g. preterm labor, malpresentation, prolonged labor). Because women attended by TBAs who were not referred or who did not comply with referral were not included in the analysis, the effect of TBA training on extent and effect of referral on PMR in the study communities is unknown [70].

Sibley et al. [64] conducted a meta-analysis in 2004 of 13 studies assessing the effect of trained TBAs on referral practices for obstetric emergencies. Six studies included outcomes on TBA knowledge related to referral (n = 441 treatment vs n = 786 control), 13 studies included outcomes on TBA referral behavior (n = 5976 treatment vs n = 5991 control), and 2 studies reported outcomes on maternal referral behavior (n = 812 treatment vs n = 1567 control). Although TBA knowledge of conditions requiring obstetric intervention was not significantly affected by training, TBA behaviors related to obstetric referral (including detection and referral of intrapartum complications) showed a small, significant increase after training: 36% over baseline (13 studies with n = 5976 treatment vs n = 5991 control). Women seen by trained TBAs had a small, significant increase in obstetric care seeking behaviors (22%). The authors concluded, however, that given the overall insufficient quality of the studies and the fact that the interventions were included within packages of services, it was not possible to attribute the small improvements in TBA and maternal behaviors to the TBA training interventions alone.

In a large, cluster-RCT (cRCT) in Sindh, Pakistan, training and integrating TBAs into the health system to provide obstetric care resulted in substantial increases in detection and referral for EmOC, as well as significant reductions in PMR and NMR [61] (Table 6). A total of 585 TBAs were trained to recognize obstetric emergencies and refer for EmOC, encourage care seeking, use clean delivery kits, and promote essential newborn care. The partnership between the TBAs and lady health workers (LHWs), and links with the formal health system, was strengthened by increasing the frequency and quality of their contacts during birth kit distribution and at community based clinics within the community. The home birth rate was about 80% in both study arms, but trained TBAs attended the majority of births in intervention clusters (75%), whereas untrained TBAs attended most births in the control clusters (76%). Pregnant women attended by trained TBAs were less likely to have puerperal sepsis (RR 0.17; 95% CI, 0.13–0.23) and hemorrhage (aRR 0.61; 95% CI, 0.47–0.79), and more likely to be diagnosed with obstructed labor (RR 1.26; 95% CI, 1.03–1.54) and referred for EmOC (RR 1.50; 95% CI, 1.19–1.90). Early recognition and referral for obstructed labor, in addition to the reduction in significant risk factors for intrapartum-related injury, would presumably reduce the IPR-NMR in the intervention group. PMR was reduced by 30% in intervention clusters (OR 0.70; 95% CI, 0.60–0.80), SBR was reduced by 31% (OR 0.69; 95% CI, 0.57–0.83), and NMR by 29% (OR 0.71; 95% CI, 0.62–0.83). The study was not sufficiently powered to detect a reduction in MMR (OR 0.74; 95% CI, 0.45–1.23). Intrapartum-related mortality was not determined; however, the significant reduction in both stillbirths and early deaths in parallel with the previously discussed intermediate outcomes suggests that the intervention successfully targeted the primary prevention of intrapartum injury. However, scale-up remains a challenge.

3.2.2.2. Trained TBAs for secondary prevention: Recognition and management of the non-breathing baby. The evidence for beneficial involvement of TBAs in the management of the non-breathing baby is discussed in detail in the third paper on neonatal resuscitation [5], and will only be discussed briefly here. In the 1980s, Daga et al. [71] trained TBAs (attended >90% of births) in essential newborn care including mouth-to-mouth resuscitation of non-breathing infants. Over the program period, the PMR fell from 74.8 to 28.7 (1987–1990); however, also reflected were concurrent improvements in the management of low birth weight, preterm infants, and infections as well as improvements in hospital-based neonatal care. In Chandigarh, India, TBAs were trained to recognize the non-breathing baby and conduct neonatal resuscitation, using mouth-to-mouth and then bag-and-mask resuscitation (Table 6)

Table 6
Evidence for impact of trained traditional birth attendants (TBAs): Mortality effect.

Intervention/study	Setting	Percentage skilled attendance	Baseline Mortality Rates	Mortality Effect: % Relative Reduction in Mortality Rate *(number of deaths in intervention or end-line group)*; RR or OR (95% CI)						Investigator and year
				SBR	ENMR	PMR	NMR	IPR-NMR	MMR	
Non-randomized comparison of perinatal outcomes between subset of TBAs trained in "advanced" resuscitation with suction and bag-and-mask as opposed to usual TBA training with mouth-to-mouth resuscitation.	Rural India	< 10%	PMR 49 IPR-NMR 5	-	-	19% [a] *(45)* RR 0.82 (0.56–1.19)	-	70% *(5)* RR 0.3 (0.1–0.8)	-	Kumar [54] 1995 Kumar [60] 1998
Before-after comparison of TBA training in basic resuscitation with mouth-to-mouth breathing.	Rural India	TBAs attend 90%	SBR 19 PMR 75 NMR 57	51% RR 0.49 (0.16–1.50)		61% RR 0.39 (0.21–0.69)	41% RR 0.59 (0.32–1.09)			Daga [107] 1992
Before-and-after comparison of referral patterns and PMR before and after a 3-month hospital-based training program for TBAs.	Rural Guatemala	< 20%	PMR of referred infants 200	-	-	27% [b] *(81)*	-		-	O'Rourke [56] 1995
Before-and-after comparison of the outcome of pregnancy for 1 year before and 3 years after introduction of primary health care including trained TBAs in 41 villages, and in control villages without a Primary Health Center (PHC).	Rural Gambia	< 7%	NMR 60	Apparent increase (better surveillance)	15% *(64)*	Apparent rise in stillbirths meant only 8% reduction in PMR	33% [c] *(101)*		26% [d] *(24)*	Greenwood et al. [57] 1990
Quasi-experimental study of TBA training especially in recognition of complications and referral. Establishment of "mini- maternities" with telephones for TBA births. Non-randomized comparison of trained TBAs with high case load (>29 births per year) versus unattended home births.	Brazil rural NE	< 40%	NMR 26	-	-		40% [e] *(23)*			Janowitz et al. [58] 1988
Meta-analysis comparing trained and untrained TBAs. Evaluated differences. on TBA knowledge, attitudes, and behaviors; PMR/NMR (including asphyxia specific mortality). Two studies trained TBAs in neonatal resuscitation. [NMR analysis n = 15 286 treatment and n = 12 786 control; "asphyxia" analysis n = 6217 treatment and n = 5170 control].	Meta-analysis of 60 studies/ 90 datasets ranging 1971-1999 from 24 countries, Asia, Africa and Latin America-Caribbean; For IPR-NMR 3 datasets	Range	Range	-	-	Combined peri-neonatal 6% (4%–9%)		IPR-NMR 11% (2%–21%)	-	Sibley et al. [50] 2004
Cluster randomized, controlled trial of TBA training in antepartum, intrapartum, postpartum, and neonatal care; distribution of clean delivery kits; referral for emergency obstetrical care. Lady health workers also trained to support TBA and link community-health center services. Trained TBAs attended 74% of births in intervention group.	Rural Pakistan, Larkana, Sindh province	10%	PMR 120 [f] SBR 71 NMR 53 MMR 268	31% *(483)* aOR 0.69 (0.57–0.83)		30% [f] *(823)* aOR 0.70 (0.59–0.82)	29% *(340)* aOR 0.71 (0.62–0.83)		26% *(27)* aOR 0.74 (0.45–1.23)	Jokhio et al. [61] 2005
Before-and-after study of training of community birth attendants (TBAs, nurses) in WHO Essential Newborn Care [108], including basic resuscitation with bag-and-mask in 6 countries.	Argentina, DR Congo, Guatamala, India, Pakistan, Zambia	TBAs attend average 37% of births	PMR 46 ENMR 23 SBR 23	31% *(557)* RR 0.69 (0.54–0.88)	NS RR 0.99 (0.81–1.22)	15% *(1367)* RR 0.85 (0.70–1.02)				Carlo et al. [71] 2009

Abbreviations: SBR, Stillbirth Rate; ENMR, Early Neonatal Mortality rate; PMR, Perinatal Mortality Rate; NMR, Neonatal Mortality Rate; IPR-NMR, Intrapartum-related Neonatal Mortality Rate.

[a] Non significant reduction in PMR among babies with "asphyxia" due to small numbers. Also note the prevalence of asphyxia was lower (0.9%) in the advanced resuscitation group, compared to the basic group (2.4%).

[b] Before-after comparison.

[c] Significant reduction but mainly late neonatal so probably more related to reduction in infections.

[d] 61% reduction between before-and-after. Control villages fell by 35% so comparative fall of 26%, but not significant.

[e] Non-significant reduction comparing TBAs with highest case load (>29 births /year) with unattended home births.

[f] PMR defined as stillbirth and neonatal death up to 28 days.

[59,60]. There was a non-significant 19% reduction in PMR, and 20% lower case fatality among non-breathing babies for births attended by TBAs trained in advanced neonatal resuscitation. The "asphyxia" mortality rate was significantly reduced; however, some of the effect may also reflect the reduction in the mortality of preterm non-breathing infants.

In a recent multicenter trial, TBAs were trained in 6 countries in essential newborn care including basic neonatal resuscitation with a bag-and-mask device [71]. In a before-and-after comparison including over 57 000 births, there was a 22% reduction in PMR among those delivered by trained TBAs (RR 0.78; 95% CI, 0.63–0.96) and a 31% reduction in SBR (RR 0.69; 95% CI, 0.54–0.88), likely due to a shift in classification of babies from stillbirth to early neonatal death.

3.2.2.3. TBA training programs: Intrapartum-related mortality effect. In 2004, Sibley et al. [50] conducted a meta-analysis of 17 studies with 18 datasets (n = 15 286 in treatment vs n = 12 786 in control), and reported a 6% reduction in deaths in the perinatal and neonatal period in the areas served by trained TBAs (Table 6). "Birth asphyxia" mortality (3 studies, 6217 neonates in the treatment group vs 5170 controls) was significantly reduced by 11%. In the 3 studies included in the analysis of "asphyxia" mortality, TBAs conducted neonatal resuscitation—Gadichiroli, India (initial TBA training period [82]; Chandigarh, India [60] and Ethiopia [65]. However, in the recent Cochrane review [70], these studies were excluded and only 2 studies reporting PMR met methodological quality inclusion criteria (Pakistan [61] and Guatemala [56]), and were not pooled because of differences in study design. After reviewing the data, we did not identify new evidence that had comparable study design, intervention, and outcome measures for which to conduct a meta-analysis. The First Breath trial has not yet reported cause-specific mortality [71], and the before-and-after study design was not pooled with studies of quasi-experimental or cRCT design. There are 3 recently completed RCTs of TBA training that will soon help better inform this evidence base [5].

3.2.3. Cost of TBA training

The cost of TBA training per TBA may range from US $44 in Uganda [72], US $60 in Nepal [49], to US $45–$95 in Ghana, Mexico, and Bangladesh [73]. The estimated cost per TBA assisting 30 births per year would be US $110, assuming training/supervision at US $50 per year and supplies at US $2 per birth [74]; training costs may be reduced after the first year but costs for supervision would remain. The cost per neonatal life saved by primary prevention of intrapartum-related hypoxia because of better management in labor by TBAs can be estimated based on an assumed reduction of 11% in IPR-NMR from a baseline rate of 10 IPR-neonatal deaths per 1000 live births [2,50]. A TBA assisting 30 births a year would then save about 1 neonate for every 1000 births or 1 neonate every 33 years, at a cost of US $3630 per life saved, is greater than the range considered as cost-effective in low-resource settings based on 3 times gross national income per capita (per DALY averted) [2,75]. In addition, it should be noted that many TBAs perform fewer than 30 births per year, further reducing cost-effectiveness. More systematic assessment of outcomes and cost is required.

3.2.4. Implications

While the role of TBAs remains controversial, there is emerging evidence that TBA training may have positive direct effects on neonatal outcomes through primary and secondary prevention of intrapartum-related events, provided that the volume of births is sufficient to maintain skills. A previous meta-analysis demonstrated an 11% reduction in intrapartum-related mortality [50], and in a recent cRCT, TBA training resulted in 30% reduction in PMR. However, the GRADE level of evidence is low, since there is only one cRCT which reported intrapartum-specific outcomes and one meta-analysis, primarily of lower quality program experience (Table 4). More data are required before making recommendations to initiate training of TBAs for these purposes. Future studies should include at least the following information on participants, the intervention, and outcomes, to permit analyses to inform policy and programs: (1) TBA age, socioeconomic status, educational attainment, experience, number and proportion of births attended; (2) maternal age, parity, socioeconomic status, and educational attainment; (3) training method, content, duration, contact hours, trainer/trainee ratio, supportive supervision and education after training, context, for example whether training is a single invention or part of a complex intervention, and whether it is situated within an enabling environment that includes elements such as advocacy, community mobilization, emergency transportation or adequate accessible referral sites; (4) timing of measurement relative to the intervention, data collection method and sources; (5) definition of intrapartum-related neonatal deaths and stillbirths, and inclusion of preterm deaths; and (6) cost-effectiveness [70].

The decision-making process regarding TBA training will also vary by setting. In rural settings where there are no SBAs and little hope of sustaining sufficient numbers of skilled attendants, and where access to emergency care facilities is lacking, TBA training may be considered. While TBAs cannot substitute for SBAs, they may play valuable roles in partnering with SBAs, and in providing information and support to the woman and her family. Moreover, in many settings, poor women still chose to deliver with TBAs even when skilled attendance is a possibility, illustrating that TBAs may bring value to families, particularly social and cultural skills from which SBAs could learn.

3.3. Using CHWs to promote birth preparedness and care-seeking, with or without provision of newborn care at birth

3.3.1. Background

CHWs are defined by WHO as "members of the communities where they work, selected by the communities, answerable to the communities for their activities, supported by the health system but not necessarily a part of its organization, and have shorter training than professional workers [76]" (Table 1). CHWs may play a critical role in healthcare delivery in rural, under-resourced regions and have proven to be effective in promoting childhood immunization and the management of acute respiratory infections and malaria [77–79]. The provision of newborn care by CHWs is less controversial than the role of TBAs [13,80–83], as the selection process and the objectives, as well as the evidence for effect, are different. CHWs differ from TBAs in that they tend to be younger, more educated, and less closely bound to traditional care practices. Characteristics and training of CHWs may vary by region and even within countries, however, depending on local policy. For example in South Asia, CHWs tend to be women from the village who are trained in aspects of maternal, newborn and child health; the extensive network of CHWs in Nepal is made up largely of women volunteers [81]. In contrast, in some studies and programs in South Asia [84], and in several African countries, CHWs are male, compounding the challenge of accessing mothers and newborns during the traditional postpartum period of seclusion widely practiced in many low-resource settings [85]. In China, which promoted broad coverage with male "barefoot doctors," particularly during the 1970s, 2-3 years of training was the norm and there was good back-up by a referral system [38].

3.3.2. Evidence for CHW packages

The evidence for CHWs in averting intrapartum-related hypoxic injury falls into 3 main categories: (1) education to increase birth preparedness and care-seeking during childbirth; (2) community mobilization activities to increase access to skilled childbirth care (detailed in the fourth paper in this series) [6]; (3) and the provision of care at delivery to recognize and manage the non-breathing baby.

3.3.2.1. CHWs for primary prevention: Improving birth preparedness and care seeking. CHWs may play an instrumental role in the primary prevention of intrapartum-related injury by educating women and

families about birth preparedness and mobilizing communities to seek skilled care during childbirth (Table 7). There are limited data on the mortality effect of birth-preparedness programs. Community mobilization is discussed in detail in the fourth paper in this series [5].

In Sylhet and 10 additional districts in Bangladesh, CHWs were trained in interventions targeting birth preparedness and essential newborn care [80,86]. After the intervention, mothers' knowledge of danger signs in pregnancy, labor and delivery, and the postnatal period significantly increased. Immediate newborn care practices, including immediately drying, warming, and stimulating the infant also improved. Furthermore, in Mirzapur district, there were some improvements in care seeking for newborn illness after CHW training, via both self-referrals and increased compliance with CHW referral [81,87,88].

In Kebemer, Senegal, CHW training was associated with significant increases in women who identified their place of delivery with a qualified provider and who had identified emergency funds or transport [89]. Pregnant women were 3-times more likely to recognize at least 4 dangers signs during labor and delivery. Furthermore, the facility birth rate significantly increased from 53% to 75%, and CHWs were more likely to attend home births.

3.3.2.2. Comprehensive CHW packages targeting primary prevention: Intrapartum-related mortality effect. Several trials involving CHW training to promote birth preparedness and care seeking during pregnancy reported mortality effects; however, delivery attendance or the provision of neonatal resuscitation by CHWs did not feature prominently in most intervention packages, except for the SEARCH trial [90] (Table 8).

In Pakistan, the LHW program was established by the Ministry of Health in the early 1990s to provide primary maternal and child health services to rural and poor urban regions. In the Hala and Matiari subdistricts of rural Sindh province [83], LHWs were trained in home-based essential newborn care, provision of prenatal and postnatal care, leading group education meetings and village health committees, and working with TBAs to follow pregnancies in the community. LHWs attended few births: 5% of births in the intervention villages versus 1% in the control arm. Intervention clusters, however, had improved rates of prenatal care, skilled birth attendance at public sector facilities, reductions in home births, and significantly reduced SBR (65.9 to 43.1 per 1000) and NMR (57.3 to 41.3 per 1000). Although cause-specific mortality data are not yet available, the substantial reductions in early neonatal mortality and stillbirths may reflect the effect of these interventions on intrapartum-related deaths.

In a cRCT in Shivgarh, India, CHWs held collective meetings with community stakeholders in newborn care, and additionally made two prenatal and two postnatal home visits, covering birth preparedness, hygienic delivery, umbilical/skin care, thermal care, breastfeeding, and care seeking from trained providers [13]. The interventions were focused primarily on hypothermia and neonatal infection; however, primary prevention of intrapartum complications was addressed via improving birth preparedness, hygiene, and care-seeking activities. Pregnant mothers from CHW clusters had significant improvements in prenatal care attendance; birth preparedness indicators such as identification of a health facility and birth attendant, and arrangement of money in case of emergency prior to delivery; and care seeking during pregnancy. Furthermore, newborns in the intervention arms were more likely to be wiped-stimulated, wrapped, and receive skin-to-skin contact. PMR was significantly reduced in the essential newborn care group (aRR 0.54; 95% CI, 0.38–0.76). While IPR-NMR was not reported, the reductions in SBR (aRR 0.72; 95% CI, 0.51–1.01; essential newborn care vs control) and in ENMR (62 per 1000 live births in the control group vs 35 per 1000 in the essential newborn care group) suggest that primary prevention was effective in reducing adverse intrapartum events.

3.3.2.3. Comprehensive CHW packages including secondary prevention: Intrapartum-related mortality effect. In the SEARCH study [82] in Gadchiroli, India, CHWs partnered with TBAs to provide childbirth care and manage the non-breathing baby in the home. This study is discussed in detail in the third paper [5]. In brief, CHWs were trained to use a tube-and-mask (1996–1999) and bag-and-mask device (1999–2003) for neonatal resuscitation and attended 78%–84% of births over the study periods. The "asphyxia" specific mortality was significantly reduced by 65%, and case fatality of "severe asphyxia" was reduced by 48% from before to after the intervention [90]. In a comparison of the intervention versus control areas during the CHW period of tube-and-mask resuscitation, "asphyxia" specific mortality was reduced by 42%. The SBR in the intervention area was lower by 49% (95% CI, 31–66), and the ENMR lower by 64% (95% CI, 49–79) versus the control area [91].

3.3.2.4. Integrated CHW packages: Meta-analysis of effect on intrapartum-related mortality. In a meta-analysis that included all the available higher-quality evaluations of primary and secondary prevention of intrapartum-related outcomes through CHWs (2 cRCTs [13,80] and 2 quasi-experimental trials [80,83]), the pooled effect on PMR was RR 0.72 (95% CI, 0.62–0.84) (Fig. 3A) and on ENMR was RR 0.64 (95% CI, 0.56–0.73) (Fig. 3B). There was only one trial that reported intrapartum-related mortality. We did not include the study by Jokhio et al. [61] because its focus was on TBA linkages with the health system, rather than program implementation through CHWs. The studies by Pratinidhi et al. [92] and Sundararaman et al. [93] were excluded because of the lower-quality, before-and-after, or historical control study designs. For the SEARCH study, the standard error was adjusted by the highest design effect of the RCTs to account for the difference in study design and small number of study clusters (2 clusters). For the Hala trial [83], we did not apply a correction and used the cluster adjusted data.

3.3.3. Cost of CHW training

The limited data on cost-effectiveness indicate that CHW programs may help improve equity in coverage for programs for the poor [91,92,94,95]. Non-recurring costs of home-based care in Gadchiroli, India came to US $0.89 and recurring costs of care were US $6.06 per neonate, giving a total of approximately US $7 [91]. The estimated cost per death averted was US $150.5 for home-based care, and in a subsequent analysis, US $13 for equipment (bag-and-mask resuscitator) per death averted (US $6.50 for tube mask) [91], although cost-effectiveness for the management of intrapartum-related hypoxia alone will differ from this estimate. Additional data using state-of-the art methods for determining cost-effectiveness are needed.

3.3.4. Implications

There is growing and substantial high-quality evidence that CHWs, working within the community and often with TBAs, may effectively provide packages of newborn care and significantly improve neonatal and perinatal outcomes. However, there are limited data on cause-specific mortality, therefore the GRADE level of evidence is moderate (Table 4). CHW packages may result in 36% reduction in ENMR, a substantial fraction owing to intrapartum-related neonatal deaths. Bang et al. [82] achieved high rates of birth attendance in Gadchiroli and observed a 42% reduction in intrapartum-related mortality in the area where CHWs were trained in tube-and-mask resuscitation of the non-breathing baby versus the control area. While intrapartum-related mortality data are not yet available for many other community-based RCTs, the reductions in perinatal mortality, early neonatal and stillbirth suggest that deaths due to intrapartum-related events may have been reduced in these studies as well [13,83]. However, any reduction in intrapartum-related deaths was probably mediated through primary prevention and increased care seeking for complicated births, given the low rates of birth attendance by CHWs and absence of training in neonatal resuscitation with positive pressure ventilation.

Table 7
Evidence for community health worker (CHW) packages: Intermediate outcomes 2005–2008.

Intervention/study	Setting	% skilled attendance	Baseline mortality rates	Changes in knowledge/attitudes	Changes in Care-seeking/Demand	Other Intermediate Outcomes	Investigator and year
Training of CHWs in essential newborn care, communication/education program through CHWs and mass media, and strengthening of health facilities with staff training and equipment upgrades. Before and after comparisons.	Kebemer district, Senegal Pop 67 000	~50%	NMR 31	• Significant increases in knowledge of birth preparedness (identify place of delivery 22% to 34%, identify source of emergency funding 23% to 76%, identify transport 8% to 30%) • Significant increases in knowledge of hypothermia management (skin to skin 22 % to 63%, wiping dry 19% to 48%), clean cord care (clean blade 26% to 55%, no topical application 43% to 90%) • Significant increases in recognition of at least 4 danger signs (18% to 54%)	• Increase in facility based births (53% to 75%) • Increase in proportion of home births attended by matrons (CHWs) from 29% to 39%	• Significant increase in birth-preparedness practices: pre-identifying place of delivery (57% vs 68%); choice of delivery location with qualified person (34% vs 39%) emergency fund (44% vs 78%), emergency transport (10% vs 30%) • Improvement in essential newborn care practices: skin to skin contact (2% vs 14%), drying (54% vs 73%), delayed first bath at least 6 hrs (20% vs 53%), breastfeeding in first hour (60% vs 78%)	Ndoye et al. [89] 2004
Longitudinal before-and-after comparison of package of newborn home-based care (extension of original observation period from above study). Baseline period (1993-1995): trained TBA using mouth to mouth resuscitation. Intervention: team of TBA and semi-skilled CHW; training of CHW in tube-and-mask (1996-1999) and later bag-and-mask (1999-2003) ventilation.	Rural India Maharashtra state Intervention area: 39 312 Control area: 42 520	<5%	SBR 32 ENMR 37.5 PMR 68.3	• In last year of intervention (1997-8) in cross sectional survey of 726 mothers: 79% of mothers were prepared for delivery, 77% recognized signs for which VHW should be called, 85% knew delivery room should be clean, 68% could identify neonates at high risk	• VHWs attend 78% of home births in 1995-1996 to 84% in 1996-2003	• Incidence of "Mild asphyxia" (not breathing at 1 minute) 14.2% in 1995-1996 to 5.7% in 2000-1003 • Incidence of "Severe asphyxia" (not breathing at 5minutes) 4.6% in 1995-1996 to 4.9% in 2000-2003 • Delayed breastfeeding decreased from 9.3% to 1%	Bang et al. [90] 2005
CHWs trained in essential newborn care conducted door-to-door visits to identify and follow women during pregnancy and post-natal period, educate mothers about newborn care and danger signs. Before and after comparisons.	Rural Bangladesh, 10 upazilas (subdistricts)		NMR 41	• Mothers' knowledge of at least 2 danger signs during pregnancy increased from 31.1% to 77.6% • Maternal knowledge of at least 2 danger signs during labor and delivery increased from 77.8 to 91.1% • Maternal knowledge of at least 2 postnatal danger signs increased from 47.1% to 64.3%	• Postnatal check up of infant within 24 hrs by trained provider increased from 14% to 27% • Postnatal check up of mother within 24 hrs by trained provider increased from 2% to 27%	• Increase in newborn drying and wrapping after birth (14% to 55%) • Increase in breastfeeding within 1 hour of birth (39% to 76%) • Delayed bathing by 24 hours increased (22% to 82%)	Syed et al. [86] 2006
Promotion of family care-seeking for maternal-newborn care through behavior change communication, identification and referral of sick infants by CHWs and strengthening of neonatal care in health facilities. Mid-study CHWs received emphasized training on management of birth asphyxia and antepartum family counseling on asphyxia.	Mirzapur upazila, Rural central Bangladesh				• Increased family compliance with CHW referral to hospital over study period (56% baseline vs 80% end line) • Significant increase in proportion of sick newborns seeking care from qualified providers in intervention area (31% vs 60% end line, OR 2.98; 95% CI, 2.00–4.44) • Significant increase in care seeking from Kumudini Hospital 18% vs 46%, OR 2.90; 95% CI, 1.91–4.41) • Significant		Bari et al. [109] 2006

Promotion of Birth-Preparedness Package (BPP) by community mobilizers (CHWs, trained TBAs) who conducted inter-personal counseling and mother's groups with flipcharts covering topics including: antenatal care, care for mother and newborn during/ after delivery, danger signs, and financial/transport planning. Before and after comparison.	Rural Siraha, eastern Nepal Pop: 615 000	17% at baseline 18% at end line	IMR 81	• Increase in antenatal (84% vs 60% with 1+ ANC visit) and post natal care (25% vs 11% within 1 wk of delivery) • No change in use of skilled birth attendant (18% vs 17%) • No change in care seeking during emergency (85% vs 83%)	• Significant increase in birth-preparedness index (54 vs 33) • Improvements in essential newborn care practices by 20-30% compared to baseline (use of clean delivery kit, breastfed within 1 hr, delayed bathing, nothing applied to cord, wrapped immediately)	McPherson et al. [110] 2006
Pilot study training of Lady health workers (LHW, CHW) and Dais (TBAs) in home based newborn care (including basic resuscitation)[e], improvement of linkages between LHWs and Dais, and community mobilization with group educational sessions and establishment of health committees and emergency transport funds. Strengthening of health facilities in intervention/control areas with training and upgrading equipment.	Hala and Matiari subdistricts, rural Sindh province, Pakistan Intervention: 2672 Control: 2462	Baseline skilled attendance 18% (30% endline in intervention areas) LHWs attended 12% of births in intervention areas (1.4% in control)	NMR 57.3	• Proportion of births with skilled attendant in public sector facility increased from 18 to 30% in intervention clusters • Antenatal care during pregnancy 79% in intervention villages vs 66% in control • Presence of LHW during delivery 12% in intervention areas vs 1.4% control	• Improvements in immediate breastfeeding (66% vs 21% in control), delayed bathing at least 4 hours after birth (50% vs 30% control), colostrums administration (76% vs 40%) • Newborn exam within 48 hours (56% vs 39%)	Bhutta et al. [83] 2008
Cluster randomized controlled trial (cRCT) of package of birth and newborn care preparedness (BNCP) interventions in Home vs Community care. In Home-care group CHWs provided antenatal visit, promoted BNCP, postnatal visits in first week of live, referred sick newborns, and treated sepsis at home with injectable antibiotics. In Community care arm, community mobilizers promoted BNCP in group sessions. In comparison and intervention arms improvement of government health facilities.	Rural Sylhet district, Bangladesh Home care: 14 880 Community care: 16 449 Comparison: 15 779	CHWs attended 5% of births	in study area NMR 48	• Higher proportion with an antenatal visit in Home care vs comparison arms at endline (72% vs 49%)	• Higher proportion taking iron-folate supplementation in home care vs comparison (84% vs 25%) • Delayed first bath at least until day 3 (78% vs 25%) • Breastfeeding within 1 hr (81% vs 57%) • Clean cutting of the umbilical cord (95% vs 61%)	Baqui et al. [80] 2008
cRCT of essential newborn care package delivered by CHWs via collective meetings, antenatal and postnatal visits. Extensive participatory social mapping and formative research conducted in local community to develop behavior change strategies for intervention package. Intervention clusters received either essential newborn care (ENC) package or ENC plus use of a hypothermia indicator.	Shivgarh, Rural Uttar Pradesh province India Total population of study area: 104 123	Baseline skilled attendance in all groups <5%	stillbirth 24.4 (ENC) 27.2 (control) NMR 64.1 (ENC) 54.2 (control)	• Increased Routine antenatal care checkup in ENC vs comparison (RR 1.84; 95% CI, 1.08–3.14) • Maternal Care seeking from nurse midwife in ENC vs comparison (RR 1.42; 95% CI, 1.09–1.85) • Delivery in Health Facility ENC vs comparison • (RR 1.41; 95% CI, 0.93–2.13)	Improved birth preparedness in ENC vs comparison • Identification of health facility (RR 3.43; 95% CI 2.12-5.54) • Identification of delivery supervisor (RR 5.79; 95% CI 4.16-8.06) • Identification of newborn attendant (RR 4.94; 95% CI 3.19-7.63) • Previous arrangement of money (RR 1.55; 95% CI 1.15-2.09) • Wiping of body right after delivery (RR 5.05, 95% CI 4.20-6.06)	Kumar et al. [13] 2008

Table 8
Evidence for impact of community health worker (CHW) packages: Mortality effect.

Intervention/study	Setting	Percentage skilled attendance	Baseline mortality rates	Mortality Effect: % Relative Reduction in Mortality Rate *(number of deaths in intervention or end-line group)*; RR or OR (95% CI)						Investigator and year
				SBR	ENMR	PMR	NMR	IPR-NMR	MMR	
Before-after study where CHWs made 3 post-natal home visits over the first month of life, performed essential care and screened for risk factors/referral; attended some births.	Rural India near Pune	25%	NMR 52	-	-	-	25% *(60)* RR 0.74 (0.52–1.04)		-	Pratinidhi et al. [92] 1986
Quasi-experimental controlled field trial of a package of newborn home-based care mainly implemented through trained and supervised CHWs. The package included health education of pregnant women and the community, attending delivery, neonatal resuscitation, essential newborn care and management of neonatal infections. Mortality as well as morbidity outcomes were recorded.	Rural India Maharashtra state Intervention area: 39 312 Control area: 42 520	< 5%	SBR 32 ENMR 37.5 PMR 68.3	49% [a] *(26)* RR 0.51 (0.34–0.69)	64% [a] *(22)* RR 0.36 (0.21–0.51)	50% [a] *(48)* RR 0.50 (0.35–0.71)	62% [a] *(25)* RR 0.48 (0.31–0.75)	48% [b] *(5)*	-	Bang et al. [82] [66] 1999
Longitudinal before-and-after comparison of package of newborn home-based care (extension of original observation period from above study). Baseline period (1993-1995): trained TBA using mouth-to-mouth resuscitation. Intervention: team of TBA and semi-skilled CHW; training of CHW in tube-and-mask (1996-1999) and later bag-and-mask (1999-2003) ventilation.	Rural India Maharashtra state 39 villages: total population 38 998; 4033 home births during study period	89-95% Home births, 92-97% conducted by TBAs; 77-84% attended by CHWs	NMR 52/1000 ASMR 10.5/1000 Incidence: "Mild birth asphyxia" 14.2% "Severe birth asphyxia" 4.6%	32.6% reduction in fresh stillbirth rate [c]				65% [d] reduction in IPR-NMR *(20)* 42% reduction in IPR-NMR with tube and mask *(37)* [e]		Bang et al. [90] 2005
Historical study of broad range of government sponsored activities to improve rural child health, including training of 54,000 community volunteers (Mitanins) to provide child survival interventions and essential newborn care, community mobilization, and family outreach/counseling	Chhattisgarh, Rural India Madya Pradesh	Not stated	IMR 95 in 2000				IMR 32% [g]			Sundararaman et al. [93] 2007
Cluster randomized controlled trial (cRCT) of package of birth and newborn care preparedness (BNCP) interventions in Home vs Community care. In Home-care group CHWs provided antenatal visit, promoted BNCP, postnatal visits in first week of live, referred sick newborns, and treated sepsis at home with injectable antibiotics. In Community care arm, community mobilizers promoted BNCP in group sessions. In comparison and intervention arms improvement of government health facilities.	Rural Sylhet district, Bangladesh Home care: 14 880 Community care: 16 449 Comparison: 15 779	CHWs attended 5% of births	Baseline in study area 48				Home Care arm 34% [h] *(82)* aRR 0.66 (0.47–0.93)			Baqui et al. [80] 2008
Quasi-experimental study training of Lady health workers (LHW, CHW) and Dais (TBAs) in home based newborn care (including basic resuscitation)[e], improvement of linkages between LHWs and Dais, and community mobilization with group educational sessions and establishment of health committees and emergency transport funds. Strengthening of health facilities in intervention/control areas with training and upgrading equipment.	Hala and Matiari subdistricts, rural Sindh province, Pakistan Intervention pop: 74 083 Control pop: 64 517	Baseline skilled attendance 18% (30% endline in intervention areas) LHWs attended 12% of births in intervention areas (1.4% in control) Baseline home births 79% (65% endline in intervention areas)	Baseline stillbirth 65.9 (intervention) Baseline NMR 57.3 (intervention)	35% [i] *(132)*	36.2% [i] *(90)*	34.6% [i] *(222)*	28% [i] *(121)*			Bhutta et al. [83] 2008
cRCT of essential newborn care package delivered by CHWs via collective meetings, antenatal and postnatal visits. Extensive participatory social mapping and formative research conducted in local community to develop behavior change strategies for intervention package. Intervention clusters received either essential newborn care (ENC) package or ENC plus use of a hypothermia indicator (TS).	Shivgarh, Rural Uttar Pradesh province India Total population of study area: 104 123	Baseline skilled attendance in all groups <5%	Baseline stillbirth 24.4 (ENC) 27.2 (control) Baseline NMR 64.1 (ENC) 54.2 (control)	ENC: 28% *(59)* RR 0.72 (0.52–.00) ENC + TS: 15% *(48)* RR 0.85 (0.56–1.29)	ENC: 44% *(51)* ENC + TS: 47% *(36)*	ENC: 41% *(113)* aRR 0.59 (0.47–0.74) ENC + TS: 38% *(96)* aRR 0.62 (0.47–0.81)	ENC: 54% *(64)* aRR 0.46 (0.35–0.60) ENC + TS: 52% *(48)* aRR 0.48 (035–0.66)			Kumar et al. [13] 2008

Abbreviations: SBR, Stillbirth Rate; ENMR, Early Neonatal Mortality rate; PMR, Perinatal Mortality Rate; NMR, Neonatal Mortality Rate; IPR-NMR, Intrapartum-related Neonatal Mortality Rate. [a] Comparison of rate in intervention vs comparison areas in last year of study 1997-1998. [b] Change in cause-specific NMR in intervention area from 1995-6 to 1997-8. [c] Data on "fresh" stillbirth only available after 1996 in intervention regions. Comparison in rate from 1996-1999 to 1999-2003. [d] Change in cause-specific NMR in intervention area from 1995-6 to 1997-2003. [e] Comparison of IPR-NMR in intervention vs comparison areas 1996-1999. [f] Comparison of IPR-NMR in intervention vs comparison areas 1993-1995. [g] Historical data and should be interpreted with caution as many other factors may have influenced the reduction. [h] NMR reduction in neonates receiving Home care was likely due to reduction in infection related deaths, given low birth attendance of CHWs (5%). [i] Before-after comparison in intervention arm.

While our recommendation for use of CHWs in programs to reduce intrapartum stillbirths and IPR-NMR is strong (Table 4), there is a need to further assess the effect and cost-effectiveness of community-based CHW packages on intrapartum-specific mortality and examine the mechanisms (e.g. better management in labor or better resuscitation) more closely under a variety of conditions. Furthermore, as with the other community-based providers, the linkages to the formal health system are paramount for the ultimate success of these programs.

4. Discussion

While striving to achieve universal skilled childbirth attendance, it may be years before this can be realized, particularly in rural, remote, and resource-limited settings. As part of health systems strengthening, the utilization and mobilization of community-based providers, including trained TBAs and CHWs, but preferably community-based SBAs, is a potential strategy to increase access to essential pregnancy and childbirth care for the poor, link pregnant women to the formal health system, and improve perinatal outcomes [3,9]. There is growing program experience and observational data that training SBAs in the community may reduce IPR-NMR by around 20%. The evidence is strong that CHWs help mobilize communities to seek care and provide essential newborn care—our new meta-analysis suggests approximately 30% reduction of PMR (Fig. 3A). There is lower quality evidence for neonatal resuscitation by CHWs [5]. While the role of TBAs is controversial, there is some evidence from a previous meta-analysis that trained TBAs may reduce IPR-NMR by 11% [63]. Additional evidence from a recent cRCT reports that when TBAs are linked with the formal health system, use of EmOC may be increased and associated with a similar PMR reduction (30%) [61].

In high mortality regions with low skilled birth attendance rates, increasing coverage of both community and facility-based care to 90% could avert up to 67% of all neonatal deaths [96]. Phased scale up of evidence-based community outreach services in parallel with continued health system strengthening may also reduce inequities in access for the rural poor [3,97]. Community and outreach care have been estimated to reduce neonatal deaths by around a third, and are feasible even in settings with weaker health systems [96]. Impact at community level may be further increased through adaptation and introduction of selected tools and technologies, including some that are currently in use in referral-level facilities (Fig. 3).

The primary prevention of intrapartum-related hypoxia by community cadres requires the rapid recognition of obstetric complications, functioning referral and transport systems, and timely access to CEmOC, including cesarean delivery in cases of severe complications. Studies of all three community cadres (i.e. community-based midwives, TBAs, CHWs) have demonstrated that with adequate training, danger signs can be identified during pregnancy and labor, and referral facilitated [10,19,22–29,33,36,40,52]. There is convincing evidence from cRCTs demonstrating that CHW interventions may mobilize communities to increase rates of care seeking and skilled birth attendance [83,98], and that properly trained and supervised TBAs can successfully identify and refer cases for CEmOC [61]. However, ongoing supervision remains a challenge, and cost-effectiveness data are needed. SBAs may monitor the progress of labor and reduce delays to CEmOC by directly providing potentially life-saving emergency obstetric interventions in the home or in birthing centers [29,40]; the private sector can potentially play an important role in the establishment of birthing centers (e.g. nursing homes in India) within the community. An unresolved issue is what proportion of community-based SBAs actually perform advanced interventions such as vacuum extraction, and what the competency, safety, and effect of conducting these procedures are in the home setting. This is a critical programmatic issue that requires improved monitoring, evaluation, safety, and cost-effectiveness evaluation, particularly as several national programs (Indonesia, Bangladesh) have been instituted to scale up SBAs in communities [10,20]. Finally, in cases of severely obstructed labor, operative delivery may be the only intervention to prevent intrapartum-related hypoxic injury, and community-based care must be adequately linked to CEmOC to reduce this burden; further consideration should be given to task shifting to cadres closer to the community to reduce this burden [4].

Community cadres may engage in the secondary prevention of intrapartum-related deaths by the early recognition of the non-breathing baby, and intervening through drying, stimulation, and/or provision of positive pressure ventilation [5]. There is low-quality evidence that neonatal resuscitation may be performed by community midwives [33], CHWs [99], and even potentially TBAs [60], resulting in reductions in IPR-NMR [5]. In a recent Delphi expert panel, community-based neonatal resuscitation was estimated to reduce IPR-NMR by 20% [100]. However, there are many programmatic and setting-specific considerations, including the effect of this approach on long-term neuro-developmental outcomes that must be carefully weighed in regions where births commonly occur at home and resources are limited. Neonatal resuscitation and specifically programmatic issues in the implementation of this intervention in low-resource settings are discussed in detail in the third paper in this Supplement [5].

The success of maternal-child health interventions within a community requires a careful understanding of the local culture and customs surrounding childbirth and the role of key stakeholders [13]. Interventions should be developed for and tailored to the epidemiological context of the local setting and the cultural beliefs and practices surrounding the disease process, and be targeted to reduce risk factors for mortality. Traditional birth practices for the baby who is not breathing at birth may vary widely between cultures (see first paper in this Supplement). While many practices are healthy methods of physical stimulation, others may be harmful for the newborn or delay the time to a more appropriate action, such as establishing effective ventilation. Framing community-based interventions for intrapartum-related hypoxia within local beliefs and customs may increase the adoption of healthy community practices and acceptance of interventions by community-based providers and families.

Innovative tools and technology are an important potential means for increasing coverage of effective interventions. Developing and adapting tools and technologies for use in more peripheral health systems settings may help bring pregnant mothers in the community closer to facility care, such as the use of cellular phones or resourceful transport vehicles like bicycle stretchers. This approach may also bring improved childbirth care directly to the home, such as clean birth kits, home birth and immediate newborn care kits with bag-and-mask and suction devices, or Doppler ultrasound-fetal heart rate monitors. Several key current tools in use and future development needs are highlighted in Fig. 4.

There are many considerations and challenges to feasibility and scale up of community-based interventions during pregnancy and childbirth that will reduce the effect of intrapartum-events, and several are highlighted in Table 9. First, the availability and skill capacity of the existing cadre providing childbirth care in the community must be carefully considered. While the ideal cadre is the SBA or midwife, in most low- and middle-income settings there is insufficient human resource capacity to staff hospital facilities and, thus, even lower potential to retain skilled providers in remote or rural settings. In some settings, TBAs may already attend the majority of births, and incentives may be offered to engage them in the formal health system to encourage partnership with CHWs, midwives, or medical doctors and change behaviors with culturally contextualized training programs; however, evidence for the effect of such an incentivized approach is needed. Secondly, the skills and competence of community cadres need to be carefully evaluated, monitored, and supervised. Whether ranging from danger sign recognition to neonatal resuscitation or extensive measures such as administration of uterotonics or assisted delivery, training does not equate to adequate

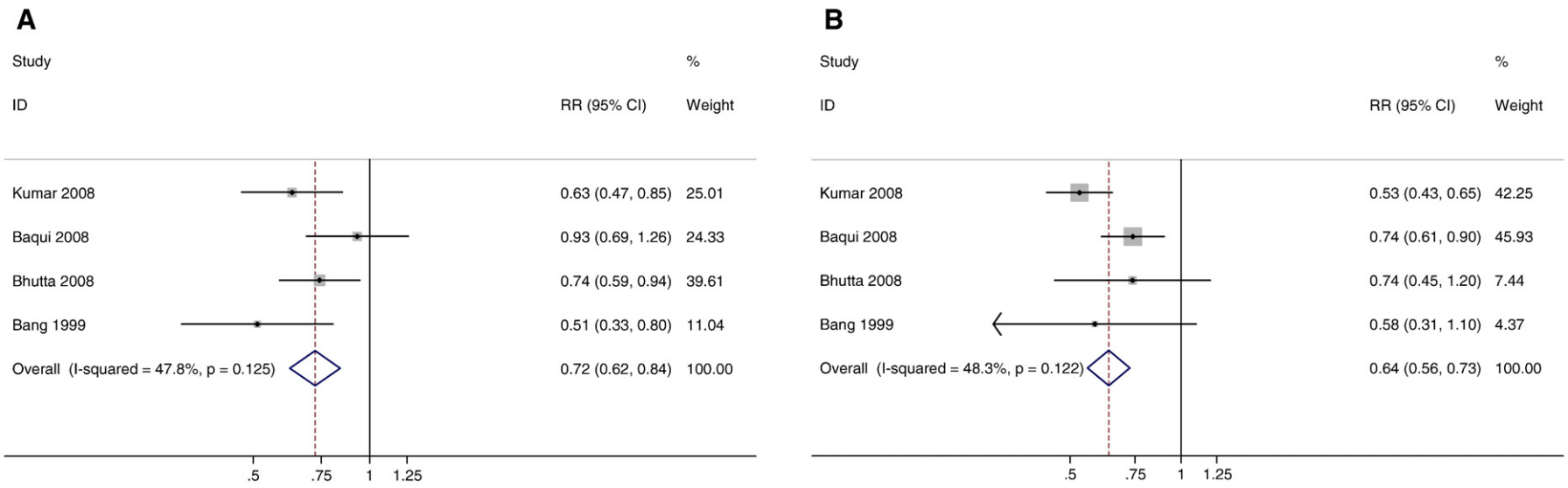


Fig. 3. Meta-analysis of mortality effect of community health worker packages. (A) Perinatal mortality. (B) Early neonatal death.

care provision, and skill competence, retention, and health outcomes must be carefully monitored and ongoing retraining and supervision ensured [19].

5. Conclusion

The majority of maternal and newborn deaths occur in regions where most births occur outside facilities and without skilled childbirth care. In systems with the resources to train SBAs, community midwives may provide elements of EmOC, which may have the potential to avert intrapartum-related stillbirth and neonatal deaths, although the evidence is presently limited. Other community cadres may be formally linked to the healthcare system, and their roles may be adapted and/or enhanced to include community education and empowerment, identification and referral for obstetric complications, birth and newborn care preparedness, or even neonatal resuscitation. These strategies have proven to be effective in several cRCTs with CHWs and/or TBAs. Community-based approaches require a functioning continuum of care and effective linkages with CEmOC health facilities. More research is needed to determine the cost-

Current Technology/Tools	Development needs
Preparation for birth	
Community mobilization materials e.g. puzzles used in Nepal Communication tools such as folk songs used to disseminate birth preparedness messages 	Generic set of community mobilization materials for local adaptation organized per visit (e.g. 2 during pregnancy and 2-3 after birth) Generic communications toolkit for local adaptation Effectiveness of picture cards for counseling and recognizing complications with mother and newborn.
Identifying complications and facilitating referral	
Communication technology such as 2 way radios or cell phone technologies (see Paper 4) Transport vehicles and mechanisms for pregnant women (stretchers, bicycle ambulances, motorcycle ambulances) (see Paper 4) [6] 	Refine and test information communication technology tools and approaches in various settings. Lower cost Local adaptation and production Effectiveness of picture partograph for recognition of complications during labor and childbirth.
Home Births	
Clean birth kit (ideally locally made and marketed) • Plastic sheet • New/sterilized blade • Soap • Sterilized cord tie • Pictographic instructions with behavior change messages on hygiene and use of items in the kit 	Evaluate use of clean birth kits by various cadres for effectiveness and cost Evaluate barriers to community demand and inform strategies to overcome them
Home birth and immediate newborn care kit (in addition to clean birth kit) • Low-reading Digital thermometer • Weighing scale • Simple suction device • Bag-and-mouth device • Pictographic instructions on danger signs for referral to facility 	Evaluate use of home birth and immediate newborn care kits by various cadres for effectiveness and cost Advance designs for low cost, robust fetal heart rate monitors, ultrasound for pelvimetry, and user-friendly blood pressure devices Test use of needle-free or simplified injection technology (eg Uniject for administering oxytocin or antibiotics)
Equipment for birthing center or first level facility with skilled attendants • Doppler ultrasound-fetal heart rate monitor • Oxytoxin for active management of third stage of labor 	Test effectiveness of oral misoprostol for postpartum hemorrhage

Community mobilization maternal and partograph images reprinted with permission granted by Uganda MoH/Save the Children, clean birth kit image reprinted with permission granted by Program for Appropriate Technology in Health (PATH), home birth kit image reprinted with permission granted by SEARCH, Gadchiroli, India, Doppler ultrasound-fetal heart monitor image reprinted with permission granted by Healthcheck Systems/www.healthchecksystems.com

Sources: PATH. 2001. Basic Delivery Kit Guide. Washington, DC: PATH.
PATH. Birth weight scale

Fig. 4. Community level care: Tools, technologies, and further development innovations required.

Table 9
Implementation considerations for programs.

Skilled Birth Attendants	Provider qualifications • Supply of potential candidates/skilled providers for training • Existing cadres • Selection and prerequisite education, medical experience Training • Duration, methodology and quality of training – lecture vs clinical • Soft skills – counseling, negotiation, behavior change management • Skill retention and need for frequent re-training • Frequency of births • Need for supervision and mentoring • Referral management Scope of practice (Basic emergency obstetric care, BEmOC) • Performing of assisted births (vacuum, forceps) in community setting • Partograph use • Oxytocin administration • Anti hypertensive medications for pre-eclampsia • Manual removal of placenta • Neonatal resuscitation Retention and quality of care • Work force retention in rural areas, eg compensation, incentives, professional development • Quality audits • Community appraisal Linkages with community • Synergy with other cadre of community-based health providers • Partnership and dialogue with key stake-holders for optimal utilization of community resources Linkages with health system • Access to emergency fund, referral and transport systems to EmOC • Capacity, timeliness and quality of emergency obstetric care • Clinical audit and quality assurance Monitoring and Evaluation • % births attended, maternal and neonatal outcomes • Procedures and resuscitation conducted, competence • Key indicators: intrapartum stillbirths, early neonatal death, neonatal encephalopathy
Traditional Birth Attendants	Provider qualifications • Education level, literacy • Living within community • Linkages with other cadres, and relationships • Volume of births conducted • Preferred care provider by community Training • Modification of her current practices by incorporating useful techniques and skills and avoiding harmful practices and advocating towards shifting social norms • Scope of training – e.g. counseling, behavior change, detection and referral, or also additional skills • Sustaining acquired skills and practices, skill retention and need for re-training, motivation of behavior change • Need for supervision and mentoring Retention • Compensation, incentives, Linkages with health system • Access to emergency funds, referral and transport systems • Incentives for referral Monitoring and evaluation • % births attended, outcomes, newborns resuscitated if relevant, maternal and neonatal outcomes • Proportion of pregnancies attended, uptake of ANC by mothers • Adherence to safe birthing practices • Number of appropriate referrals made for labor-delivery complications • Key indicators: intrapartum stillbirth, early neonatal death, neonatal encephalopathy
Community Health Workers	Provider qualifications • Education level, literacy • Living in community • Existing cadres, and relationship with them Training • Duration and methods of training • Participatory action learning cycle methods to lead community groups • Behavior change management skills (including communication and negotiation skills) birth preparedness and recognition of danger signs • Neonatal resuscitation if appropriate and likely to be present at birth • Competence, skill retention and need for frequent re-training, supervision-mentoring Retention • Compensation, incentives Linkages with health system • Access to emergency fund, referral and transport systems to EmOC • Incentives for referral Linkages with community • Synergy with other cadre of community-based health providers • Partnership and dialogue with key stake-holders for optimal utilization of community resources Monitoring and evaluation • % high risk cases screened during antenatal period • % sought appropriate and timely care from trained providers • % births attended; % facility births; maternal and neonatal outcomes • Number of referrals made and followed (for labor or delivery complications) • Number of infants resuscitated at home and transported to higher center • Key indicators: intrapartum stillbirths, early neonatal death, neonatal encephalopathy

effectiveness, sustainability, scalability and long-term impact, including neurodevelopmental outcomes, of such approaches. While the goal is to have a skilled attendant at every birth, innovative community strategies with health systems strengthening may provide childbirth care to the poor, help reduce the gross inequities in maternal and newborn survival and stillbirth rates, and provide an effective transition to higher coverage for facility births.

6. Conflict of interest

All authors have no conflicts of interest to declare.

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INTRAPARTUM-RELATED DEATHS: EVIDENCE FOR ACTION 6

Perinatal mortality audit: Counting, accountability, and overcoming challenges in scaling up in low- and middle-income countries

Robert Pattinson [a,*], Kate Kerber [b], Peter Waiswa [c,d,e], Louise T. Day [f], Felicity Mussell [f], Sk Asiruddin [g], Hannah Blencowe [h], Joy E. Lawn [b,i]

[a] MRC Maternal and Infant Health Care Strategies Research Unit, University of Pretoria, Pretoria, South Africa
[b] Saving Newborn Lives, Save the Children-US, Cape Town, South Africa
[c] Makerere University School of Public Health, Kampala, Uganda
[d] Iganga District Health Department, Iganga, Uganda
[e] International Health, Department of Public Health Sciences (IHCAR), Karolinska Institute, Sweden
[f] LAMB Hospital, Parbatipur, Dinajpur District, Bangladesh
[g] Saving Newborn Lives, Save the Children-US, Dhaka, Bangladesh
[h] London School of Hygiene and Tropical Medicine, London, UK
[i] Health Systems Research Unit, Medical Research Council of South Africa, Cape Town, South Africa

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ABSTRACT

Background: In high-income countries, national mortality audits are associated with improved quality of care, but there has been no previous systematic review of perinatal audit in low- and middle-income settings. *Objectives:* To present a systematic review of facility-based perinatal mortality audit in low- and middle-income countries, and review information regarding community audit. *Results:* Ten low-quality evaluations with mortality outcome data were identified. Meta-analysis of 7 before-and-after studies indicated a reduction in perinatal mortality of 30% (95% confidence interval, 21%–38%) after introduction of perinatal audit. The consistency of effect suggests that audit may be a useful tool for decreasing perinatal mortality rates in facilities and improving quality of care, although none of these evaluations were large scale. Few of the identified studies reported intrapartum-related perinatal outcomes. Novel experience of community audit and social autopsy is described, but data reporting mortality outcome effect are lacking. There are few examples of wide-scale, sustained perinatal audit in low-income settings. Two national cases studies (South Africa and Bangladesh) are presented. Programmatic decision points, challenges, and key factors for national or wide scale-up of sustained perinatal mortality audit are discussed. As a minimum standard, facilities should track intrapartum stillbirth and pre-discharge intrapartum-related neonatal mortality rates. *Conclusion:* The effect of perinatal audit depends on the ability to close the audit loop; without effectively implementing the solutions to the problems identified, audit alone cannot improve quality of care.
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1. Introduction

Each year an estimated 904 000 neonates die soon after birth as a result of intrapartum-related neonatal death, previously loosely termed "birth asphyxia" [1]. These deaths are closely linked to at least 1.02 million intrapartum stillbirths occurring during the time of labor, giving a total of nearly 2 million stillbirths and neonatal deaths related to acute intrapartum events, primarily in low- and middle-income countries [2]. In addition, an unknown number of "near-miss" babies survive the hypoxic event, only to suffer long-term impairments that prevent attainment of their educational potential [3]. When these deaths occur in high-income countries, they are usually reported and investigated. In low-income countries most neonates are born and die without any record [4]. Peer reviewed literature has drawn attention to the absence of reliable data for births, deaths, and causes of death, and the need to count and account for these deaths to set priorities for action and strengthen health systems [5].

While neonatal deaths due to infection and preterm complications have solutions that can potentially be taken to scale [6], even in weak health systems [7], solutions for intrapartum-related outcomes are more challenging and require strengthening the quality and responsiveness of the health system at all levels [8]. Mortality audit and feedback appears to be a promising tool to address delays and suboptimal care practices, given that lack of progress in addressing both neonatal and maternal deaths is often attributed to the need for better individual case management around the time of birth. However, the

* Corresponding author. MRC Maternal and Infant Health Care Strategies Research Unit, University of Pretoria, Gauteng, South Africa. Tel.: +27 12 373 1002; fax: +27 12 373 1045.
E-mail address: robert.pattinson@up.ac.za (R. Pattinson).

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use of audit has been limited in low- and middle-income countries, and yet this is where 98% of the world's maternal deaths, stillbirths, and neonatal deaths occur.

National enquiries into maternal deaths, stillbirths, and neonatal deaths have been used in high-income countries for decades [9]. In low-income countries, experience with mortality audit has been tried primarily at the facility level, often limited to tertiary or referral centers, and has more commonly focused on maternal deaths, notably influenced by the World Health Organization's "Beyond the Numbers" guide for reviewing maternal deaths in low-resource settings [10]. Perinatal mortality audit has been used less frequently and its implementation in low-income countries a community research site. However, there are notable examples of audit at scale in such countries. Furthermore, given that 60 million births occur outside facilities each year, there are a growing number of strategies for examining avoidable factors outside facilities and even conducting mortality audits at the community level.

1.1. Objective

This paper is the sixth in a series that focuses on reduction of intrapartum-related neonatal deaths. Here we present the results of a systematic review of perinatal mortality audit in low- and middle-income settings to facilitate health system strengthening, particularly at the time of birth, and examine the effect on perinatal outcomes, particularly intrapartum-related, where data allow. We intentionally focus on the potential for wide-scale, sustainable implementation in low- and middle-income settings, discussing two national case studies.

2. What is perinatal mortality audit?

The principal aim of audit in the healthcare setting is to identify deficiencies and address them to improve the quality of care provided [9]. Audit can be a means to increase efficiency, or improve patient satisfaction, or to save lives. Types of audit include:

- *Structural audit*, which includes an examination of the resources in the system;
- *Satisfaction audit* involving surveys or focus groups to obtain users' views about the quality of care they have received;
- *Process audit* to assess case management;
- *Outcome audit* to identify the end results of care.

Perinatal audit has been defined as: "The systematic, critical analysis of the quality of perinatal care, including the procedures used for diagnosis and treatment, the use of resources and the resultant outcome and quality of life for women and their babies" [11]. Outcome audit is often the first priority to determine a profile of facility-based causes of death. The outcome in perinatal mortality audit is death. It is simpler to use as there is little difficulty in defining the end point compared, for example, with morbidity. In the future, as perinatal mortality rates improve in low-income settings, there will be a need to focus on morbidity or "near miss" as an outcome for audit. Neonatal "near-miss" definitions have been used either for a specific condition like neonatal encephalopathy, or neonatal care in general [12–14].

In an ideal situation, the quality of care provided to all babies would be assessed. Focusing on deaths and making every death count is a justifiable alternative—but it is more feasible in high-income settings where perinatal deaths account for around 0.5% of births, compared with low-income countries where perhaps 10% of births may result in perinatal death, and the health staff are already few and under pressure. One facility-based audit in Tanzania found that among 385 perinatal deaths, 3 mothers died [15]. Where perinatal mortality is high, the assumption is that the factors related to each individual death are widespread and not particular to the specific case. Thus, the correction of factors involved in one death has the potential to improve the quality of care for many pregnant women and babies. This assumption may be less valid in high-income settings and some middle-income countries when related to maternal death, where deaths may be linked to fewer modifiable factors [16].

This paper focuses on perinatal mortality audit. The classic audit cycle can be adapted for perinatal audit with 6 steps, forming a circle or ideally an upward spiral of continuous improvement (Fig. 1):

Step 1: Identify perinatal deaths as well as ensure all births are recorded.

Step 2: Collect information on causes of death and avoidable or modifiable factors using a standard classification system.

Step 3: Analyze the results and generate mortality rates and trends over time.

Step 4: Recommend solutions to address modifiable factors.

Step 5: Implement recommendations arising from the modifiable factors identified.

Step 6: Evaluate and refine the process.

Information on clinical history, case management, and findings are captured either on paper or electronically. These data can remain at the point of collection or be compiled regionally or nationally for analysis and review. Either all cases or a selection of cases are discussed at a multidisciplinary meeting with a purpose toward improving future management rather than assigning blame [17].

Outcome audit can be combined with an analysis of factors contributing to avoidable deaths, modifiable factors, or substandard care. Wilkinson defines an avoidable death as one that is "judged to be directly due to an error or omission on the part of the health service" [18]. To determine which deaths could have been avoidable, a criterion-based audit is used to measure quality of care against explicit standards [19]. The term "modifiable factors" is preferred as a positive alternative to "avoidable factors" in many settings to indicate that there is an action that can be taken to correct the problem. Recognizing modifiable factors could open pathways to primary or secondary prevention of the identified causes of death or near misses.

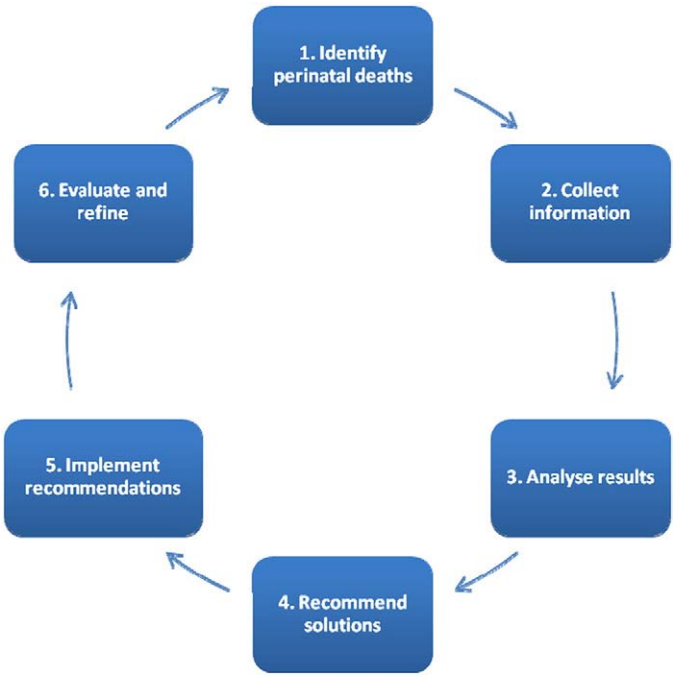

Fig. 1. Six-step cycle for perinatal mortality audit.

3. Evidence for audit

Searches of the following medical literature databases were conducted: PubMed, Popline, EMBASE, LILACS, IMEM, African Index Medicus, Cochrane, and WHO documents. The details of the search strategy and selection criteria for inclusion of papers are described in detail in the first paper in this series [8]. Keyword searches relevant for this paper included "perinatal," "neonatal," "stillbirth," "asphyxia,"

Table 1
Evidence for the impact of facility-based perinatal audit in low- and middle-income countries.

Intervention and type of study (data order)	Setting	Skilled birth attendance	Mortality effect (% reduction)					Outcome notes	Investigator and year
			SBR	ENMR	PMR[a]	NMR	MMR		
Comparison of avoidable perinatal deaths in hospital between 1971–76 and 1977–79.	Iringa, Tanzania, Lugarawa hospital, population of 75 000 (1971–1979)	24%	–	–	***44%***	–	–	1971–76 audit data showed high rate of avoidable intrapartum stillbirths. PMR declined with use of a partograph and standard protocols	Van Roosmalen [50] 1989
Before and after evaluation of maternal and child health project with regular audit and self appraisal. Crude birth rate declined 28% during intervention period, and primary focus was on family planning.	Lahore, Pakistan. 8 urban and 2 rural areas with population ~6000 (1984–1987)	–	–	–	**–**	–	61% [x]	[x]Number of cases not given. Infant mortality rate 41% reduction	Awan et al. [51] 1989
Examination of the effect of a routine, internal audit of perinatal deaths to identify avoidable factors.	Lebowa, a South African district hospital and clinics (10 months)	–	–	–	***31%****	–	–	*Perinatal deaths with potential avoidable factors decreased from 30% to 13%	Wilkinson [32] 1991
Data from the delivery register summarized at weekly meetings and then complied. 1982 data capture of perinatal deaths incomplete. Cesarean deliveries increased from 7% to16%.	Maputo, Mozambique. Maputo Central Hospital with 134 408 births registered (1982–1991)	>90%	61%[+]	–	***20%***[x]	–	–	[+]Intrapartum SBR only [x]Overall PMR remained constant – attributed to Mozambique war and an increase in fetal deaths due to STIs. PMR declined from 1983 (first year with full data collection) compared with 1990 (last year before war effect). Paper reports 20%, data gives 17% Most effect on IP SBs	Bugalho and Bergstrom [36] 1993
Retrospective assessment of perinatal audit over 2 years utilizing the Identification, Cause, Avoidable Factor (ICA) solution system on perinatal deaths (n=1060).	Port Elizabeth, South Africa. Central referral hospital and 2 district hospitals with 22 585 deliveries assessed (1991–1992)	_	55%*	_	***24%***	_	_	*Intrapartum fetal deaths	Ward et al. [52] 1995
Internal audit of deliveries >1000 g with avoidable factors defined and analyzed and software system tested.	Pretoria, South Africa. Urban population (1992–1994)	>90%	–	–	***38%***	–	–	Pilot for later scale-up of PPIP system in South Africa	Pattinson et al. [45] 1995
Assessment of quality of care improvement based on audit recommendations from perinatal deaths (n=653) involving rearrangement of the district maternity service, implementing protocols, and regular in-service education.	Hlabisa, South Africa. Hlabisa Hospital, 8 village clinics, and 20 mobile clinic points with 21 112 consecutive births (May 1991–Dec 1995)	–	–	–	***39%***	–	–	Proportion of perinatal deaths occurring in clinics decreased over this time from 17% in 1995 to 6.3% in 1991. PMR reduced 39% from 1992 (when number of high-risk deliveries stabilized – previously all high-risk deliveries transferred out to other facilities) to 1995	Wilkinson et al. [18] 1997
Description of rates and causes of perinatal mortality using classification according to Wigglesworth classification.	Kathmandu, Nepal. Teaching hospital (2003–2005)	–	–	56%	38%	*	–	*Intrapartum-related neonatal deaths from decreased from 41% to 13% Cesarean deliveries from 26% to 30% over this period Excluded from meta as inadequate numerator/ denominator data in the paper	Shrestha et al. [53] 2006
Weekly multi-disciplinary perinatal mortality reviews with classification of modifiable factors.	Kampala, Uganda. Nsambya Hospital (2008–2009)	56%	–	–	32%	–	–	Excluded from meta as inadequate numerator/ denominator data available	Byaruhanga and Nakibuuka (unpublished)
Perinatal mortality audit using South African PPIP software and cases presented at monthly multi-disciplinary meetings.	Bangladesh. LAMB Hospital, 23 731 babies >1000 g. (2001–2008)	32%	34%	1%	***26%***	–	–	Most of the reduction in PMR was related to SBR reduction	Mussell et al. (unpublished)

Abbreviations: SBR, stillbirth rate; ENMR, early neonatal mortality rate; PMR, perinatal mortality rate; NMR, neonatal mortality rate; MMR, maternal mortality ratio; PPIP, Perinatal Problem Identification Programme.

[a] PMR data in bold italics included in meta-analysis (see Fig. 2) also with 95% confidence intervals.

"mortality audit," and "death audit." Each study was assessed and graded according to the CHERG adaptation [20] of the GRADE technique [21]. We conducted a random effects meta-analysis using STATA version 10.0 statistical software (STATA Corp, College Station, TX, USA) and report the Mantel-Haenszel pooled risk ratio and corresponding 95% confidence interval (CI).

Assessment of the impact of perinatal mortality audit is complex because the audit cycle and implementation of recommended actions are rarely carried out as part of a randomized trial [22] and other factors may also contribute to a measured reduction in mortality. One recent systematic review of interventions to prevent stillbirths identified 1 review and 12 intervention studies on the impact of perinatal mortality audit, with the majority from high-income countries. The authors reported some evidence of benefit of mortality audit through changes in clinical practice and strongly recommended the practice of mortality audit where practical [23].

3.1. Perinatal mortality audit at the facility level

3.1.1. Evidence of mortality effect

Facility-based mortality audit often begins with a single individual or team coordinating data collection and review meetings that are most commonly conducted at referral or academic centers. A number of studies from high-income settings have shown that perinatal mortality audit is feasible and effective in reducing deaths [24–31]. There are fewer studies from low- and middle- income countries. Ten studies reporting the impact of facility-based perinatal mortality audit on maternal, perinatal, or infant outcomes were identified, including two unpublished datasets identified through conference proceedings (Table 1). All recorded a reduction in deaths following the introduction of perinatal mortality audit, which raises the issue of publication bias as an audit with no measured change is less likely to be published or presented.

Seven low quality or very low quality before-and-after studies were identified that reported improvements in perinatal mortality and with adequate numerator and denominator data. The quality of evidence was upgraded to low/moderate since the effect sizes were very consistent and the studies were from multiple regions. These studies were combined in a random effects meta-analysis with a resultant relative risk of 0.70 (95% CI, 0.62–0.79) (Fig. 2).

3.1.2. Experience in perinatal audit process and sustainability

Perinatal mortality audit in a rural district hospital in Eastern Cape, South Africa, was associated with a significant reduction in avoidable perinatal deaths over a 10-month period in 1991. Perinatal mortality fell by 32% and avoidable factors reduced from 28% to 13% of perinatal deaths [32]. The mortality audit process informed the intervention strategies, an important part of which was training midwives to advanced diploma status using the distance-learning Perinatal Education Programme [33]. More recently, Murchison Hospital in KwaZulu-Natal province has seen a substantial decline in perinatal deaths after commencement of a mortality audit process in 2003. This included introducing the Perinatal Problem Identification Programme (PPIP), which involves a database for perinatal mortality audits and monthly perinatal mortality meetings, conducted in a no-fault atmosphere. Meeting attendance was compulsory for all healthcare providers in the hospital and a representative from each clinic. Mortality meetings were accompanied by in-service training on the use of the partograph, interpreting fetal heart rate patterns, neonatal resuscitation, and newborn care. Midwives displayed perinatal care indices on bar charts on the wall of their labor ward, and these were updated monthly after the mortality meeting. The total perinatal mortality rate (PMR) decreased from 42 per 1000 births in 2003 to 29 per 1000 births in 2007/08. Early neonatal mortality rate (ENMR) declined by half and deaths due to intrapartum asphyxia and trauma showed a 26% reduction (from 8.7 to 6.4 per 1000 births) [34].

In North-West Bangladesh, LAMB is a 150-bed general hospital, which includes a comprehensive emergency obstetric care unit that is part of an integrated rural health and development project serving a community population of 600 000 with 13 Safe Delivery Units with obstetric first aid, bringing care closer to home. In the region, the use of skilled birth attendance was 32% in 2007, which was higher than the national average of 18%. Since January 2001, all maternal and perinatal (>1000 g birth weight) deaths have been audited. Primary obstetric and final causes of death are coded and modifiable factors are identified by a consultant obstetrician. Cases with learning points are presented at a monthly multidisciplinary meeting in a confidential and non-blame environment. Data are analyzed using South Africa's PPIP software. From January 2001 to December 2008, 23 731 neonates were born at LAMB Hospital. The perinatal mortality rate at the facility was 75 per 1000 births and stillbirths accounted for two-thirds of perinatal deaths (47 per 1000 births). Of the stillbirths 46% were dead on admission to the facility and another 18% died in labor after admission. Facility perinatal mortality and stillbirth rates have decreased significantly since the introduction of audit (Table 1, Fig. 3). The data show an increase in mortality around 2003, which is likely to be a measurement artefact due to improved information capture. The decreases between 2001 and 2008 are statistically significant for the stillbirth rate (χ^2 for linear trend = 25.8; $P<0.001$) and overall perinatal mortality (χ^2 for linear trend = 22.6; $P<0.001$). The leading causes of perinatal mortality are hypoxia (48%), preterm birth complications (22%), and infection (15%). Probable modifiable factors were present in 45% of cases and possible modifiable factors in 80% of

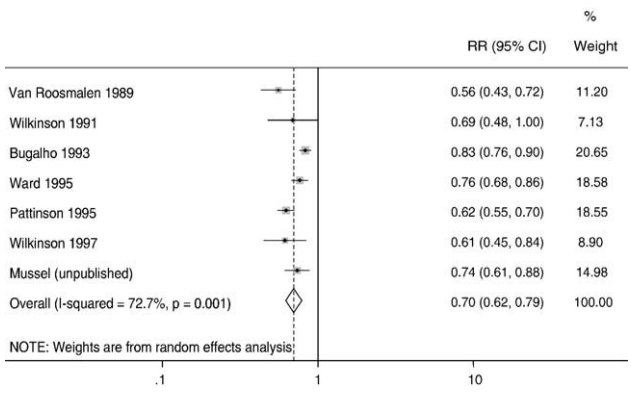

Fig. 2. Meta-analysis of the effect on perinatal mortality rate associated with introduction of perinatal audit in low- and middle-income countries. Notes: Bugalho 1993: Results from 1983 (the first year of full data collection) to 1990 (the last year before the effects of the civil war). Wilkinson 1997: Results comparing 1992 (when number of high-risk deliveries stabilized – previously all high-risk deliveries transferred out to other facilities) with 1995.

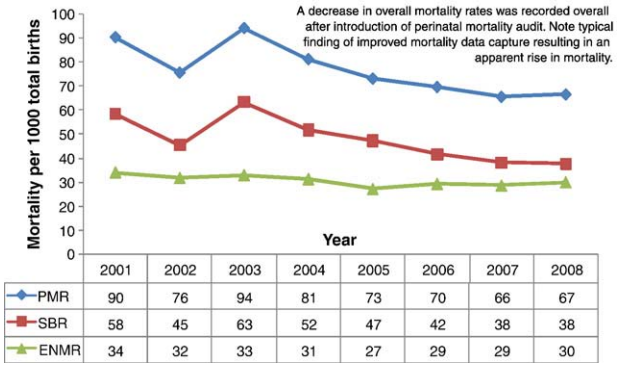

Fig. 3. Perinatal and early neonatal mortality rate and stillbirth rate at LAMB Hospital, Bangladesh. Abbreviations: PMR, perinatal mortality rate; SBR, stillbirth rate; ENMR, early neonatal mortality rate.

Table 2
Community audit – small scale examples from Africa and Asia.

Verbal and social autopsy in research settings
Guinea pathway to survival The Guinea Ministry of Health together with Save the Children and BASICS conducted a verbal and social autopsy of 330 deaths among children younger than 5 years old in Mandiana, Guinea, from October 1998 through September 1999 [54]. As well as mortality rates and direct causes, the delays along the pathway to survival were assessed. Almost two-thirds (61%) of children were never taken to a health facility before death, although most sought some care outside the home. The lowest care-seeking was for "birth asphyxia" with only 9% being taken outside the home compared with 83% for pneumonia and 76% for diarrhea. Over one-third of children who visited a health facility received average to poor treatment. This study did not examine stillbirths.
Uganda social autopsy A pilot project in the Makerere University-operated Iganga/Mayuge Demographic Surveillance Site (DSS) investigated the care-seeking delays and causes contributing to 64 neonatal deaths using social autopsy. A panel of 2 physicians employed verbal autopsy using a hierarchical model to determine direct causes of newborn deaths. The leading causes of death were sepsis or pneumonia (20/64, 31%) and birth asphyxia (19/64, 30%), preterm births (16/64, 25%), and in 6 cases (9%) a cause of death could not be determined. In addition social autopsy was used as a tool to supplement the direct cause-of-death data to understand modifiable factors at household/community and health facility levels. They used a modified "3 delays" model [55] to identify the delays contributing to newborn death. Delay 1 (delay in deciding to seek care outside the home) was the greatest contributor to death (32/64, 50%), followed by delay 2 (delay in transportation to the health facility) (19/64, 30%), whereas delay 3 (delay in receiving care after arriving at a facility) contributed to (13/64, 20%) of deaths. Among the 19 intrapartum-related ("birth asphyxia") deaths, the distribution of delays was similar (7 deaths for delay 1 and 6 deaths for each of delays 2 and 3) .There were more intrapartum-related deaths in health facilities (11/19) than in the community (8/19). However, the study had limitations, including a small number of newborn deaths and excluding stillbirths. The process was descriptive, and did not link back to community action, although this will be included in the larger newborn care study commencing in the same site.
Participatory audit involving the community
Community audit in Uttar Pradesh A community level "Social Audit for Community Action" was conducted in rural Uttar Pradesh [56]. Community members from 152 villages were asked to recall the causes of deaths among children under 5 years in the prior year and identify preventive measures that could have been taken by the family or community. Intrapartum-related events accounted for 13.5% of neonatal deaths. Delay in recognizing the seriousness of the problem and arranging for transport and funds were identified as major contributors of neonatal deaths and to be targeted for behavior change by the community mobilizers. Another study to examine the feasibility of community audit was undertaken in Shivgarh, Uttar Pradesh, India involved in-depth interviews with family members of deceased neonates, and focus group with family and community members [38]. Approaches involved the community in identifying avoidable factors in each death and discussing solutions. Community neonatal death audit was found to be acceptable and feasible. Presence of an educated/experienced community member or health worker served as a catalyst.

cases. Leading modifiable factors were patient related: not initiating prenatal care (32%), delay in seeking medical attention in labor (17%). Medical personnel-associated avoidable factors included not detecting fetal distress in the intrapartum period despite intermittent fetal monitoring. One strategy identified through audit that has improved patient management has been the improvement of clinical guidelines [35]. There is still the ongoing challenge of a large burden of perinatal deaths in the comprehensive emergency obstetric care facility, and the unaddressed emotional burden on staff.

Perinatal mortality audit can be sustained and effective in low-resource settings. One study from Maputo Central Hospital, Mozambique, analyzed changes in mortality over 10 years of maternal and perinatal mortality audit through weekly meetings and regular feedback of perinatal data via wall charts [36]. Over this time period, a 61% reduction in intrapartum fetal deaths and a 20% reduction in perinatal mortality overall were recorded. While many factors may have played a role, the authors cite frequent open communication between obstetric and pediatric staff and involvement of staff at all levels as contributing to this large decline.

Nsambya Hospital, a large tertiary mission hospital in Kampala, Uganda, has been conducting maternal audits for several years, and introduced perinatal and under-5 mortality audits in 2008. Weekly perinatal death reviews were conducted by a team of midwives, pediatricians, administrators, and obstetricians to identify gaps, mistakes, and cause of death. A total of 120 perinatal deaths were audited, almost equally split between macerated stillbirths, fresh stillbirths, and neonatal deaths. "Birth asphyxia" or intrapartum-related neonatal deaths accounted for around 30% of the neonatal deaths. The introduction of perinatal audit was associated with a 32% reduction in perinatal mortality rate from 62 per 1000 total births in 2007 to 42 per 1000 total births in 2008 (Table 1) [37].

3.2. Perinatal mortality audit at the community level

Sixty million women around the world still give birth at home each year and in low-income countries the majority of births and perinatal deaths occur at home or soon after admission. Babies that die at home are often not captured in any health records. Social audits may be used at the community level as a tool to identify strategies for community motivation of behavior change, or for addressing delays and promoting linkages for care. Community audit can be difficult to implement because of multiple role-players, but if conducted in a culturally acceptable and participatory process, audit is feasible, empowering, and may lead to behavior change [38]. This can be a descriptive process to gather information, as seen in Guinea and Uganda, or a participatory activity involving community members in implementing change as in rural Uttar Pradesh, India (Table 2). Verbal and social autopsy are tools used in community-level perinatal mortality audit to ascertain the cause of death profile as well as contextual factors such as care-seeking delays related to these deaths. An audit cycle is used to translate that information into recommendations and action, involving community members in the quality improvement process.

In Malawi, the "Safe Motherhood from below" project used a local music and drama troop to facilitate community meetings to discuss maternal and early infant deaths, and discuss actions needed to avoid another death. For example, discussing the death of a woman caused by infection after surgical delivery in hospital led to improvements in the hospital sterilizing equipment, a new refrigerator for the blood bank, and the provision of antibiotics to rural clinics so that treatment could be commenced earlier [39].

In the "Mother Care Indonesia" project, both facility and community maternal and perinatal mortality audits were conducted as part of a district-based strategy to reduce mortality and improve care [40]. A sector-wide approach was undertaken that involved community members, such as village and religious leaders, in discussing the deaths and possible solutions. The audits led to changes in obstetric practice including better drug and equipment supply to village midwives. Unfortunately, although the paper describes the inclusion of perinatal deaths in the process, results are only given for maternal deaths.

4. Considerations for implementing and scaling up audit

4.1. Getting to scale with perinatal audit: national case studies

In some cases, the audit process is led at the national level with central coordination. This often involves a directive that health facilities must be involved in audit and often involves confidentiality. Confidential enquiries and "near-miss" audits into maternal deaths have been employed successfully at national level in a limited number of low/middle-income countries, including South Africa and Malaysia. There is less evidence for wide-scale quality improvement arising from a national process for perinatal audits, but there are lessons to be learned.

In the UK, the national Confidential Enquiry into Stillbirths and Deaths in Infancy (CESDI), established in 1992, provides an annual overview of the numbers and causes of stillbirth and infant deaths, together with a detailed enquiry. The process identifies approximately 10 000 deaths annually in England, Wales, and Northern Ireland. Public recommendations for action are made on the basis of the findings of the enquiries. The additional social and political pressure of public reports has mobilized national attention, and resulted in channeling more resources to the problems identified [41].

In South Africa, the growth of PPIP has come from the ground up by committed individuals who wanted a tool to help improve patient care. Following the lead of the National Committee for Confidential Enquiries into Maternal Deaths in South Africa, PPIP is linked to a wide-scale national process (see Panel 2 at the end of the paper). Leadership for PPIP is currently being transferred to national and provincial departments of health with an aim to introduce perinatal mortality audit to all sites that conduct births. In 2007, the audit committees in South Africa for perinatal, maternal, and child deaths came together to facilitate a national process to harmonize the recommendations detailed in each of the 3 audit reports in a summary publication [42]. This process resulted in national media coverage and was linked to the set-up of national-level committees for maternal, perinatal, and child deaths. Other countries in the region are asking for support looking to scale-up audit, including support from the African Union and partners. Despite national support and continued roll-out to sites, there are still challenges with sustaining implementation.

Similarly, it has been shown that confidential, non-blame audit is possible in Bangladesh (see Panel 3 at the end of the paper). Health professionals together with development partners and the Government of Bangladesh joined together in 2004 to introduce perinatal mortality audit in 5 pilot sites. Training, supervision, and advocacy for perinatal mortality audit were provided with a view toward expanding perinatal mortality audit to all government health facilities.

In Uganda, a national maternal mortality audit committee has been set up under the Ministry of Health's National Road Map for Maternal and Neonatal Health. Recently, the Ministry of Health has expanded this to integrate maternal and neonatal death audits and scale up countrywide. The process has started with the national, regional, and district hospitals. Initial experience shows that health workers are interested in the process. However, there are challenges, mainly related to resources for scaling up training as well as follow-up of trained sites to ensure sustainability of the process.

4.2. Sustainability and effectiveness of perinatal audit

There are a number of options available and decisions to consider in terms of both design and implementation when instituting perinatal mortality audit, particularly to maximize the likelihood of reaching wide-scale coverage, with sustainability and linking to change (Figs. 3 and 4). Initiation may vary from one facility to a whole country, although even with a plan for national scale-up, the process must start in a few facilities first. Choices regarding the scope of outcomes covered and methods of data collection (paper-based or electronic) will depend on local factors. Although a wider scope that encompasses maternal, newborn and child health (MNCH), a larger scale, and the use of data outside health facilities would be a more comprehensive approach, this is a much more ambitious remit. A phased approach—for example, adding perinatal to more established maternal audit—may be more achievable. One recommendation is to start by tracking intrapartum stillbirths and pre-discharge intrapartum-related neonatal deaths as a minimum indicator of the quality of obstetric care [43].

Sustainability is a challenge. Audit may be initiated by donors or research projects in one facility or area without government involvement or plans to reach wide scale. Ongoing meetings, data collection, and change depend on local champions, local and national ownership and leadership, a feasible data collection system and a method of disseminating the information (see Panel 2). Audit is most effective if all levels of staff are involved in the process of case review and putting forth recommendations [17]. At the same time, audit is time-consuming and requires commitment and motivation of staff at various levels. In particular, the emotional impact on staff working in an environment with high perinatal mortality has been raised as an issue in Bangladesh. In Nsambya Hospital, Uganda both good events (e.g. a successful severe birth asphyxia rescue) and bad ones (e.g. a death) are reviewed in order to keep staff motivated (personal communication, Romano Byaruhanga). Staff turnover could be a

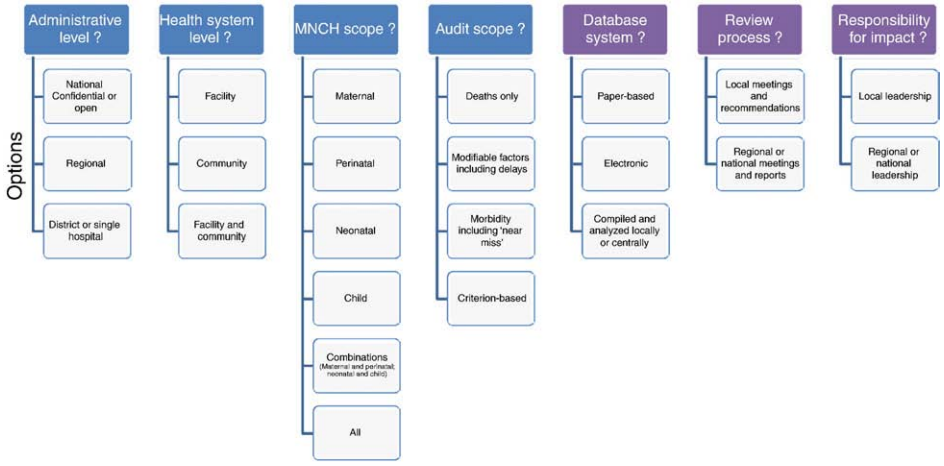

Fig. 4. Considerations around initiating and scaling up perinatal mortality audit.

contributing factor to lack of sustainability. In Murchison Hospital, South Africa throughout the process the doctor-in-charge of the labor ward, the senior midwife, and the information officer remained in the same positions, possibly contributing to the ongoing high quality of PPIP data collected.

Community-level audit can be part of a dialogue between the broader health system, involving health facilities and communities [38]. Similarly, community involvement has been identified as a crucial component of improving facility-based care and a feedback mechanism for communicating patient-related modifiable factors [44]. Potential entry points for community audit can include facility audit itself, in which every death is also audited at the community level. Other entry points can include community-based vital registration systems (which identify pregnancies, births, and deaths) and may include a cadre of multi-purpose community health workers that is already present in many low/middle-income countries. One project in Uganda, as part of maternal death audits, trained health workers to audit every maternal death in health facilities [45]. This was then followed-up by community mobilization, sensitization, and dialogue in the affected villages. Through this initiative it became common to identify many maternal deaths that were not previously identified. In some communities this led to improving the quality of care in some health facilities, e.g. by posting of a midwife, supervision of a traditional birth attendant, and equipping of maternity health units. Confidentiality is difficult in the village setting, opening up blame of either affected families or care givers as negligent. Other challenges include inability for communities to effect change due to lack of empowerment, and lack of comparability of data due to nonstandard tools or definitions.

Impact is dependent on the ability to close the audit cycle. Problems are often identified and solutions suggested, but the changes are not implemented effectively. The whole audit cycle is necessary, but the fifth step of implementing recommendations is crucial to saving lives. This step requires strong leadership and support from health service managers. Self-criticism is difficult, perhaps especially among health professionals. One potential pitfall in mortality audit is to overemphasize the responsibility of the mother or family in delaying to seek appropriate care. One facility-based perinatal mortality audit in Tanzania found that the majority (73%) of perinatal deaths were linked to a crucial delay within the health facility [15].

While perinatal mortality audit has been shown to improve overall perinatal mortality and also intrapartum stillbirths, reducing intrapartum-related neonatal deaths appears to be especially challenging (Table 1). Even within long-standing Confidential Enquiries into Maternal Deaths in the UK, some recommendations result in immediate service improvements, yet other recommendations may be repeated report after report without action [9]. Since the CESDI has combined with the National Institute for Health and Clinical Excellence (NICE), and more recently is being run by the National Patient Safety Agency, the recommendations have been more likely to be implemented [41]. In South Africa, despite a significant reduction in neonatal deaths (106 per 1000 live births in 2003 to 73 per 1000 live births in 2007, $P<0.05$) between 1–2 kg, in all 35 hospitals with serial PPIP data for 5 or more years there was no significant reduction in deaths due to "birth asphyxia." Intrapartum-related perinatal deaths are the top cause of death in rural areas, and second only to preterm birth overall. Avoidable factors were identified in 83% of such deaths, including missed diagnosis of fetal distress and delays of over an hour in undertaking cesarean delivery.

4.3. Cost of perinatal mortality audit

National perinatal mortality audit is achievable even amidst budget constraints. The running cost of the South Africa PPIP process at national level by the South African Medical Research Council with some donor input is approximately US $35 000 per year. This cost includes software program maintenance and development costs, office running costs, collating data, printing bi-annual reports, and attendance at provincial workshops and technical task team meetings. Over 1000 healthcare professionals have been trained in the use of PPIP, mostly through donor funding. Approximately 4 hours per month is spent by clerks entering data, but there is a much larger undocumented cost involved in staff collecting cases and preparing for the mortality and morbidity meetings. The major input is the time to collect and analyze the data, and the opportunity costs of staff time to attend mortality meetings and enquiry panels. At regional or national level, it might be more efficient to select a random sample of all cases across a region or reviewing all cases in a single unit where an excess of cases has been identified [46]. The cost of implementing the changes identified by audit is part of ongoing system improvement and should result in more targeted investment and efficient use of services as a result of the audit.

4.4. Research and data gaps

Local perinatal mortality audits function best as a quality improvement exercise, rather than an epidemiological tool. Amalgamation of data to generate mortality rates and causes of death generated from audit should not be used as nationally representative unless the vast majority of births and deaths occur in health facilities and the data collection is systematic. Perinatal mortality audits can miss late neonatal deaths and deaths that occur after discharge, thereby giving a false impression of the overall neonatal mortality rate. While perinatal mortality rates are the commonly used indicator for these audits, stillbirths and neonatal mortality rates should be analyzed and reported separately to address the different solutions they may require. Furthermore, causes of death will be different in facilities to those that occur in the population as a whole and national priority-setting can be misled if facility-based information alone is used as input data.

The quality of the mortality data collected is also crucial for ensuring that information connects to the right solutions. Even within facilities, without post mortems, determining the cause of death can be difficult guesswork. The concepts and tools described for maternal audit in the WHO's "Beyond the Numbers" guide can also be applied to perinatal audit [10]. Case definitions for hierarchy and cause of death should be included in all perinatal audit reports, such as those developed for neonatal by the United Nations Expert Group (Child Health Epidemiology Reference Group) [47,48]. Standardized, easy-to-use classification systems are needed, particularly for classifying stillbirths because over 35 classification systems are currently in use [49]. A new system is being developed in conjunction with the WHO International Classification of Diseases unit to allow comparability of low- and high-income country data, and to allow cross-tabulation with maternal complications [49]. More standardized social autopsy evaluations are also needed and teams from Uganda, Kenya, Ghana, and Guinea Bissau are working together to standardize social autopsy tools linked to the INDEPTH network (www.indepth-network.org).

The effectiveness and feasibility of audit, particularly to address delays in accessing maternal and newborn care has been demonstrated. However, stillbirths have often been excluded in community audits because of social and cultural constraints that need to be quantified [49]. More research is needed to investigate how to operationalize linkages between community and facility perinatal mortality audits and their effect on changing quality of care.

5. Conclusions

Perinatal mortality audit involves different approaches in different settings, varying from community or clinical meetings following an individual death, to a computerized data entry system assessing thousands of deaths with national level notification. While perinatal mortality audit is often associated with high-income hospital settings,

it has great potential in low-resource settings and also appears to be feasible at the community level, although there are limited experiences as yet. Our new meta-analysis of 7 before-and-after studies in low- and middle-income countries indicates a reduction in perinatal mortality of 30% (95% CI, 21%–38%) after introduction of facility-based perinatal audit. These are low or very low quality studies but, because of consistency of effect across 7 studies in different regions, and all the studies being from low- or middle- income countries, the evidence GRADE may be increased to moderate [20]. Hence, despite the complexities of assessing the impact of perinatal mortality audit, there is increasing evidence to recommend it as a process to facilitate improvement in perinatal mortality outcomes.

Intrapartum-related neonatal deaths are consistently one of the most common causes of neonatal deaths, and in low-income settings, stillbirths also have a large component of intrapartum causation [2]. There is some evidence to suggest that these deaths specifically have decreased through perinatal mortality audit. Given the sensitivity of mother and baby to delays in accessing care and the well-documented challenges with quality of intrapartum care, there is obvious value in a process identifying these and targeting them with solutions. However, based on the limited data available here, it appears more difficult to implement changes to reduce intrapartum-related neonatal deaths than for intrapartum stillbirths.

The public health impact of perinatal mortality audit depends upon scale of operation and sustainability, which are reliant on motivating health workers, having champions, and involving stakeholders at all levels, as well as a locally feasible data collection system. There are lessons to be learned from the widespread experience of maternal mortality audit that is more frequently implemented at national scale.

There is untapped potential for perinatal mortality audit to identify and address deadly delays and modifiable factors in care around the time of birth that lead to intrapartum stillbirths and intrapartum-related neonatal deaths, as well as to maternal deaths. However, without effectively implementing local solutions or national recommendations to close the audit cycle, audit alone cannot save lives or improve quality of care.

6. Conflict of interest

The authors have no conflicts of interest to declare.

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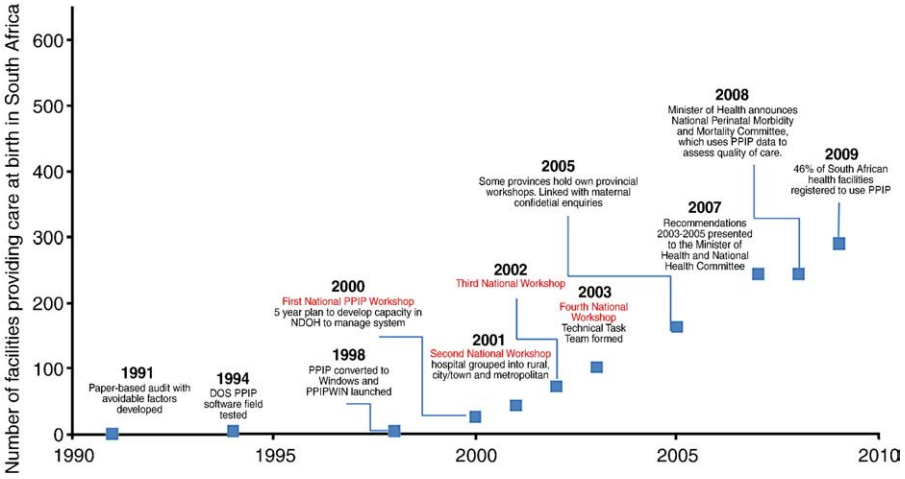
Panel 1. National process toward scaling up perinatal mortality audit in South Africa

There are 664 healthcare facilities that conduct deliveries in South Africa, and in 2009, 305 (46%) of these health facilities have been registered with Perinatal Problem Identification Programme (PPIP), a computer-based perinatal audit system. The database in 2006–07 had information on almost 40% of all births in South Africa and 35% of all sites conducting births. The national *Saving Babies* reports and recommendations based on PPIP findings are presented to the Minister of Health via a national committee appointed to make recommendations for priorities to reduce the perinatal mortality. The system is gradually becoming institutionalized as the data become increasingly used (Panel 1. Fig. 1).

So far, 146 (48%) sites have submitted data in 2009, including 35 sites with continuous data for 5 or more years, 16 that stopped at some point and restarted, and 38 are new registrations with no new data yet. Some 48 sites have not responded for this year and 73 sites (24% of those registered) are known to have stopped collecting data. The main reason for discontinuing the process has been the removal of the driving force behind the process within the institution, either by promotion to another position, rotation within the hospital or resignation from the public service. PPIP is voluntary and database maintenance at each audit site is performed by doctors and midwives as an integral part of clinical practice. The sites that use PPIP were trained in its use by other PPIP users. Recently some of the country's 9 provinces have appointed provincial coordinators that visit PPIP sites to sustain the process and help promote change based on the data.

Factors contributing to successful scale-up and sustainable implementation

- *Champions:* Interested healthcare providers have driven the process in their hospitals, in their provinces, or nationally. These champions have been obstetricians, midwives, and pediatricians.
- *National Department of Health links*: This has facilitated the spread of the program to all of the provinces and provided a method of communicating the recommendations to the Department so that they can impact on their strategic planning.



Panel 1. Fig. 1. Timeline for scale up of national perinatal audit in South Africa (1991–2009).

- *Collaborative network:* In 1981 a group of pediatricians, obstetricians, epidemiologists, midwives, and neonatal nurses initiated an annual meeting to identify priorities in perinatal care in South Africa. This group has continued to meet annually and expand, providing an effective communication network where the data can be presented and discussed, promoting ongoing improvements and use for PPIP, as well as enabling recruitment of new PPIP sites.
- *Computer-based user-friendly tool:* PPIP was developed from a paper-based audit system to a computer program that is continually being improved. The software is free and can be downloaded from the web site (www.ppip.co.za). A system provides support for users.
- *Compilation and dissemination of reports and recommendations:* Initially annual and now biannual reports were produced by the group and were sent to all sites conducting births. Funders covered the costs of meetings to produce the reports and of printing. The report was disseminated by the National Department of Health.

Panel 2. National process toward scaling up perinatal audit in Bangladesh

Although over 90% of births in Bangladesh occur at home, complicated cases are often referred to health facilities with an imperative to improve facility outcomes for mothers and babies. During the first annual International Perinatal Congress in Dhaka, February 2003, the government and many stakeholders explored the potential for perinatal mortality audit in Bangladesh. The South African PPIP software and process was presented for consideration for adaptation. Later meetings were held with key stakeholders, existing data collection systems were reviewed, and LAMB Hospital Bangladesh shared their experience of using PPIP for the previous 3 years.

The government of Bangladesh selected 5 pilot facilities based on capacity to provide emergency obstetric care and to represent varying levels of the health system. A 3-day training course was created by LAMB for health workers from these pilot facilities. The training provided the software and job aids as well as an exploration of values involved in perinatal mortality audit, such as accuracy, honesty, and an acknowledgement that every life matters. A 1-day Training of Trainers course was subsequently developed. Follow-up visits were made to each of the facilities to monitor progress and to gather feedback from users. This feedback led to the creation of a birth register and an easy-to-read wall poster to assist with PPIP data entry. In response to challenges with the PPIP software where computer access is limited, a paper-based system was developed.

Perinatal mortality audit has now expanded to 22 health facilities in Bangladesh. In 2006, an assessment was conducted of the first 17 facilities. Several challenges were identified:

Challenge	Proposed solution
Communication between teams	Complete perinatal death records depend on communication between the obstetric unit where births and stillbirths occur and the pediatric unit where neonatal deaths occur. One forum for this is the monthly facility coordination meeting, but this may not involve all the necessary staff.
Fear of blame	Staff fear failure and embarrassment for wrongdoing. Managers of perinatal audit meetings shifted focus from blame to learning.
Extra work for already over-stretched health staff	Filling out audit forms and monthly meetings can be seen as an additional burden. To recognize the extra effort, a token compensation (Tk. 500, or US $8) was paid monthly to the focal person at each pilot facility.
Software issues	Computer-based data collection and analysis relies on trained staff and requires capacity for updating and troubleshooting the software. Ultimately, the objective is more for health workers to properly record deaths than to learn how to use specific software and technology must be appropriate to the setting. If collation is required, it should be done centrally.
Inability to address modifiable factors	Even when audit runs well, many health facilities have a high patient load and are under-staffed. Drugs and supplies logistics may not be reliable. Change requires involvement of higher level decision makers.

While the expansion of perinatal mortality audit in Bangladesh has not yet reached desired levels, there is high level commitment to the process of counting every death. The Director General of Health has recently called for notification of all maternal and perinatal deaths in facilities using a modified version of the perinatal mortality audit form. The Ministry of Health and Family Welfare of Bangladesh included perinatal mortality audit in its 3-year policy document, in-service training, and annual program implementation plans. The introduction of perinatal mortality audits has led to increased awareness of the need for accurate record keeping, a better understanding among health workers of the data in their own facilities, and in several facilities quality of care for mothers and newborns is improving.

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INTRAPARTUM-RELATED DEATHS: EVIDENCE FOR ACTION 7

Reducing intrapartum-related deaths and disability: Can the health system deliver?

Joy E. Lawn [a,b,*], Mary Kinney [a], Anne CC Lee [c], Mickey Chopra [b], France Donnay [d], Vinod K. Paul [e,f], Zulfiqar A. Bhutta [g], Massee Bateman [a], Gary L. Darmstadt [c,d]

[a] Saving Newborn Lives/Save the Children-US, Cape Town, South Africa
[b] Health Systems Strengthening Unit, MRC, South Africa
[c] Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA
[d] Integrated Health Solutions Development, Global Health Program, Bill & Melinda Gates Foundation, Seattle, WA, USA
[e] Department of Pediatrics, All India Institute of Medical Sciences, New Delhi, India
[f] WHO Collaborating Centre for Training and Research in Newborn Care, Delhi, India
[g] Aga Khan University, Karachi, Pakistan

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ABSTRACT

Background: Each year 1.02 million intrapartum stillbirths and 904 000 intrapartum-related neonatal deaths (formerly called "birth asphyxia") occur, closely linked to 536 000 maternal deaths, an estimated 42% of which are intrapartum-related. *Objective:* To summarize the results of a systematic evidence review, and synthesize actions required to strengthen healthcare delivery systems and home care to reduce intrapartum-related deaths. *Methods:* For this series, systematic searches were undertaken, data synthesized, and meta-analyses carried out for various aspects of intrapartum care, including: obstetric care, neonatal resuscitation, strategies to link communities with facility-based care, care within communities for 60 million non-facility births, and perinatal audit. We used the Lives Saved Tool (LiST) to estimate neonatal deaths prevented with relevant interventions under 2 scenarios: (1) to address missed opportunities for facility and home births; and (2) assuming full coverage of comprehensive emergency obstetric care and emergency newborn care. Countries were first grouped into 5 Categories according to level of neonatal mortality rate and examined, and then priorities were suggested to reduce intrapartum-related deaths for each Category based on health performance and possible lives saved. *Results:* There is moderate GRADE evidence of effectiveness for the reduction of intrapartum-related mortality through facility-based neonatal resuscitation, perinatal audit, integrated community health worker packages, and community mobilization. The quality of evidence for obstetric care is low, requiring further evaluation for effect on perinatal outcomes, but is expected to be high impact. Over three-quarters of intrapartum-related deaths occur in settings with weak health systems marked by low coverage of skilled birth attendance (<50%), low density of skilled human resources (<0.9 per 1000 population) and low per capita spending on health (<US $20 per year). By providing comprehensive emergency obstetric care and emergency newborn care for births already occurring in facilities, 327 200 intrapartum-related neonatal deaths could be averted globally, and with full (90%) coverage, 613 000 intrapartum-related neonatal deaths could be saved, primarily in high mortality settings. *Conclusion:* Even in high-performance settings, there is scope to improve intrapartum care and especially reduce impairment and disability. Addressing missed opportunities for births already occurring in facilities could avert 36% of intrapartum-related deaths. Improved quality of care through drills and audit are promising strategies. However, the majority of deaths occur in poorly performing health systems requiring urgent strategic planning and investment to scale up effective care at birth, neonatal resuscitation, and community mobilization as well as to develop, adapt, and introduce tools, technologies, and task shifting to reach the poorest.
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1. Introduction

This is the final paper in a series of 7 reviews summarizing the size of the burden of intrapartum-related stillbirths and intrapartum-related neonatal deaths, and the evidence to reduce these, especially in low-resource settings where most of these deaths occur. The first paper mapped the staggering size of the problem [1]—almost 2 million deaths, comprised of an estimated 904 000 (uncertainty range, 650 000–1.17 million) intrapartum-related neonatal deaths, formerly referred to as "birth asphyxia," and 1.02 million (uncertainty range, 660 000–1.48 million) intrapartum stillbirths [2], as well as a poorly measured burden of long-term impairment and disability. Global Burden of Disease, Millennium Development Goals, and Countdown to 2015 metrics do not currently include stillbirths [3], illustrating the

* Corresponding author. Saving Newborn Lives/Save the Children USA, 11 South Way, Cape Town 7405, South Africa. Tel.: +27 21 532 3494.
E-mail address: joylawn@yahoo.co.uk (J.E. Lawn).

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legacy of invisibility of this massive loss of life [4]. Perinatal deaths are intimately linked with the annual global toll of approximately half a million maternal deaths [5].

This burden is not just a disease metric, but represents immeasurable loss for families just at a point when new life is expected. Globally, intrapartum-related conditions are implicated in 23% of neonatal deaths, 32% of stillbirths, and 42% of maternal deaths [1]. Yet the time when the risk of these deaths is highest—during childbirth and the immediate postnatal period—is also the time in the continuum of care when women and newborns in high mortality settings are least likely to have contact with health care, particularly skilled care during childbirth and follow-up care in the early postnatal period [6,7]. While two-thirds of women in high mortality settings attend prenatal care, only one-third access skilled care at birth, and a much lower number receives early postnatal care. In addition, more than half the world's births occur in high mortality countries with a neonatal mortality rate (NMR) greater than 30 per 1000 and coverage of skilled attendance at birth of approximately 50% (Fig. 1). These high mortality settings, mainly in South Asia and Sub-Saharan Africa, account for approximately three-fourths (77%) of neonatal deaths and a similar proportion of maternal deaths [8]. Hence, where the burden is highest, the probability of effective care is lowest [9]. In addition, within countries, it is the poorest families, often in rural areas and urban slums, who continue to have the highest risk, and yet the greatest delays in accessing obstetric and early postnatal care [10,11]. These delays may not be due to distance, or even financial barriers alone, but also gender, ethnicity, fatalism, or different perceptions of complications at birth [1].

This burden is large, yet, as summarized in this Supplement, interventions exist even if the GRADE quality of evidence is often moderate or low. The fact that there is a 24-fold difference in intrapartum-related neonatal mortality between high-income and low-income countries [1] indicates that solutions are possible. It has been convincingly argued that the greatest test of health system function is the ability to provide timely care at birth [12]. Delays can be important for many of the critical conditions that cause neonatal and maternal mortality and stillbirth, but delays of even a few hours can be the difference between life and death for a woman with obstetric hemorrhage, or a delay even of minutes can contribute to the death of a baby not breathing at birth. A health system that can provide timely cesarean delivery and resuscitate a non-breathing baby is likely to be able to respond to other acute and chronic conditions; hence, we propose that effective care at the time of birth is a litmus test of health systems performance.

The huge challenge remains how to implement these solutions—especially high-quality obstetric care and immediate newborn care—in low-income settings and particularly how to reach 60 million home births a year. Strategies to better link communities to effective obstetric and immediate newborn care are also critical and yet often not systematically implemented [11]. Can interventions be prioritized for varying levels of health system performance, and are there some interventions that can also be adapted for effective delivery now in lower levels of the health system or even at community level? [13].

1.1. Objective

In this paper, the concluding paper in a series entitled "Intrapartum-related neonatal deaths: Evidence for action," we summarize the evidence for interventions to reduce intrapartum stillbirths and intrapartum-related neonatal deaths based on a systematic review of almost 30 000 article titles or abstracts as detailed in the preceding 6 papers. The level of evidence was assessed using the GRADE system criteria, to evaluate the quality of the evidence (high, moderate, low, or very low) and make recommendations (strong, conditional, weak) based on standard criteria [1,14]. Here we place the problem and solutions in a health systems context, integrating effective interventions and strategies with existing health system packages, and synthesizing evidence and experience regarding delivery strategies across the continuum of maternal, neonatal, and child health (MNCH) programs. Statistical modeling based on the Lives Saved tool (LiST) is used to estimate the lives saved through immediate and medium/long-term program priorities for 5 different health system settings categorized by level of NMR as an outcome marker of health system performance. Finally, we highlight evidence gaps and priorities for innovation and further research with a focus on reaching under-served populations, and on current experience with large-scale programs.

2. Intrapartum-related outcomes: Evidence and integration into health system

2.1. Interventions and strategies: Overview of the evidence

In this systematic literature review of strategies to reduce intrapartum-related mortality, we screened approximately 30 000 article titles or abstracts, but identified fewer than 100 trials that reported an effect on neonatal mortality rate (NMR), stillbirth rate (SBR), or perinatal mortality (PMR), and even fewer that reported intrapartum-related outcomes, specifically intrapartum-related neonatal deaths or intrapartum stillbirths. Furthermore, many of the reports identified were primarily set in high-income settings, thus, the results or comparisons may not be readily generalized to low-income settings. In many of the

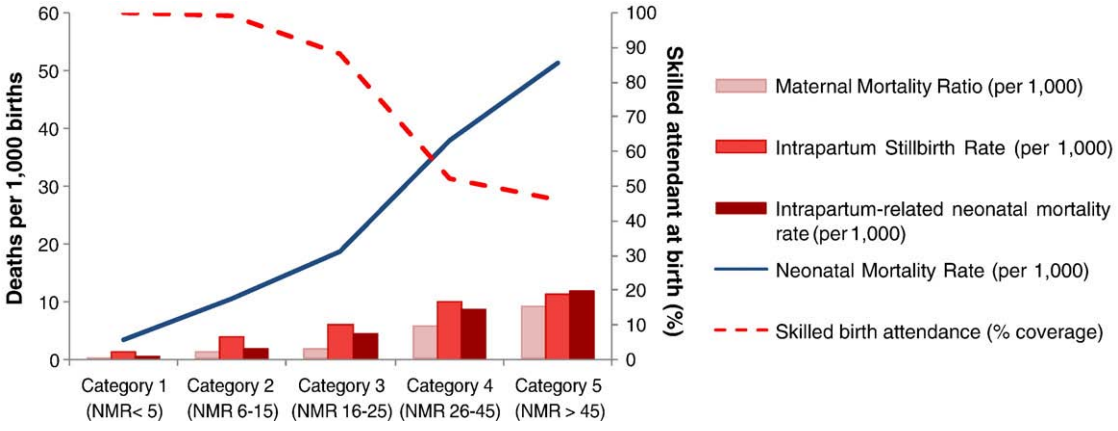

Fig. 1. Countries (193) organized according to 5 Categories of neonatal mortality rate as a marker of health system performance, showing the associated variation in maternal mortality, as well as intrapartum mortality outcomes for stillbirths and neonatal deaths, and an inverse association with skilled attendance at birth. Abbreviation: NMR, neonatal mortality rate. Note that the association between skilled neonatal mortality and skilled attendance is at ecological level and cannot be assumed to be causal based on this data. Country groupings by category of NMR level are adapted from *The Lancet* Neonatal Series 2005 [74]. Updated for 2009 births and mortality rates. Sources: Maternal mortality ratio data from Hill et al. [5]; intrapartum stillbirth data from Lawn et al. [2]; neonatal mortality rate data WHO (UNICEF [75]); intrapartum-related neonatal deaths ("birth asphyxia") from Countdown 2008 [26] based on methods from Lawn et al. [76].

studies of maternal health interventions, only maternal outcomes were reported, missing an opportunity to also evaluate intervention effect on perinatal outcomes. The converse may also be true—with trials reporting only on neonatal outcomes. It was disappointing to identify how many trials missed the opportunity for integrated evaluations of relevant outcomes for stillbirth, neonate, and mother, as noted in another recent large systematic review process for stillbirths [3]. Interpretation is also simpler if stillbirth and neonatal outcomes are reported separately, rather than always combined as perinatal.

We did not identify any interventions that had high GRADE level of evidence on intrapartum-related mortality (Table 1). This lack of high-quality evidence from randomized controlled trials (RCTs) may also reflect the ethical complexity of undertaking such trials, particularly for interventions that are already considered standard practice, such as cesarean delivery. Nevertheless, there are major knowledge gaps that could be addressed and require a more systematic research agenda, prioritized based on likely impact [15].

2.1.1. Obstetric care

Evidence for the impact of obstetric care packages (Basic and Comprehensive Emergency Obstetric Care) was very low quality based on GRADE [16], consisting primarily of ecological and historical data. Nonetheless, access to emergency obstetric care should be a universal right for all mothers and is strongly recommended. Of the individual obstetric interventions reviewed, none had strong evidence based on specific data regarding intrapartum-related mortality outcomes (Table 1) [10]. Amnioinfusion for meconium staining was associated with lower rates of neonatal encephalopathy, planned cesarean delivery for breech presentation, and post-term induction of labor were associated with lower all-cause perinatal mortality; however, further evaluation and specifically risk-benefit analysis in low-resource settings is needed before these procedures can be routinely recommended in low-resource settings. On the other hand, there are several individual obstetric interventions with a low level of GRADE evidence, yet these are conditionally or strongly recommended, given the favorable risk-benefit assessment and inability to evaluate these interventions in RCTs because of current standards of care; these include use of the partograph, external cephalic version, emergency cesarean delivery for breech presentation, management of shoulder dystocia with therapeutic maneuvers, in utero resuscitation, symphysiotomy, rapid delivery for placental abruption, and cesarean delivery for uterine rupture (Table 1). Promising intrapartum care provision strategies include obstetric drills/rapid response teams, continuous intrapartum support, safety checklists, and task-shifting to non-physician clinicians. The dearth of evidence stresses the urgent need to better evaluate obstetric care programs and packages to build this evidence base, and to also evaluate perinatal outcomes [10].

2.1.2. Neonatal resuscitation and post-resuscitation management

In a meta-analysis of observational before-after-studies, facility-based training for neonatal resuscitation resulted in a 30% reduction in intrapartum-related neonatal mortality [17]. The results were highly consistent in direction and strength of association across multiple studies, and also directly generalizable to low- and middle-income settings; thus, the GRADE level of evidence was upgraded to moderate [18]. There is moderate level evidence for therapeutic hypothermia in the reduction of neonatal encephalopathy-related morbidity and mortality; however, the evidence thus far has been derived in high-income settings. Clinical trials are underway of therapeutic hypothermia modified for use in low-resource settings, and this intervention is not presently recommended until further data is available and cost-effectiveness can be compared with primary and secondary prevention.

2.1.3. Linking community and facility

Community mobilization is an effective strategy to link families to facility-based obstetric care associated with a significant increase in facility births and a 36% reduction in ENMR in a meta-analysis of 2 RCTs and 1 quasi-experimental trial of high intensity mobilization [11]. This GRADE level of evidence is moderate and community mobilization is strongly recommended as a strategy to increase demand for skilled childbirth care, and possibly to improve intrapartum outcomes through reducing the risk for other factors, such as maternal infection, that may compound the risk. Additional evaluation is needed, however, to define impact of community mobilization strategies on intrapartum-related outcomes and cost-effectiveness. Furthermore, other potential linking strategies such as financial incentives, community referral/transport schemes, risk screening, and maternity waiting homes need to be further evaluated.

2.1.4. Delivering care in community settings

At the community level, there was moderate GRADE level evidence supporting a beneficial effect of integrated community health worker (CHW) packages on both perinatal (28% reduction) and early neonatal mortality (36% reduction). Furthermore, there is evidence that stillbirths may be reduced 28%–49%, and one quasi-experimental study of CHW training in neonatal resuscitation demonstrated a 42% reduction in "asphyxia-specific" mortality [19]. The effect of training TBA in neonatal resuscitation resulted in a smaller reduction of intrapartum-specific mortality of 11% [20]. A recently published large RCT of TBA training in primary prevention demonstrated a significant 30% reduction in PMR [21] and 2 large trials showed a 31% reduction in stillbirth [21,22]. The evidence for effect of community-based skilled birth attendants is low by GRADE criteria, and a meta-analysis of before-and-after studies of skilled birth attendant training showed a 12% reduction in PMR and 13 % reduction in early NMR (ENMR) [13]. Three low-quality studies reported intrapartum-related mortality reductions ranging from 22%–47%. However, these data on effect of skilled birth attendants must be interpreted with caution, given the low quality before-and-after studies.

2.1.5. Perinatal mortality audit

Perinatal mortality audit has been used primarily in health facility settings, and there are encouraging signs that this can be scaled up even in middle- and low-income countries; the overall GRADE of evidence is low-moderate. There are also some experiences with community-based audit [23,24]. Our new meta-analysis of 8 studies suggests a 31% effect on perinatal mortality from effective audit, linked to action [23].

2.1.6. Evidence summary

Comparing the various effect sizes, the GRADE level of evidence, and the strength of GRADE recommendations, the largest mortality effects are expected through obstetric care packages, but these also have the weakest levels of evidence (Table 1). *The Lancet* Neonatal Series estimated that obstetric care reduced all-cause neonatal mortality by 20%–60% [25]. A recent Delphi process suggests 75% (60%–85%) reduction in intrapartum-related neonatal deaths through Comprehensive Emergency Obstetric Care (see Panel 1). The strongest evidence is for facility-based neonatal resuscitation, community mobilization, and integrated CHW packages (effect size ranging from 30%–40% reduction in ENMR), with more modest reductions with the other strategies, such as training community skilled birth attendants and TBAs or therapeutic hypothermia. Caution must be applied in using these data as some of the effect estimates are based on studies with design limitations or with small numbers of subjects, or the effect may have been dependent on local factors not easily replicated [18]. However, the massive size of the burden of intrapartum-related mortality mandates cautious use now of the available evidence to guide new policy and program implementation, and a much more aggressive approach to filling key evidence gaps, especially for facility-based obstetric care.

Table 1
Evidence of effect of interventions and strategies on perinatal, neonatal, and intrapartum-related mortality outcomes.

		Mortality Effect					Morbidity effect	GRADE level of evidence	GRADE recommendation
		SBR	PMR	NMR	ENMR	IPR-NMR			
Interventions and packages	**Obstetric care: Intrapartum interventions [10]**								
	- Basic Emergency Obstetric Care					38%[2]		Low	Strong
	- Comprehensive Emergency Obstetric Care					75%[2]		Low	Strong
	- Partograph use	38%–46%	36%–40%					Low-Moderate	Strong
	- Planned elective cesarean delivery for breech		**71% (14%–90%)[1]**					Moderate	Conditional
	- Routine induction of labor at ≥41 weeks		**70% (1%–91%)[1]**					Moderate	Conditional
	- Continuous labor support						**9% (1%–17%)[3]**	Low	Strong
	- Amnioinfusion for meconium staining						**91% (51%–98%)[4]**	Moderate	Weak
	- Amnioinfusion for umbilical cord compression						**68% (30%–85%)[5]**	Moderate	Weak
	Neonatal resuscitation [17]								
	- Facility settings [94]				**40% (6%–61%)**	**30% (16%–41%)**		Moderate	Strong
	- Community settings	31%–33%	15%–29%			20%[6] [47%–70%]		Low	Conditional
	Post-resuscitation management								
	- Serum glucose-fluid management							Low	Weak
	- Anticonvulsants							Low	Weak
	- Thermal management							Low	Strong
	- Therapeutic hypothermia					**26% (6%–42%)[7]**		Moderate (high income settings)	Conditional
Linking strategies	**Increasing community demand for obstetric care [11]**								
	- Community mobilization	28%–47%[8]	**25% (4%–41%)**	5%–76%[9]	**36% (15%–52%)**			Moderate	Strong
	- Financial strategies							Very Low	Conditional
	Brining pregnant women closer to formal health system								
	- Community referral and transport schemes							Very Low/Low	Conditional
	- Risk screening							Very Low	Conditional
	- Maternity waiting homes	48%–90%	16%–51%					Low	Conditional
	Delivering care in community settings [13]								
	- Community midwives and birthing centers	15%[10]	**12% (5%–17%)**	32%–40%	**13% (3%–21%)**	22%–47%		Low	Strong
	- Trained traditional birth attendants	31%[11]	**6% (4%–9%)[13]** 30% (18%–41%)[14]	29%–41%	15%[16]	**11% (2%–21%)[13]**		Low/Moderate	Conditional
	- Integrated home-based care packages by CHWs	28%–49%[12]	**28% (16%–38%)**	25%–54%[15]	**36% (27%–44%)**	42%[17]		Moderate	Strong
	Perinatal mortality audit [23]								
	- Facility-based audit, quality of intrapartum care	34%–61%	**30% (21%–38%)**		1%–56%			Low/Moderate	Strong
	- Community-based audit							Very low	Weak

BOLD results are from meta-analysis or Cochrane review.
*Interventions without sufficient evidence demonstrating significant effect on perinatal-neonatal or intrapartum mortality (active management of labor, cesarean for failure to progress, controlled fundal pressure, instrumental delivery, symphysiotomy, induction for fetal macrosomia, maneuvers for shoulder dystocia, external cephalic version, amnioinfusion for meconium or umbilical cord compression, antihypertensives for hypertensive disorders of pregnancy, anticonvulsants for hypertensive disorders of pregnancy, ultrasound confirmation of previa, cervical cerclage, rapid delivery for placental abruption, membrane sweeping at or after 41 weeks gestation, antibiotics for chorioamnionitis, continuous electronic fetal heart rate monitoring, electronic fetal electrocardiogram, fetal pulse oximitry.
[1]From Cochrane Review, trials primarily in high-income settings.
[2]Estimate based on Delphi Expert Consensus opinion.
[3]From Cochrane Review, reduction in cesarean birth.
[4]From Cochrane Review, reduction of neonatal encephalopathy.
[5]Reduction of 5 minute Apgar <7.
[6]Estimate based on Delphi Expert Consensus, [Range] from 3 community-based studies however low quality and varying definition of non-breathing baby.
[7]From Cochrane Review, all studies from high-income settings.
[8]Range of 3 studies (O'Rourke et al. [78], Bhutta et al. [79], Kumar et al. [55]), 2 studies with no significant effect (Manandhar et al. [80], Fullerton et al. [81]).
[9]Range of packages with multiple interventions not limited to community mobilization, including case management of neonatal infections (O'Rourke et al. [78], Manandhar et al. [80], Fullerton et al. [81], Baqui et al. [82], Bhutta et al. [79], Kumar et al. [55]).
[10]Significant 15% effect in 2 studies (Ibrahim et al. [83], Ronsmans et al. [84]), 2 studies with no effect (Gloyd et al. [85], PATH [86]).
[11]Results from 1 RCT (Jokhio et al. [21]) and 1 multi-center before-after study (Carlo et al. [22]).
[12]Significant reduction in 3 studies (Bhutta et al. [79], Bang et al. [19], Kumar et al. [55]).
[13]Based on previous meta-analysis (Sibley et al. [20]).
[14]Based on new RCT (Jokhio et al. [21]).
[15]Broad range of packages and interventions, several including case management of neonatal infections.
[16]One significant result (Greenwood et al. [87]), one study with no effect (Carlo et al. [22]).
[17]Intervention to Control area comparison for SEARCH trial during tube-and-mask training period (Bang et al. [88]).

2.2. Integration of intrapartum-related interventions into health system packages in the continuum of care

Some interventions are more feasible to deliver vertically and have shown major increases in coverage, particularly those that are primarily commodity-based and are receiving major investments such as insecticide treated bed nets, immunizations, and antiretroviral therapy [26]. However, interventions based on clinical case management have made slower progress; for example, skilled birth attendance coverage has not increased in Africa in the last decade and at current rate of increase will still reach less than half of African women at birth by 2015 [1]. Interventions to avert intrapartum-related deaths are less amenable to a vertical approach than many child health interventions, and will be most effectively and efficiently delivered when integrated into existing health service delivery packages along the continuum of care for mothers, newborns, and children. Fig. 2 shows the continuum of care through the pregnancy life cycle and along the continuum of place of health service delivery, adapted from the framework of 8 service delivery packages for MNCH proposed by Kerber et al. [27]. Of these healthcare service packages, the 4 most relevant to intrapartum-related outcomes are: (1) prenatal care; (2) childbirth care; (3) postnatal care, particularly immediate care and in the first 2 days of life; and (4) care for sick neonates/children.

Specific content in each package will vary depending on local epidemiology, for example the level of NMR, the prevalence of HIV/AIDS or malaria, but also with local health system and community capacity, coverage of skilled birth attendance, access to illness management, and human resources. Prenatal care visits are more feasible and can reach higher coverage by being provided close to home in primary care clinics; aspects of prenatal care can even be provided in the home by CHWs. The content of routine prenatal care includes risk screening, birth preparedness counseling, and community mobilization. However, the quality of prenatal care may vary, and data are lacking to track this gap effectively in low-income settings.

The content of childbirth care packages will also vary, ranging from full comprehensive emergency obstetric care at referral-level health facilities to basic emergency obstetric care at first-level health facilities, and skilled community childbirth care at primary care level. The packages of care at birth should include evidence-based interventions for the baby as well as the mother. Where the birth occurs at home, at least simple immediate newborn care and essential newborn care can be provided by family members or other community cadres present. Every skilled birth attendant should be able to provide immediate newborn care—drying, warming, assessment, as well as neonatal resuscitation and stabilization if needed. It is not a rational investment to provide effective obstetric care only to have the baby die for lack of a bag-and-mask device or because someone is not competent in neonatal resuscitation. Yet currently this is the norm in many hospitals, given the fact that at least for the 6 countries for which data are available, the majority of attendants are not trained in neonatal resuscitation and more than half of the facilities do not have bag-and-mask devices (Fig. 3) [17]. Facilities that provide comprehensive emergency obstetric care should also provide emergency newborn care services for ongoing care of babies who are ill with neonatal encephalopathy after intrapartum-related injury or who have complications of preterm birth or neonatal sepsis. The United Nations (UN) has proposed that the 6 core competencies of basic emergency obstetric care be expanded to include neonatal resuscitation, and we support this proposal. A UN manual detailing the indicators for EmOC mentions this proposal, but detailed content and indicators for this have yet to be included [28].

In addition to integration of evidence-based intrapartum care interventions within existing packages, there is a need for strategies to

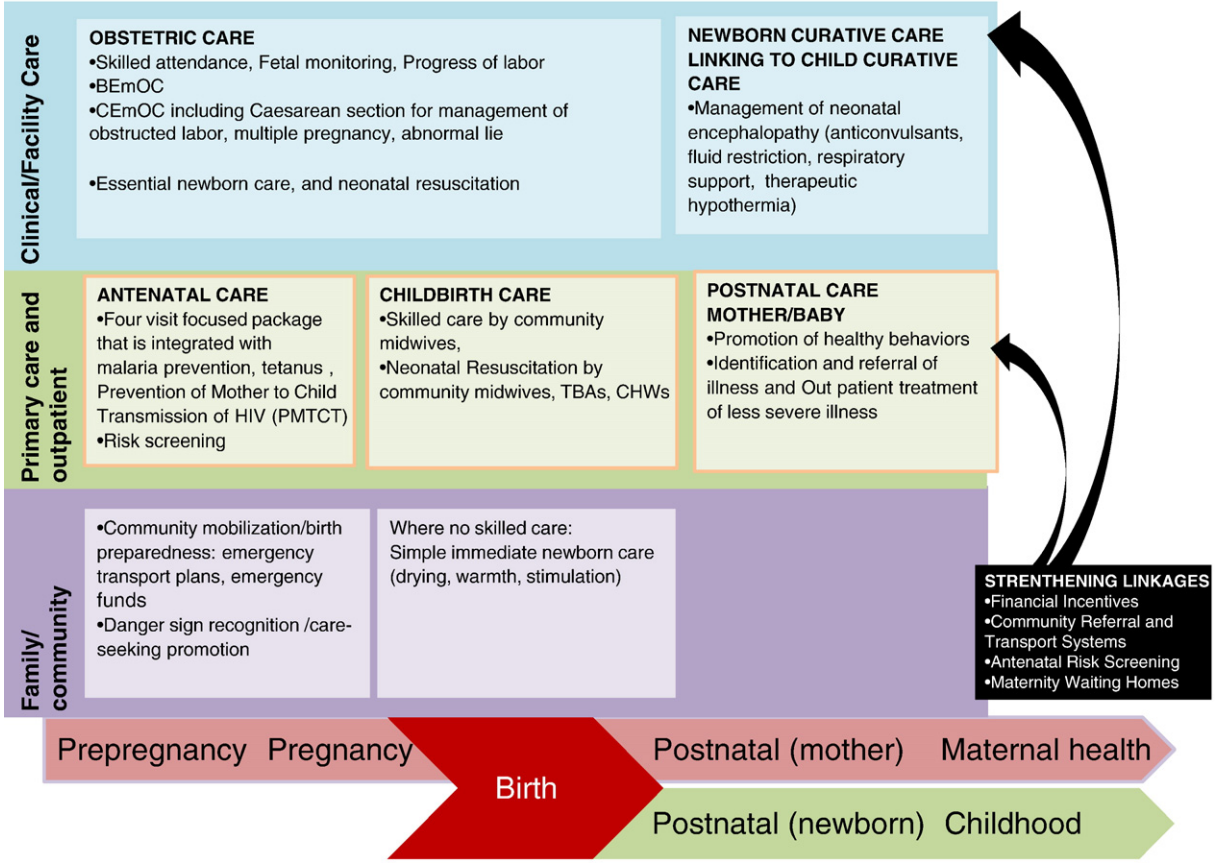

Fig. 2. Evidence-based interventions to reduce intrapartum-related stillbirths and neonatal deaths, with interventions integrated in packages of care for implementation within the continuum of care for mothers and newborns and for service delivery within facilities and communities. Adapted from Kerber et al. [27].

link the different levels of the health system in order to reduce delays in receiving referral-level obstetric care [11]. Community mobilization activities may originate via community groups, such as newborn care stakeholder groups and mass media campaigns, and be facilitated by community-based providers including community midwives, CHWs, and TBAs. Important increases in facility birth utilization are possible through such mobilization efforts. In a meta-analysis, the more intensive community mobilization activities were associated with a doubling of skilled birth attendance in a short time (1 to 3 years) [11].

2.3. Delivering interventions: Who can do what?

Table 2 highlights different delivery channels for interventions to reduce adverse intrapartum-related outcomes, ranging from a generic media/marketing approach through to the most skilled provider. A systematic approach is required to define the individual roles and responsibilities of all the providers of care, both formal and informal. A key aspect, often missed, is to clarify the interactions between providers and levels of care, as well as with the family and community. Appendices 1a, 1b, and 1c (available in the online version) provide a matrix of shared responsibilities, outlining in more detail the tasks for each actor (the woman, through community leaders, community cadres, facility-based cadres, and policymakers) during pregnancy, childbirth, and the postnatal period.

The single most critical person for effective care at the time of birth is the midwife. Expectations and competencies for the skilled birth attendant have been defined in a joint consensus statement by the International Federation of Gynecology and Obstetrics (FIGO), the International Confederation of Midwives (ICM), and the World Health Organization (WHO) [29]. However, data from national service provision assessments in 6 African countries showed that 72%–93% of such attendants were not trained in resuscitation, and basic resuscitation equipment such as bag-and-mask was missing from 53%–84% of facilities providing care at birth—a major missed opportunity for high-impact care [17]. Program reports of neonatal resuscitation being undertaken by community midwives, CHWs, and TBAs [17] warrants further research for the effectiveness of these cadres of health workers in resuscitating the non-breathing baby.

An ongoing debate is whether it should be standard practice to have more than one provider present at birth—one to look after the mother and delivery of the placenta, and another for the baby. In most high-income countries it is standard practice for a midwife to have an assistant at the time of the actual birth, although in some countries this may be another cadre of worker teaming with the midwife. In reality, this sometimes leads to the replacement of the skilled provider with another worker with lesser skills, especially during night shifts [30]. This principle of having two providers at the birth has also been applied in the most intensive home-based care studies—a CHW who is competent in resuscitation cared for the baby while another attendant looked after the mother [19]. Although a second worker makes intuitive sense since effective care simultaneously for mother and newborn even in a normal birth is challenging, there are no data available to support a measured benefit apart from some process data to support the value of a supportive companion for the mother [10,31]. However, the counter-argument is that a standard of two attendants is not feasible, given the global gap for even one skilled attendant at 45 million births a year. For very high NMR settings (>45) where the density of skilled birth attendants is only 0.7 per 1000 population, urgent attention is needed to train and retain more midwives and to evaluate work load, roles, and identify opportunities for task shifting with paired workers who may not be midwives.

Simpler tasks such as clean childbirth care and simple immediate newborn care (drying, warming, and putting the baby skin-to-skin with the mother) can potentially be provided by any helper present at birth who is given the appropriate information and skills before the birth—even family members who may be the only attendant at 32% of births in Africa and 14% in South Asia [13].

For certain interventions, the skill level required may be so high that task shifting can only pass from one skill level to the next skill level directly below it, and with built-in supervision. For example, comprehensive emergency obstetric care is typically provided by obstetrician medical officers in referral-level health facilities. Task shifting would expand the capacity of the next level of providers, including nurses or medical assistants, to perform aspects of obstetric care, such as cesarean deliveries [32]. Evaluations at scale in Malawi, Mozambique, Senegal, and Tanzania suggest that this is feasible, safe, and cost-effective [33–36]. Success for such task shifting depends on effective linkages with higher levels of the

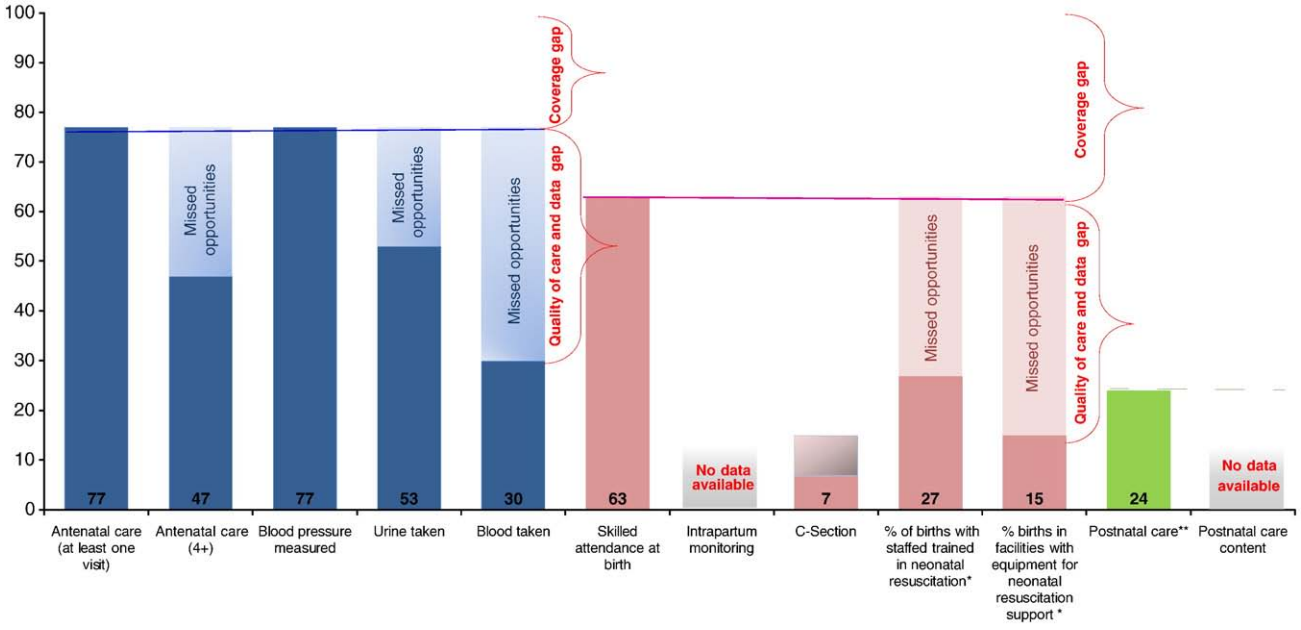

Fig. 3. Coverage of care for low-resource countries showing the missed opportunity between the interaction of a woman with the health system for a given package and the delivery of relevant, effective interventions. Source: New analysis of data from UNICEF [75], Bryce et al. [26], DHS 2000–2007, and Service Provision Assessment Surveys (2003–2008). * Data from Service Provision Assessment Surveys in: Egypt, Ghana, Kenya, Rwanda, Tanzania, and Uganda. ** Postnatal care is the median from 12 countries based on analysis for Countdown 2008 [54].

Table 2
Delivery channels for interventions to reduce intrapartum-related adverse outcomes.

	Mass media (including social marketing, health days, etc.)	Community and women's groups	Traditional birth attendants	Trained outreach workers or CHWs	Skilled birth attendants (in community or primary care facility)	Facility-based health workers providing care at birth	Medical staff and clinical officers in first-level facilities
Comprehensive Emergency Obstetric care	*	*	* Facilitate referral for CEmOC	+/−	* Facilitate referral for CEmOC	Task shifting for cesarean delivery	✓ Task shifting for cesarean delivery
Basic Emergency Obstetric Care	*	*	*	*	✓ Task shifting for vacuum extraction	✓	✓
Skilled care at birth	*	*	*	*	✓	✓	✓
Clean birth care and facilitating referral	*	*	✓	✓	✓	✓	✓
Neonatal resuscitation with bag-and-mask			+/−	+/−	✓	✓	✓
Simple immediate newborn care (drying, warming, immediate breastfeeding)			✓	✓	✓	✓	✓
Post-resuscitation management						+/−	✓
Perinatal audit		✓		+/−	✓	✓	✓
Mobilzation of families to seek skilled care for mothers, newborns and children	✓	✓	✓	✓	+/−		✓

* Promotion ✓ Care provision +/− Situational/more evidence required.
Adapted from *Lancet* Maternal Survival Series, Campbell and Graham [89], and Bhutta et al. [90].

health system and effective supervision [10,37]. In fact, in 28 district hospitals in Malawi, non-physician clinicians carried out 90% of cesarean deliveries in a 3-month study period: 70% of those for emergency indications were with subtotal hysterectomy, 60% of those combined with total hysterectomy, and 89% of those combined with repair of uterine rupture [34]. Similarly, basic emergency obstetric care procedures, such as vacuum extraction, have been performed by midwives in many countries. In conflict and post-conflict settings, there are small-scale examples of community extension workers undertaking such procedures, for example in refugee camps in Burma [10,38].

3. Health system performance and context

3.1. Health system performance categories

There is enormous variation in healthcare systems around the world, particularly for care at the time of childbirth. Classifying the strength and performance of a country health system requires data. The WHO health system framework describes health systems in terms of 6 core building blocks: service delivery; health workforce; information; medical products, vaccines and technologies; financing; and leadership and governance (stewardship) [39]. Collectively these affect access, quality, affordability, and safety of personal and public health services, and subsequently, coverage of high impact interventions, theoretically resulting in improved health outcomes. Whilst this describes the components of the system, it does not capture how they articulate and perform in particular settings to produce the required outcomes. There have been many attempts to measure health systems performance and a detailed review of this is not an aim of this paper. However, we note that most previous attempts have focused on national economic indicators such as Gross National Income per capita (GNI) [40], but there are several outliers, for example low-income countries with high performance based on mortality outcomes, coverage of care, and equity, such as Cuba, Thailand, and Sri Lanka [41]. Conversely, there are also countries with high income and relatively poor performance such as South Africa and the USA [41].

The performance of the health system should be measured primarily by the effect on mortality and, for the purpose of this series, the focus is the reduction of intrapartum-related mortality. The key process target of relevance is timely access to high-quality care for every birth. Possible mortality outcome indicators may include child mortality, maternal mortality, or neonatal mortality. Stillbirth rates would also be a useful marker of mortality outcome, but are frequently unavailable or unreliable at population level [4]. Under-five mortality is an equally important mortality outcome, but it is possible to substantially reduce under-five deaths through interventions that are less dependent on health systems function such as oral rehydration solution, immunization campaigns, and bed nets. Facility-based care may only become more critical as under-five deaths fall to lower levels [41]. Hence, under-five mortality appears to be a less discriminatory outcome measure of more complex health system function necessary for effective care at birth. Maternal mortality is a newly accepted indicator of human rights [42], but is also clearly related to effective care at birth. However, routine measurement of maternal mortality ratio (MMR) is challenging [5] and may not be a simple choice to measure health system performance. As shown in Fig. 1 and described in the first paper in this series [1], there is a close relationship between MMR and NMR. Given that NMR is nearly 10 times more common, and is measured routinely in Demographic and Health Surveys, we propose that NMR is a useful surrogate marker of health systems performance to track mortality outcome for care at childbirth. Intrapartum-related NMR or intrapartum stillbirth rate or a composite of the two may be an even more sensitive mortality indicator for childbirth care [43]. However, these data are less available, especially at population level, and are more complex (with different denominators for the two components) than NMR. We endorse the UNFPA proposal of this composite (intrapartum stillbirth and day 1 neonatal mortality) indicator as a useful marker of quality of facility-based childbirth care, as

discussed under innovative data needs later in this paper, although, further evaluation of validity is required [43]. Skilled attendance at birth has also been used as a discriminatory marker of access to care, progress toward a comprehensive health system, and of equity, and is also widely measured and available [41]. NMR, and also MMR, however, is inversely associated with skilled attendance at birth, but this association cannot be considered here to be causal since the data is ecological (Fig. 1).

Hence, using one outcome indicator (NMR), we allocated 193 countries of the world into 5 "Categories" of NMR with an even distribution of countries per band apart from the top band (NMR>45), which has only 18 countries but still includes nearly one-fifth of global annual births (20 million). The same Categories of NMR have been used previously for setting priorities for neonatal mortality reduction in varying contexts [44,45]. Across these 5 NMR Categories shown in Fig. 1, there are also variations, up to about 90-fold, in maternal mortality ratio. Furthermore the cause-specific neonatal mortality varies. For example, in Category 5 countries (NMR>45 per 1000), around half of neonatal deaths are due to infections and the intrapartum-related NMR is around 12 per 1000, which is 20 times higher than in the Category 1 settings with the lowest mortality [1]. As described previously, these Categories act as a useful marker of variation of causes as well as magnitude of mortality. For policymakers with NMR data but no reliable cause of death data, these Categories may provide a simple surrogate that is better than no data at all [7].

The 5 Categories of NMR provide a sensitive indication of health system functioning during childbirth, including the predominant place of birth, person(s) attending the majority of births and providing essential newborn care, and availability of emergency and neonatal intensive care (Table 3). For example, the median cesarean delivery rate ranges from 17% in Category 1 (NMR ≤5), to 3% in Category 5 (NMR ≥45). Likewise, the density of skilled personnel is over 20-times higher in Category 1 (10.9 per 1000) compared with Category 4 (0.9 per 1000) and Category 5 (0.7 per 1000), the latter two of which are less than half that recommended by WHO of 2 per 1000 (Table 3).

In addition, the quality and quantity of health information varies with these 5 Categories, since the Category 1 settings have full availability of vital registration data, often recently updated, but the Category 5 settings are dependent on intermittent household surveys and verbal autopsy data for cause-of-death.

It should be noted that this approach to define a context for priority setting is not restricted to national analyses. For example, in some countries the urban capital city population may have entirely different outcomes (NMR) and health systems performance than in poor rural areas or in urban slums. Thus, while these 5 Categories were used to categorize countries, we recognize that they oversimplify the variable situations encountered in any given country and can also be applied to sub-national populations if the NMR data are available.

4. Prioritization, phasing, and potential lives saved

4.1. Principles for data-based prioritization for planning

Priorities and the menu of feasible solutions will vary across settings. Where data and a systematic decision-making process are lacking, it is more likely that choices will be swayed by the loudest voices, whether these are local or international, rather than by the true problems and priorities of the setting and local communities. A reproducible approach to defining the levels of health system performance by NMR is discriminatory and useful for priority setting and a first step in a transparent and data-driven approach to setting priorities. In all health systems, there are missed opportunities for providing life-saving interventions; thus, we focus first on addressing missed opportunities at facility and at community level. Given the major global gap for care at birth, we also examine priorities to close this gap.

The top priority should surely be given to interventions with the highest mortality impact that are also affordable and feasible, and improve equity [46]. Hence, we present modeled estimates of lives saved to inform the decision-making process. One of the reasons for ongoing lack of prioritization and investment in intrapartum care may be that advocacy has focused primarily on maternal deaths alone [47]. Linking in the numbers of intrapartum-related stillbirths and

Table 3
Countries (193) organized according to 5 Categories of neonatal mortality as a marker of health system performance, showing the variation in skilled birth attendance, health system capacity, and density of skilled human resources.

	CATEGORY 1 VERY LOW MORTALITY NMR≤5	CATEGORY 2 LOW MORTALITY 6–15	CATEGORY 3 MODERATE MORTALITY 16–30	CATEGORY 4 HIGH MORTALITY 31–45	CATEGORY 5 VERY HIGH MORTALITY ≥45
Births *# of countries* **Neonatal deaths**	12 707 000 *49* **42 000**	18 705 000 *51* **212 000**	33 577 000 *35* **627 000**	49 901 000 *40* **1 891 000**	20 727 000 *18* **1 065 000**
				77% of neonatal deaths	
Birth attendant coverage (%) Skilled attendance at birth (median) Traditional birth attendant (median)	 100 -	 99 14	 88 23	 52 23	 46 33
Cesarean delivery (median coverage)	17	15	12	3	3
Neonatal intensive care with ventilation	Full coverage Very high quality	High coverage Moderate/high quality may be variable	Low coverage (e.g. teaching hospitals) Variable quality, but increasing survival and disabled survivors	Very low coverage (e.g. capital city only) Low quality	Extremely low coverage and quality
Midwives per 100 000 populations (total number in level)	30 (225 845)	21 (274 023)	17 (174 071)	13 (596 407)	12 (111 318)
Physicians per 100 000 population (total number in level)	313 (2 901 950)	130 (1 778 614)	57 (1 905 038)	16 (863 043)	11 (203 770)
Density of physicians, nurses, and midwives per 1000 population	10.9	4.5	3.4	0.9	0.7

Abbreviation: NMR, neonatal mortality rate.
Country groupings by level of NMR adapted from Lawn et al. [7], and updated for 2009. Sources: maternal mortality rate [5]; intrapartum stillbirth rate [2]; NMR [75]; and revised neonatal cause-specific estimates for Countdown 2008 [26] based on methods from Lawn et al. [76]. The skilled birth attendance is based on median, and the range is reported in Lawn et al. [1].

intrapartum-related neonatal deaths increases the amount of deaths that are modeled by a quantum, and also allows for a broader analysis of the lives saved using the Lives Saved Tool (LiST) modeling software. *LiST* is a new module in Spectrum software based on *The Lancet* [48] Neonatal Survival [25] and Nutrition series modeling of lives saved. While many of the interventions to reduce maternal mortality and stillbirths are already included, however, an important limitation of the current version of LiST is that the output estimates for maternal lives saved and stillbirths averted are not yet available (see Panel 1). Thus, this analysis is based on national modeling using the most recent neonatal mortality rate and cause-of-death estimates, and applying mortality effect estimates in the Lives Saved Tool (LiST) whilst taking into account current national coverage of interventions. The details of the inputs and modeling are described in Panel 1, and the results are displayed in Table 4.

4.2. Identify and address missed opportunities within existing programs

The most obvious way to increase effective coverage and reduce deaths is to identify a programmatic platform that reaches the target population at the critical times (i.e. during pregnancy, childbirth, and in the immediate postnatal period) and addresses missed opportunities to provide packages of cost-effective interventions at the same contact [25,46,49]. To reduce intrapartum stillbirths and intrapartum-related neonatal deaths, some of the key interventions during pregnancy could be provided through prenatal care contacts, yet whilst many women come for one prenatal visit, fewer come for 4 visits and quality of care may be lacking (Fig. 3). It appears that some procedures such as blood pressure monitoring are carried out for almost all women, but it is unknown whether these measurements are taken properly and, even if properly performed, whether this information then leads to the appropriate case management should hypertensive disease of pregnancy be detected. Data for the details of effective care at the time of birth are almost entirely lacking—use of the partograph and tracking fetal heart rate are unknown and may not be amenable to questions in retrospective surveys [50]. While cesarean delivery data are increasingly available [51], it is unknown if the woman who received the procedure had a medical indication or not, or if so, whether the surgical intervention was timely [52] or was associated with complications [53]. The limited data on neonatal resuscitation provision suggest that there is an important missed opportunity whereby few skilled attendants are trained and equipped to provide this core intervention. There is even more limited data for postnatal care, particularly for a visit within 2 days (a global Countdown to 2015 indicator); comparable data are currently available for only 12 countries [54].

4.3. Potential for lives saved through addressing missed opportunities during contact points

Ensuring that every skilled attendant at birth can resuscitate the non-breathing newborn is a critical and achievable priority [17]. If coverage with neonatal resuscitation were increased to 90% for all current facility births alone (not including births outside facilities), 93 700 intrapartum deaths would be averted globally each year. The majority (n = 67 500) would be prevented in the two highest mortality settings (Categories 4 and 5, NMR > 30) where rates of skilled attendance at delivery are about 50%; an additional 21 900 deaths would be prevented in Category 3 (88% skilled attendance at delivery) settings. Provision of comprehensive emergency obstetric care is more challenging in weak health systems; however, if achieved for 90% of the deliveries that already occur in facilities, 232 500 neonatal lives could be saved each year, or 26% of all intrapartum-related neonatal deaths. The majority of deaths averted (n = 175 500) are in the two highest mortality settings (Categories 4 and 5, NMR > 30), and an additional 48 000 deaths would be averted in Category 3 settings. Thus, the greatest mortality effect is observed in the moderate and high NMR Categories, where the burden of deaths is concentrated, and the quality of childbirth care is deficient among babies who are born in health facilities.

There are also missed opportunities at the community level. For the 60 million home births, the person present at birth can at least dry and warm the baby, thereby providing stimulation and thermal control, and put the baby skin-to-skin with the mother. In one program in a poor, rural

Table 4
Estimates of neonatal deaths averted from intrapartum-related events for countries according to 5 Categories of neonatal mortality.

	CATEGORY 1 VERY LOW MORTALITY NMR ≤5	CATEGORY 2 LOW MORTALITY 6–15	CATEGORY 3 MODERATE MORTALITY 16–30	CATEGORY 4 HIGH MORTALITY 31–45	CATEGORY 5 VERY HIGH MORTALITY >45	Global Total
Births	12 707 000	18 705 000	33 577 000	49 901 000	20 727 000	135 617 000
# of countries	*49*	*51*	*35*	*40*	*18*	3 837 000
Neonatal deaths	42 000	212 000	627 000	1 891 000	1 065 000	
Skilled attendance (median)	**100%**	**99%**	**88%**	**52%**	**46%**	
Addressing missed opportunities						
Estimated lives saved if all births currently in facilities received effective care:						
(1) Comprehensive obstetric care	-					
(2) Neonatal resuscitation		9000	48 000	113 000	62 500	232 500
(3) Estimated lives saved if all home births had someone who could dry, and stimulate the baby		4300 <1000	21 900 1800	43 000 25 500	24 500 13 400	93 700 41 700
Reaching high (90%) coverage						
Estimated lives saved with single package of care:						
(1) Comprehensive obstetric care	Already > 90%	11 000 (8600–12 200)	51 000 (38 400–54 400)	282 000 (211 700–300 000)	150 000 (112 500–159 000)	494 000
(2) Neonatal resuscitation	-	5000 (2700–6900)	23 000 (1200–30 900)	107 000 (56 800–145 600)	57 000 (30 500–78 300)	192 000
(3) Management of neonatal encephalopathy	-	2000 (800–2500)	7500 (3800–11 300)	36 000 (17 800–53 300)	19 000 (9500–28 700)	64 500
Estimated lives saved if all 3 packages (comprehensive obstetric care, resuscitation and management of neonatal encephalopathy) are at 90% coverage [% of intrapartum deaths averted in NMR Category]	-	17 000 [47%]	83 000 [55%]	332 000 [76%]	181 000 [74%]	613 000 [68%]

Source: New analysis using data from UNICEF [75], WHO [91]. Skilled birth attendance is median percentage for each band of countries.
Modeling and inputs and methods described in Panel 1. Upper and lower range of lives saved shown for estimates with single package or intervention, based on 95% CI of meta-analysis or inter-quartile range of Delphi panel responses.

district in India, within a short time frame the community changed practices of delivering the baby onto the floor, to instead receiving the baby onto clean hands, wrapping the baby and putting the baby skin-to-skin. This change, along with others was associated with a halving of neonatal mortality in 18 months [55]. In settings where there are CHWs or health extension workers at scale, especially for communities with low access to facility care at the time of birth, options for community-based care can be explored, always bearing in mind the goal that these steps should lead toward a more comprehensive health systems solution. Simple immediate newborn care provided at all home births at 90% coverage is estimated to avert 41 700 (5%) of intrapartum-related neonatal deaths globally; the bulk of the effect (93%) would occur in Category 4 and 5 settings, where most deliveries occur in the home. Some countries are considering national scale up of community-based neonatal resuscitation. For example, in Nepal where over 80% of 796 000 annual births are at home and there is a strong community-based health care system, introduction of community-based neonatal resuscitation could save an estimated 1000 lives a year, based on LiST analysis (see Panel 1).

4.4. Invest to reduce major gaps in coverage for care at birth

Even if the health system performed to full effectiveness for every interaction that occurs antenatally, intrapartum, and postnatally between pregnant women and newborns with health system providers there remains a huge gap in coverage. Whilst 25% of women in Category 4 and 5 settings do not access prenatal care at all, a staggering 60 million a year give birth outside facilities [1]. Improving quality of care in facilities may draw more women to give birth in hospital; however, countries with high percentages of women giving birth at home urgently need to develop strategies that address both supply and demand factors to increase effective care at birth.

Countries must prioritize and commit to allocating the necessary financial resources to increase the supply of obstetric and newborn care. Several recent analyses have demonstrated the cost-effectiveness of obstetric-neonatal care packages [25,46,56]. In *The Lancet* Neonatal Survival Series, expansion to full global coverage with skilled maternal and immediate neonatal care was estimated to cost $1.8 billion international dollars and avert approximately 100 million DALYS, and met the cost-effectiveness thresholds of the Commission of Macroeconomics and Health [25]. Full coverage with emergency obstetric care packages cost $2.8 billion international dollars and averted 150 million DALYS, also meeting the criteria for cost-effectiveness. When skilled childbirth care, immediate newborn care, and emergency obstetric care are bundled as a package, cost is lowered and cost-effectiveness improved. Full coverage (90%) of emergency obstetric care was estimated to cost between $1.44–2.81 billion international dollars and avert 13%–24% of all neonatal deaths, mainly by reduction in intrapartum-related neonatal mortality [46].

Preliminary evidence suggests that removing financial hindrances and providing financial incentives may substantially increase demand for obstetric care. In Ghana, a rapid increase in facility birth coverage was observed following a Presidential decree removing charges for any care at birth or in the first month of life; institutional deliveries increased by 19% and skilled birth attendance by 14%–17% and likely more since the survey was carried out [57]. In India, the Janani Suraksha Yojna program has paid cash incentives to cover institutional delivery and transport. As a result, the total number of institutional births increased throughout the country, with some large states showing an unprecedented jump (9% in Orissa, 15% in Rajasthan, and 18% in Madhya Pradesh) between 2004 and 2007–2008 [58,59]. Although the impact on mortality outcomes is unknown, it is critical that quality maternal and newborn care is ensured.

4.5. Potential for lives saved at high (90%) coverage

Our new analysis for 193 countries suggests that if comprehensive emergency obstetric care was provided to 90% of all women in labor (regardless of place of birth) and was effectively implemented, an estimated 495 000 neonates per year could be saved that are currently dying of intrapartum-related causes. If neonatal resuscitation were to reach 90% coverage of all births, around 192 000 babies' lives could be saved. If the two packages were combined, with 90% coverage of comprehensive emergency obstetric care and neonatal resuscitation, as well as case management of babies with neonatal encephalopathy, then up to 613 000 newborn lives could be saved every year (Table 4). The majority (83%) of neonatal deaths averted would be from Categories 4 and 5, respectively, and 14% would be prevented in Category 3 settings.

An analysis of care packages in Sub-Saharan Africa and South Asia found that both skilled maternal and immediate newborn care as well as emergency obstetric care were highly cost-effective in both settings and highly recommended for universal scale up [56].

4.6. Priorities to reduce intrapartum-related burden, by the 5 Categories

In Categories 1 and 2, where the burden of intrapartum deaths is low, there is still a substantial burden of intrapartum-related morbidity. Key priorities include improved measurement of chronic disability and impairment, follow-up of long-term outcomes of disabled survivors, and the development and evaluation of early intervention programs and interventions to reduce the impact of chronic disability (Fig. 4). The prevention of risk factors such as adolescent pregnancy, and unhealthy behaviors may also be targeted to reduce future burden. In Category 3 where skilled attendance is relatively high, ensuring timely access to comprehensive emergency obstetric care and neonatal resuscitation, as well as providing post-resuscitation care is also a priority although may be lower impact, including improved recognition and basic management of neonatal encephalopathy with thermal and supportive care and referral to district or referral level facilities with neonatal intensive care facilities.

In Categories 4 and 5, programs may first address the missed opportunities for the approximately 50% of deliveries already occurring in facilities, and optimize coverage of prenatal, emergency obstetric, and neonatal care at district or referral-level hospitals. Achieving universal skilled attendance requires specific human resource plans and, simultaneously, increasing demand for skilled birth attendance may be facilitated by community mobilization efforts, financial incentives, communication and transport systems, and community birthing centers [11]. Other potential linking strategies that may deserve further evaluation include maternity waiting homes and targeted risk screening for pregnancy complications as opposed to prevalent maternal prepregnancy risk factors. For the approximately 50% of births that occur in the home, home-based care may be considered by a range of cadres for primary prevention, and even potentially neonatal resuscitation, as discussed in detail in the fifth paper in this series. Priorities must also include the training of skilled personnel and improvement of the quality and capacity of facilities for obstetric and neonatal care.

One of the strengths of the 5 Categories is the emphasis on continual health systems performance improvement, moving from one category to the next by context-specific, strategic strengthening of the health systems. While making the best of the immediate resources and opportunities, the countries must invest and act now to attain the long-term goal of universal coverage of effective care at birth (Fig. 4). High mortality settings (Categories 4 and 5) are working to move toward transitional (Categories 2 and 3) and then to lower mortality (Category 1).

5. Considerations for policy, planning, and implementation

5.1. National policy

Program managers and policy makers require more than a global review of effectiveness, or even cost-effectiveness, to decide which

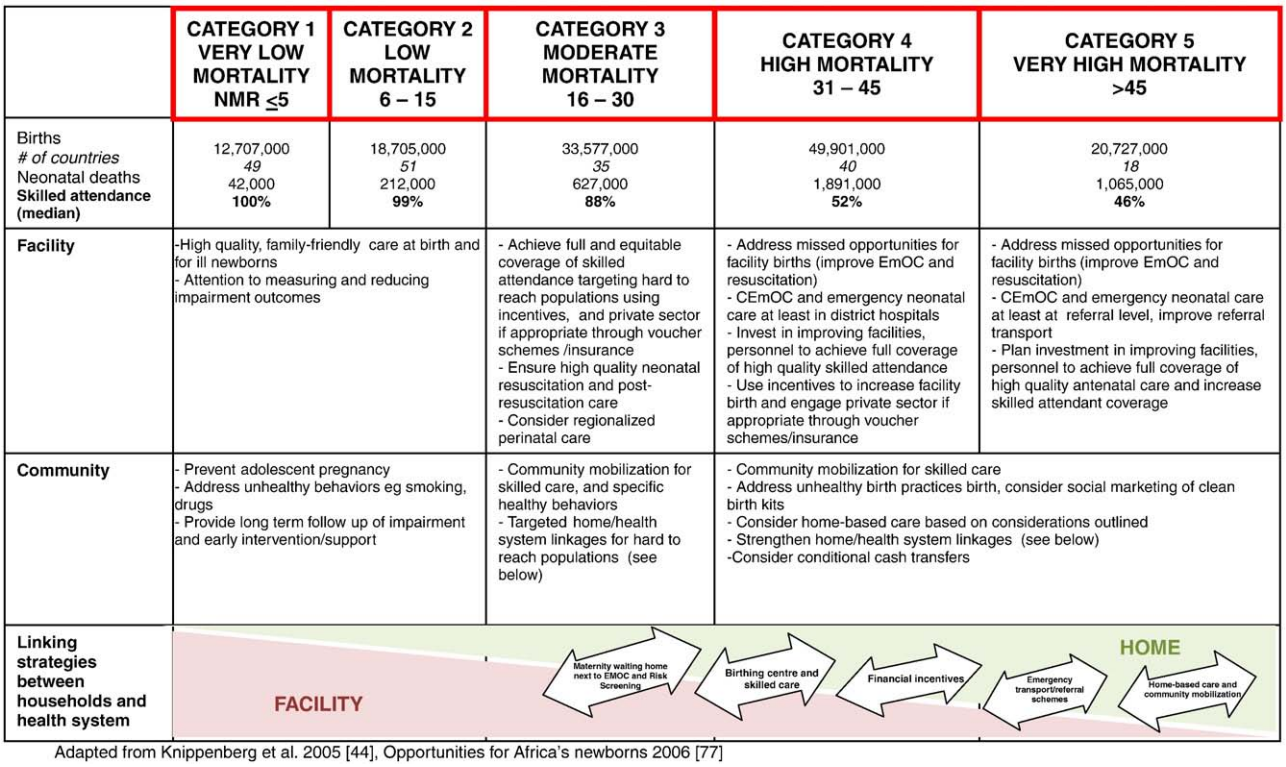

Fig. 4. Priorities to reduce intrapartum-related burden, for countries categorized by 5 Categories of neonatal mortality rate (NMR) as a marker of health system performance, showing linking strategies to increase effective coverage. Adapted from Knippenberg et al. [44], Lawn and Kerber [77].

strategies and specific interventions will be the most successful in their context. There is no magic "one size fits all" program to address intrapartum-related mortality; the local epidemiology (mortality rates, causes, and risk factors), as well as health system design and performance, financing, and community demand are key factors to consider [44].

More countries now have integrated MNCH strategies, laying out multi-year plans for scaling up key packages and the strategic approach to doing so. This is especially encouraging in large, high-burden countries such as Bangladesh, Nigeria, Tanzania, and Pakistan. The Pakistan MNCH integration and national plan was to a large extent driven by the recognition that perinatal deaths and intrapartum-related neonatal mortality could only be reduced by integrating skilled maternal and newborn care at all levels of the health system [60]. More commonly, countries have a health sector plan that includes some pages on maternal and child health and less commonly on neonatal interventions, given the recognition that to reduce this does require some specific planning and attention [61]. Stillbirths still generally remain invisible and fall outside national health plans.

Few countries have a specific national perinatal strategy, let alone a comprehensive strategy to address intrapartum-related complications. In 2008, the government of Bangladesh identified neonatal health as a critical problem gap and obstacle to meeting Millennium Development Goal 4 and developed a national neonatal health strategy via a collaborative consensus building process between the Ministry of Health, UN agencies, several NGOs, professional organizations, and the private sector. "Birth asphyxia" was identified as a top priority condition and a road map was developed to address intrapartum-related birth complications at all levels of the health system from the community to union-level and district-level hospitals, as well as along the continuum of pregnancy care, from prepregnancy, prenatal, intrapartum, and immediate postnatal care (Panel 2, at the end of the article).

However, a common theme even among those countries who have national strategic plans is a lack of either an implementation plan or a clear process to enable implementation in a decentralized, locally contextualized manner, for example at district level. Countries such as Tanzania and Ghana that have strong district health decision-making tools and processes appear to be making progress in reducing deaths [62].

5.2. Financing

Financial constraints are a critical barrier to women coming to facilities to give birth and can also be a major determining factor in lack of access or major delays in having a cesarean delivery [63]. The countries with the highest burden of perinatal mortality and the lowest performing health systems have an average GNI of only US $440; these are the poorest countries in the world (Table 5). Yet in these very countries, on average, half the costs for health care are paid out of the pockets of these extremely poor families, compared with less than 20% of the costs on average in the lowest burden/highest health system performance countries [11]. Government spending is only US $20 per capita, compared with the estimated US $34 required for a minimum package of health services [40].

Donor assistance for health has grown dramatically in the last 20 years, increasing from US $5.6 billion in 1990 to US $21.8 billion in 2007 [64]; donor spending has also increased by 66% for maternal and neonatal health and 63% for child health, resulting in nearly a US $1.4 billion increase from 2003 to 2006 [65]. However, both these analyses stress that the major increase has been for "vertical," disease-specific, commodity-driven interventions such as for HIV/AIDS, malaria, and immunizations. The investment in health systems and especially in care at the time of birth has not been commensurate to burden, or to the potential for lives saved. In addition, our analysis of Overseas Development Assistance (ODA) across the 5 NMR Categories suggests that the Category 5 countries with the highest mortality and lowest health system performance for intrapartum care receive lower ODA per birth for maternal/newborn care and lower ODA per child than the Category 3 and 4 countries (Table 5). This may be related to the countries that are post-

conflict or have governance challenges, but does raise the urgent need for more attention to MNCH care for the highest burden settings [10].

One novel approach to donor and government inputs is performance-based funding, which is defined as "transfer of money or goods conditional on taking a measurable action or achieving a predetermined performance target" [66]. To date, use of performance-based financing at scale has mainly been through the Global Fund to Fight TB, HIV/AIDS and malaria, and by the Global Alliance for Vaccines Initiative (GAVI). This strategy has potential to increase health system focus on meeting targets for increased coverage and quality of skilled care at birth. In Rwanda, increased institutional birth coverage was one of the targets set for performance-based funding and rates almost doubled (from 12% to 23%) in pilot provinces, whilst provinces with traditional input-based financing only saw a rise from 7% to 10% [66]. Given major increases in funding, more commitments including the first ever G8 statement on MNCH [67], performance-based funding focused on care at birth may help to ensure specific outputs with the greatest potential effect on MNCH.

In addition to supply-side financing, demand-side financing is crucial to remove economic barriers to care seeking. Experience from India and other countries demonstrates a rapid increase in utilization of public facilities for childbirth with conditional cash transfers [68,69].

6. Innovation to improve tools, evidence, and data

6.1. Innovation for tools and technologies

Creative and low-cost technologies may play a critical role in improving access to life-saving, intrapartum care interventions in low-resource settings. Key development needs have been highlighted in panels in several papers in the series. There is an urgent need to develop affordable and durable equipment, such as portable ultrasound devices, fetal heart rate monitors, hand-held Doptone devices, meconium suction devices, sterilizable bulb suction and self-inflating bag-mask devices. Furthermore, existing technology can be modified or utilization can be increased; for example, through the adaptation of bicycles or motorcycles for use as ambulances, or the promotion of cellular phone usage, supported by affordable and user-friendly software by community birth attendants to communicate with health centers and facilitate referral. These are discussed in more detail in second, third, and fifth papers in this series [10,13,17].

6.2. Improving the data for decision making

In order to guide policy making to monitor intrapartum-related events, there is an urgent need to refine and standardize indicators of intrapartum-related health outcomes, both fatal and non-fatal, as well as process indicators. Table 6 highlights some key considerations in developing improved and feasible indicators for use in low-income settings.

A strong argument can be made to develop a mortality outcome indicator that combines the burden of intrapartum-related injury on the fetus and newborn, given the linked pathophysiology, shared interventions to reduce both intrapartum stillbirths or neonatal deaths, and the frequent misclassification of stillbirths and non-breathing babies. Fauveau [43] suggested a new indicator of the quality of emergency obstetric care, intrapartum case fatality, which is the sum of the late stillbirth rate and first day neonatal deaths and this has recently been added to the UN list of indicators [28]. A more precise indicator of intrapartum-related mortality would be to add the intrapartum stillbirth rate ("fresh" stillbirths > 1000 g) to the rate of neonatal deaths among liveborn babies over 2000 g who die in the first 24 hours or prior to hospital discharge. This is likely to be a useful outcome indicator for care at birth that is sensitive enough to reflect quality of intrapartum care, yet common enough to be measurable, and with simple enough data to be feasible. The data in the first paper in this series demonstrates that the vast majority of intrapartum-related deaths in term babies occur within 24 hours of birth. Hence, predischarge data will capture most of these intrapartum-related neonatal deaths and may be feasible even using existing labor ward admission and discharge records. Further validation of this indicator and a standard approach to measuring and reporting the data are required.

Given that the majority of neonatal deaths occur at home, a key challenge is to develop and validate case definitions and classification systems that are feasible to apply consistently in resource-limited settings, and that allow comparability across different settings. Validation of verbal autopsy tools to differentiate stillbirths from livebirths and ascertain cause of death, particularly with hierarchies for categorizing causes of death in the presence of co-morbid conditions is a further challenge. Another critical program question with almost no useable data in low-income settings is regarding long-term disability and impairment after intrapartum-related complications [70]. In order to monitor this outcome, feasible and standard measures for neonatal encephalopathy need to be developed for low-resource, community

Table 5
Countries (193) organized according to 5 Categories of neonatal mortality, as a marker of health system performance showing the variation in gross national income per capita (GNI) and health system financing from government and donor sources.

	CATEGORY 1 VERY LOW MORTALITY NMR ≤5	CATEGORY 2 LOW MORTALITY 6–15	CATEGORY 3 MODERATE MORTALITY 16–30	CATEGORY 4 HIGH MORTALITY 31–45	CATEGORY 5 VERY HIGH MORTALITY >45
Births *# of countries* Neonatal deaths **Skilled birth attendance (median)**	12 707 000 *49* 42 000 **100%**	18 705 000 *51* 212 000 **99%**	33 577 000 *35* 627 000 **88%**	49 901 000 *40* 1 891 000 **52%**	20 727 000 *18* 1 065 000 **46%**
Gross national income per capita (GNI) (US$ median)	28 780	4590	2185	590	440
Government spending on health per capita % of all budget (Abuja target 15%)* (US$ median)	1507	327	137	35	20
Out-of-pocket expenditure on health as percentage of total expenditure on health (median %)	19%	30%	33%	39%	51%
Overseas development assistance (US$) To maternal/neonatal per livebirth (min/max range) To child health per child (min/max range) *# of countries*		0.9 (0.2–7.8) 0.45 (0.1–2.8) *4*	11 (0.8–33) 5.1 (0.3–15) *9*	12 (0.6–39) 8 (1.3–24) *35*	7.6 (1–38) 5.8 (2.4–38) *18*

Source: New analysis using data from Greco et al. [65], UNICEF [75], WHO [91].
Skilled birth attendance is median percentage for each band of countries.
* The Abuja target calls for African countries to allocate 15% of national budgets to health.

Table 6
Improving the data for decision making for intrapartum care.

Improved measurement of outcome data
Intrapartum stillbirths
- Improved measurement of the numbers/rates of stillbirths, especially in settings where most births occur at home and/or where stillbirths are normally a taboo subject
- Consistent definitions and classification systems to allow comparability of causes of death measurement across low- and high-income settings
- Tools to assess the causes of stillbirths, and to better distinguish intrapartum stillbirths versus antepartum stillbirths versus intrapartum-related neonatal deaths e.g. through verbal autopsy
- Linking to other data collection mechanisms e.g. vital registration, household surveys, demographic surveillance systems

Intrapartum-related neonatal deaths
- Improved measurement of intrapartum-related outcomes (mortality and morbidity)
- Consistent definitions and classification systems to allow comparability of measurement of intrapartum-related neonatal outcomes across low- and high-income settings
- Verbal autopsy tools and hierarchical methods to distinguish intrapartum-related neonatal deaths from other causes of very early death such as early-onset sepsis and preterm birth

Combined marker of intrapartum-related stillbirths and neonatal deaths, and/or intrapartum-related maternal deaths
- Validation of a composite indicator of quality of intrapartum care [43] e.g. intrapartum stillbirths plus first day (or predischarge if earlier) neonatal deaths >2000 g as a surrogate for intrapartum-related neonatal deaths, consider addition of intrapartum-related maternal deaths
- Classification systems to cross tabulate stillbirth and neonatal outcomes with maternal deaths, complications, and risk factors

Impairment and disability
- Feasible case definitions for neonatal encephalopathy in low-income and community settings (for example, surrogate marker proposed is seizures in first 24 hours in neonate with birth weight >2500 g)
- Screening methods (e.g. application of surveillance or screening tool followed by definitive testing of screen positives) for identification of infants at high risk of disability or impairment and who may benefit from early intervention
- Feasible, sustainable instruments to measure disability that are validated at population level to ensure that improved newborn survival (from intrapartum-related or other conditions such as preterm birth or infection) is not contributing to an increase in disability rates

Improvement in measurement of service coverage data
Obstetric care coverage indicators (refinement, consensus, and consistent reporting)
- Attendance at birth
  - Skilled birth attendance coverage, monitoring of skills, competence, and procedures performed by skilled birth attendants
  - Place of delivery, and other birth attendants
  - Cross tabulation by rural/urban and by socioeconomic status
- Emergency Obstetric Care services
  - Access, utilization, and met need for EmOC services, better determination of baseline marker of 'need' in different settings
  - Consistent definitions of maternal indications, complications, and life-saving interventions
  - Cesarean deliveries as % of all births: specify those for maternal-fetal indications
- Indicators to track referral systems for obstetric and newborn care from community to facility and between facilities

Neonatal care coverage (refinement, consensus, and consistent reporting)
- Indicators of newborn care at birth: Proportion of facilities with capacity for neonatal resuscitation (training and equipment), proportion of staff competent in neonatal resuscitation, neonates receiving neonatal resuscitation, validation of data collected through facility assessments or through retrospective surveys
- Routine postnatal care: Timing, frequency, cadres, and content of postnatal care visit in facility and at home, validation of data collected through retrospective surveys
- Emergency newborn care: Proportion of facilities with capacity for ongoing care for neonatal encephalopathy (neonatal intensive care, assisted ventilation, nutrition support, and fluid management)

settings. Furthermore, simple screening methods and tools to measure neurodevelopment and disability need to be developed, standardized, and validated on population-based cohorts in low-income settings.

Improved use of process indicators, including measurement of obstetric and neonatal service coverage and quality, is essential to tracking progress to improved intrapartum health outcomes. The UN process indicators of emergency obstetric care are relatively young and may benefit from refinement and improvement over time, for example the proportion of births in emergency obstetric care facilities or cesarean delivery may be more valuable if they specify the proportion of medically-indicated cases [71,72]. The indicator, met need for emergency obstetric care, requires clearer guidelines for the definitions of maternal indications and life-saving interventions, as well as clarity in the inclusion of abortion-related care. Consistent information needs to be collected on the quality of the content of interactions between healthcare providers and women during pregnancy, childbirth, and in the postnatal period, in order to quantify missed opportunities for interventions. Certain data, such as the proportion of deliveries that receive intrapartum monitoring or postnatal care, are almost completely lacking. This coverage data may be collected in national Demographic Health Surveys or Service Provision surveys and need to be consistently reported. Furthermore, the measurement of EmOC indicators can and should be linked with neonatal indicators, such as markers of the immediate neonatal care capacity including the proportion of newborns that receive neonatal resuscitation or proportion of skilled birth attendants trained in neonatal resuscitation. Other neonatal indicators may include the capacity of facilities to provide neonatal resuscitation and care for neonatal encephalopathy.

6.3. Implementation research

A systematic research pipeline has been framed for neonatal health interventions and may be applied for research priorities related to intrapartum-related injury [15]. In this model, research and implementation questions are grouped into 4 major categories:

(1) Definitions, descriptive data, and determinants of health: epidemiologic research;
(2) Discovery: basic and new science;
(3) Development: modifying or further developing new solutions; and
(4) Delivery: testing and monitoring delivery of solutions in "real world" settings.

The pipeline starts with the epidemiologic description and identification of major determinants of intrapartum injury, which is covered in the first paper in this series. Key areas and challenges for future epidemiologic research include the development of consistent case definitions of intrapartum-related neonatal deaths, classification systems, and terminology; comparable cause-specific data across different settings; and identification of reliable data on births and deaths in high-mortality settings. In the discovery phase, mechanisms of disease are investigated to guide the development of new interventions, ranging from elucidating the synergistic inflammatory response of maternal infections and hypoxic brain injury, to neuroprotective mechanisms of xanthine oxidate inhibitors and therapeutic hypothermia. In the development phase, interventions are developed or modified to reduce cost, increase effect or improve deliverability, such as low-cost and durable bag-and-mask resuscitators, wind-up Doptone devices, or CHW training materials. Finally in the delivery phase, existing interventions are implemented in new settings, with appropriate monitoring and evaluation to determine cost-effectiveness and mechanisms for scale up, and to guide the earlier steps of implementation research including the discovery and development science. Delivery research is urgently needed to increase the delivery of evidence-based interventions such as neonatal resuscitation in low-income settings, and to define challenges to effective scale up.

In Table 7, we summarize some of the key research and implementation questions identified in this series of papers. An innovative method to systematically prioritize research questions has been developed by the Child Health and Nutrition Research Initiative (CHNRI) [73], and is being applied to research questions for intrapartum-related neonatal deaths.

7. Conclusions

Care at birth is a sensitive marker of a responsive health system. There is a range of intervention strategies to select from to address

Table 7
Research questions organized by the research pipeline of definition, discovery, development, and service delivery.

Obstetric Care	
Definition and description	• Refining consistent, feasible approaches to data collection for intrapartum-related outcomes (perinatal mortality, neonatal encephalopathy, intrapartum stillbirths, intrapartum-related neonatal mortality)
	• Differentiating intrapartum-related events from preterm birth complications, especially in verbal autopsy
	• Developing and testing valid and feasible definitions of EmOC service indicators in different settings
Discovery	• Further research on pathophysiology and synergy between maternal infection and hypoxic brain injury, and mechanisms or medications to intervene
	• Mechanisms linking risk factors with intrapartum stillbirths or neonatal deaths
Development	• Development of low-cost hand held ultrasound device to connect with personal computer, simplified Doppler umbilical artery ultrasound
	• Simple training aids for use of fetal heart rate tracking devices and interpretation of findings (pinard stethoscope, Doppler fetal heart rate monitor)
	• Additional user-friendly, low-cost, durable, accurate alternative-powered fetal heart rate monitors capable of detecting late decelerations without need for complex interpretation
	• Oxygen condenser for adults using alternative power
	• Low-cost, durable training mannequins
	• Solar powered lighting for surgery, refrigerator for blood-banking
Delivery	• Rigorous evaluation of major intrapartum obstetric interventions on intrapartum related morbidity and mortality
	• Evaluation with field trials of widespread distribution of vacuum/forceps, hand held Doppler fetal heart rate monitor and effect on intrapartum-related outcomes
	• Trials with symphysiotomy training and kits/training aids
	• Effectiveness of obstetric drills and emergency obstetric training on intrapartum-related outcomes (fatal and non-fatal)
	• Safe methods of delivery induction in low-resource setting with limited monitoring
	• Effect of obstetric safety or delivery checklists on Intrapartum related morbidity and mortality
Neonatal Resuscitation	
Definition and description	• Refining consistent, feasible approaches to data collection for intrapartum-related outcomes (perinatal mortality, neonatal encephalopathy, intrapartum stillbirths, intrapartum-related neonatal mortality)
	• Differentiating intrapartum-related events from preterm birth complications, especially in verbal autopsy
	• Developing and testing valid and feasible definitions of resuscitation services indicators in different settings, including follow-up for long-term morbidity
	• Cohort studies to assess the long-term (2, 5, 10 year) outcome of neonatal encephalopathy at the community level. Do resuscitation programs reduce mortality but increase survivors with chronic disability?
Discovery	• Novel therapeutic interventions for treatment of babies with neonatal encephalopathy
Development	• Development/refining of more robust, simple, low-cost resuscitation equipment for use at the community level
	• Oxygen condenser for neonates using alternative power
	• Low cost, durable, pulse oximeters, with alternative power options
	• Low-cost, durable training mannequins
	• Develop and assess lower cost approaches for therapeutic hypothermia
	• Effect of oropharyngeal suctioning performed routinely for the non-vigorous infant with meconium staining
	• What is the effectiveness of a clean cloth on a finger to clear the mouth at birth?
Delivery	• Validation of an algorithm to recognize and resuscitate a non-breathing baby in the facility and in the community? What are the sensitivity and specificity and effect of these methods?
	• What are key selection criteria for successful providers of neonatal resuscitation? What are the best methods for testing competency?
	• Refining and testing the training process - key content and methods of resuscitation for lower-skill cadres and in the community, especially if they are illiterate, and frequency of re-training and supervision

Linking Families and Facilities	
Definition and description	• Developing and validating feasible indicators to monitor the functioning of referral and transport systems, community financing, birth preparedness, levels of community mobilization • Testing simple, feasible and more accurate risk screening algorithms with better predictive value focusing on pregnancy complications as opposed to prevalent maternal prepregnancy risk factors for use at the community setting and/or first level facilities
Development	• Assessing the role of new technologies for communication for arranging transport, and/or management of simple conditions in the community (mobile phones, GPS, satellite phones, internet, and options without electricity - solar powered systems, longer lasting batteries etc.) • Interactive methods and teaching tools for community mobilization activities, such as participatory women's group and community newborn stakeholder meetings (folk songs, puzzles, games) • Feasible means for CHWs or TBAs to identify maternal /fetal/neonatal complications during labor (such as a pictorial partogram). If so, will earlier referral and improved outcomes result? • What are strategies to promote community acceptance of and involvement in maternity waiting homes? Should risk-based approaches be used to determine who is referred?
Delivery	• The impact and cost of community mobilization, emergency transport systems, financial strategies, risk screening algorithms, and maternity waiting homes on perinatal-neonatal outcomes, and specifically intrapartum-related mortality (intrapartum stillbirth, intrapartum related neonatal death, or early neonatal mortality) • What are effective methods to communicate a list of danger signs for the mother and the newborn? What are effective methods to communicate danger signs with alternate health cadres? • Sustainability of community mobilization, - the optimal ratio of 'mobilizers': population and at what frequency do contacts need to occur? What are pathways for community mobilization to be taken to national scale? • How to sustain costs of fuel and repairs for emergency transport vehicles? • If women are identified to be at major risk, will they be able to act on this and access facilities with emergency obstetric and newborn care at the appropriate time? If not, what are the barriers to them doing so (e.g. money, time, other children, social acceptability)? • Assess social marketing to promote demand for community birthing centers or maternity waiting homes
Delivering Care at Birth in Community Settings	
Definition and description	• Increased understanding of traditional practices at birth and after birth that are commonly performed in different contexts-and may be amenable to change
Development	• Incentives for attracting and retaining skilled attendants to work in isolated birthing centers • Content and methods for training TBAs and CHWs in newborn resuscitation should be locally appropriate • Content, cost, and sustainability of clean delivery kit (target families) and home birth kit (skilled birth attendance or community cadre) • Effectiveness of "picture partographs" in assisting TBAs and CHWs in referring women with complications earlier or other methods to specifically improve TBA recognition and early referral of complications • Content and methods for training CHWs and TBAs in newborn resuscitation • Action for skilled birth attendant, CHW or TBA to do to stabilize a baby with "asphyxia" and assist in transport/referral
Delivery	• The effect and cost on maternal and fetal-neonatal outcomes of birthing centers, skilled birth attendants, TBAs, CHWs established within the community • Assessment of whether BEmOC skills can be safely, effectively, and feasibly done in the home setting vs facility settings • What are the outcomes for home-based BEmOC procedures? • Does CHW or TBA training with adequate on-going support result in a significant impact on the incidence of asphyxia-related fetal and neonatal mortality? • Does provision of community-based resuscitation reduce NMR without increasing disability? • What can be achieved at community level for babies with neonatal encephalopathy if referral is not an option? • What is the relative contribution of improved management of labor compared with neonatal resuscitation on PMR? • What is the social acceptability of community birthing centers, particularly in cultures where childbirth is a private family affair? • What are the key selection criteria for "successful" SBAs, TBAs, CHWs (e.g. age, literacy, number of deliveries per year)?
Perinatal Audit	
Development	• Development and testing of core perinatal audit module with paper-based and computer database that can be adapted and used in varying settings with comparable outputs with consistent results for cause of death and avoidable factors
Delivery	• Effect, cost and enabling factors for wide scale, sustainable implementation of audit • Linking perinatal audit with maternal audit, and/or with child mortality audit – feasibility, practical issues • Approaches to mortality audit meeting to overcome challenges of "blame" and "loss of face" • Further studies of community audit and models for joint community/facility audit

intrapartum stillbirths and intrapartum-related neonatal deaths, and almost all of these also benefit maternal survival and health. The call for new global attention to improve and scale up intrapartum care is clear, given the number of deaths, the lack of progress in the last two decades, and the feasibility of action at surprisingly low cost per life saved (Table 8). Global cries are empty, however, without local action. Every family, every facility, and every community member can play a role (see online appendix), but policymakers and clinicians responsible for care at the time of birth have a particular responsibility in leading change. New attention for MNCH health systems strengthening by the G8, even in the midst of global economic crisis, is encouraging [67].

Addressing missed opportunities to improve quality of care for current facility births is critical and immediately feasible—ensuring effective emergency obstetric care and neonatal resuscitation could save 327 200 neonates every year. There are also missed opportunities at community level where simple immediate newborn care may save 41 700 lives annually, and education on the recognition and rapid care seeking for complications could save many more (Table 4). However, to close the major gap in coverage for 60 million non-facility births will require new and strategic investments in service supply—bringing care closer to home and addressing the global shortfall of 1 million midwives needed, especially in Africa. Closing this coverage gap and providing universal coverage of emergency obstetric and neonatal care would avert an estimated 613 000 intrapartum-related neonatal deaths, and likely a similar number of intrapartum stillbirths, each year, as well as maternal deaths. In order to maximize these supply-side investments, more attention to demand strategies, including financial incentives and community mobilization, is also required.

Table 8
Key messages for evidence-based action to reduce intrapartum-related burden.

Paper	Problem	Policy and program actions
1	Intrapartum-related neonatal deaths: 904 000 Intrapartum stillbirths: 1.02 million Neonatal encephalopathy: uncertain Intrapartum-related maternal deaths: ~225 000	• More visibility of numbers, linking this burden with maternal health advocacy, better use of existing data to set priorities and track progress. • Consistency in terminology and classification systems. • Improve the data for pregnancy tracking and perinatal outcomes, especially intrapartum-related outcomes, particularly in low-income and community settings, including: ◦ use of NMR Category as marker of health system performance to help set priorities for action; ◦ new indicators for intrapartum care, including aggregate measure of intrapartum stillbirths and intrapartum-related neonatal deaths; ◦ measurement of impairment and disability related to intrapartum-related injury.
2	Missed opportunities for effective obstetric care for facility births Coverage of care at the time of birth is low, progress for scale up of skilled birth attendance is slow, and there is a gap in care for rural and poor populations, especially for cesarean delivery and EmOC.	Identify and address missed opportunities – quality gap • Intrapartum care that is focused on the highest impact components, but feasible for low-income settings. • Improve quality: training and drills, checklists, audit. • Innovative and robust equipment. Invest to close the coverage gap • Innovative task sharing with good supervision. • Strategic attention to solutions for care at birth for 60 million non facility births.
3	Lack of resuscitation and post resuscitation care, even for those born in facilities in low-income countries Major gap for home births	Identify and address missed opportunities – quality • All births to have someone who can dry and stimulate/rub the newborn. • Basic resuscitation available for all facility births, especially at primary care level. • Post-resuscitation care package at district hospital and above. • Innovative and robust equipment. Invest to close the coverage gap • Strategic attention to solutions for resuscitation for 60 million non-facility births.
4	Delays 1. Decision to seek care 2. Transportation to facility 3. Receiving effective care at facility	*Increasing community demand for obstetric care* • Community mobilization to increase birth preparedness, recognition of danger signs, and obstetric care seeking. • Financial strategies to reduce barriers to care seeking and provide incentives for obstetric care. *Formal healthcare system outreach towards community* • Community referral and transport schemes to reduce transportation delays. • Risk screening to bring high-risk women/babies closer to skilled care, need for new algorithms focusing on obstetric complications at high-risk for intrapartum-related injury (as opposed to old strategies using prepregnancy maternal characteristics). • Maternity waiting homes to bring higher risk mothers closer to skilled obstetric care.
5	Gap for service provision −60 million home births Lack of demand Policy conflict regarding use of community cadres	• Training of skilled birth attendants with capacity to provide intrapartum monitoring, BEmOC, and neonatal resuscitation in community settings; creation of community birthing centers. • Training TBAs in primary and potentially secondary prevention and encouraging partnership with the formal health system. • Integrated home-based care packages by CHWs, including community mobilization and pregnancy/delivery care with focus on primary and secondary prevention. • Linking with community cadres as part of process to build stronger, integrated health systems.
6	Missed opportunities, delays lack of accountability	• Audit as a tool to improve quality of care and accountability. • Only effective if the data links to action.
7	Weak health systems	• Integration of MNCH – with focus on high impact care at high coverage. • Variation of solutions based on context (mortality level, health system capacity). • Identify and address missed opportunities in existing health system packages (e.g. adding resuscitation to obstetric care). • Invest to reduce major gaps in coverage for care at birth. • Innovate – new tools and technologies and new delivery strategies to extend the reach of the health system. • Validate and promote an indicator of quality of intrapartum care with a composite indicator of intrapartum stillbirths and intrapartum-related neonatal deaths.
Overall message: The most sensitive test of a health system is provision of effective care at the time of birth and the ability to respond quickly to intrapartum emergencies for mother and/or baby; addressing missed opportunities increases the quality of current facility care, and closing the gap for 60 million non-facility births is critical for accelerating progress toward achieving MDGs 4 and 5.		

A more aggressive approach to innovation to increase health system performance at the time of birth as well as closing the huge gaps in data and evidence are urgently needed. Unless more priority is given, the world will continue to miss the unheard cry of the 230 babies who die every hour, almost three-quarters of whom could be saved through community mobilization, resuscitation, immediate postnatal care, and well-known obstetric interventions that also save mothers' lives.

8. Conflict of interest

The authors have no conflicts of interest to declare.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.ijgo.2009.07.021.

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Panel 1. Inputs and methods for modeling of impact using Lives Saved Tool (LiST)

Basis of the modeling

The Lives Saved Tool (LiST) gives a menu of interventions already loaded with current national coverage estimates. The user then sets coverage targets for each intervention by year up to 2015. The increases in coverage are linked to cause-specific mortality effect estimates resulting in estimates of lives saved by intervention and by cause per year for that country.

LiST is a new module in the Spectrum software based on *The Lancet* Child Survival [48], Neonatal Survival [25], and Nutrition [92] series modeling of lives saved. Many of the interventions to reduce maternal mortality and stillbirths are already included, but the output estimates for maternal lives saved and stillbirths averted are not yet available because modules for cause of death and intervention reviews of cause-specific mortality effect size have not been completed. A linked cost module is also being developed. The tool has been designed for use by country and district policymakers, planners, and managers in low- and middle-income countries, and by partner organizations (NGOs, multilaterals, bilaterals). The current format is in English, but the final version and training materials will be available in French, English, and Spanish.

Spectrum is a widely used, free demographic software package based on a demographic projection model called DemProj, developed and refined over the last 20 years and projecting the population by age and sex based on United Nations estimates. The software was originally to model the effect of family planning interventions and works on a country by country dataset. Several years ago a module was developed with UNAIDS and added to include lives saved and cost of AIDS interventions, and teams have been trained in over 150 countries [93].

Mortality inputs

We used numbers of neonatal deaths based on 2004 estimates of NMR and 2009 birth cohort per country [75]. Causes of death were based on the current UN estimated causes of death for neonates 2004 estimates of cause of death by country [26,76].

Mortality effect size due to each intervention

LiST includes a range of MNCH interventions, based on the strength of recommendation applying the GRADE criteria. The mortality effect estimates are based on a consistent review process using an adapted version of GRADE to review the level of evidence [18]. In some cases there are multiple high-quality studies (for example antenatal steroids. For others (e.g. cesarean delivery) there is a low quality of evidence because randomization to placebo would be considered unethical, but a strong recommendation for implementation based on GRADE. A series of systematic reviews are in press (*International Journal of Epidemiology*) [16,94]. The cause-specific mortality effect estimates used here are as follows:

- Comprehensive Emergency obstetric care: 75% [1]
- Resuscitation (facility): 30% [2]
- Immediate simple newborn care: 10% [1]
- Care of the baby with neonatal encephalopathy: 10% [1]

Current coverage of interventions

Coverage data are available for many interventions for most populous low- and middle-income countries through Demographic and Health Surveys as per the latest in UNICEF databases for 2009. However, for some interventions comparable data are lacking (for example cesarean delivery coverage or neonatal resuscitation) so assumptions were applied as described previously [25].

Combining interventions, estimating overall effect size

The estimates of lives saved are modeled such that lives cannot be saved twice by linked interventions affecting the same cause of death; for example, the prevention of intrapartum-related neonatal deaths by obstetric care, or prevention of the death by neonatal resuscitation or by care of the baby who has neonatal encephalopathy [25]. In addition, a cohort-based approach is used so that if a death is averted in the neonatal period, that baby then is at risk of dying in infancy from other causes of death. The software allows output to be displayed as tables or graphically, and can be by mortality rate change over time (e.g. to 2015), or by numbers of deaths averted for example by intervention or by cause of death.

Limitations

All modeled estimates have uncertainty. There are uncertainties around all the data inputs in LiST: the numbers of deaths, causes of death, mortality effect estimates, and the coverage data. Certain interventions that are already at high coverage will not result in many lives saved.

Notes:

[1] Based on results of a Delphi expert consensus process [16].

[2] Based on new meta-analysis [17,94].

Link to tool software: http://www.policyproject.com/software.cfm

Link to LiST manual: http://www.policyproject.com/software-Download.cfm?name=Spectrum&file=CSManual.pdf&site=Policy

Panel 2. Bangladesh National Strategy to reduce deaths related to "birth asphyxia"

Situation and health system context

Bangladesh has a population of 158 million and 4 million births each year [75]. From 1990 to 2007, the under-five mortality rate decreased from 151 to 65 per 1000 births (57% reduction), and from 1995 to 2007 the NMR decreased from 52 to 37 per 1000 births (29% reduction). Although Bangladesh is on track to achieve MDG 4 [56], neonatal mortality now comprises 57% of all under-five deaths. "Birth asphyxia" was estimated to account for 22% of neonatal deaths and the intrapartum-related mortality rate was 8.7 per 1000 live births, which is or nearly 17% of under-five deaths. From 2000–2007, coverage with a skilled attendant at birth was 18%, and the proportion of institutional deliveries was 15%. Thus, Bangladesh falls in the Category 4 "high" neonatal mortality setting (NMR 31–45), with a corresponding low coverage with skilled birth attendance (Table 3). Despite the low skilled attendance, there has been remarkable progress in reducing maternal deaths [95].

Political commitment

The constitution of Bangladesh ensures that "health is the basic right of every citizen of the republic" and the Health, Nutrition and Population Sector plan prioritizes universal access and equity in health care for all citizens, focusing on the women, children, and marginalized poor populations.

Strategic plan

Two independent evaluations of the national Health Nutrition Population Sector Plan (HNPSP 2003) identified neonatal health as critical problem areas. To address this gap, a National Neonatal Health Strategy and guidelines for implementation were developed in 2008 by the Ministry of Health and Family Welfare through a consensus building process with UN agencies, several NGOs including Saving Newborn Lives/Save the Children, professional bodies, ICDDRB, and the private sector [96]. The primary aims of the strategy were to: define interventions to be followed in public-private sectors for improving newborn health, outline essential services for newborns along the continuum of care, integrate neonatal and maternal health services, outline human resource development needs, provide guidance for community-level mobilization and capacity building, and define critical issues in program monitoring and evaluation. National research supported by Saving Newborn Lives through a grant from the Bill & Melinda Gates Foundation and by USAID provided evidence to guide program design [82,97,98]. The National Neonatal Health Strategy takes a comprehensive, health systems approach to reducing neonatal mortality. Intrapartum care is critical to the success of the strategy. The strategy document furthermore includes management guidelines for implementation of the strategy.

Interventions in the strategy for "birth asphyxia" along the continuum of care

Prepregnancy interventions

Education on risk factors and preventive measures such as delayed age at first pregnancy, birth spacing.

Pregnancy Intervensions

Four prenatal care visits including management/referral for high-risk conditions and counseling in birth and emergency preparedness, prenatal iron-folic acid supplementation, education on maternal and newborn danger signs, promotion of essential newborn care and avoidance of inappropriate oxytocin use.

Care during childbirth

- *Community/home birth*: Presence of community skilled birth attendant (CSBA) at all births, training in identification of risk factors and harmful practices contributing to birth asphyxia (oxytocin overuse); for eclampsia, CSBA may give first dose of magnesium sulphate at community level and refer to EmOC facility.
- *Facility level childbirth care*: Use of partograph, use corticosteroids for preterm birth, magnesium sulphate for eclampsia, management of breech (external cephalic version after 37 weeks, possible cesarean), labor induction after 41 weeks; calcium supplementation for prevention of pre-eclampsia to be explored.

Neonatal resuscitation

- *Immediate essential newborn care and neonatal resuscitation*: Training of all health providers in recognition of the non-breathing baby, training of community based providers in basic neonatal resuscitation with mouth-to-mouth resuscitation, training of facility level providers in advanced neonatal resuscitation including bag-mask, and cardiac massage based on the WHO algorithm [17].
- *Post-resuscitation referral and management:* Referral of all newborns resuscitated in the community for facility-based care; improvement in special neonatal units at district level hospitals, backup support of neonatal intensive care at tertiary level institutes.

Implementation approaches

Community implementation

Establish Government of Bangladesh–NGO partnerships to improve community and union-level maternal and neonatal health services; mobilization of community cadres (e.g. Family Welfare Assistant, Female Health Assistant, community skilled birth attendant, community health worker) to provide essential newborn care and recognize and resuscitate the non-breathing baby; community skilled birth attendants may initiate eclampsia management at the community level.

Strengthen referral linkages

Strengthen links between communities and facilities. Improve awareness on danger signs and care seeking.

Facility implementation

Increase capacity of facility-based paramedics, midwives, and physicians to provide emergency obstetric care, resuscitate, and manage post-resuscitation complications, including competency-based training in pre-service and in-service training. Increase coverage of interventions addressing maternal conditions that increase risk for intrapartum injury (e.g. eclampsia, infections in pregnancy).

Status of implementation, monitoring, and evaluation

The Core Committee for the National Neonatal Health Strategy has initiated the development of Action Plans to implement the strategy. The Action Plans will have detailed activities, approaches, roles of various partner organizations, budget and funding sources. A core set of indicators is also being developed with targets to measure progress.

Posters from Bangladesh for counseling on birth preparedness and maternal and newborn danger signs.
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