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

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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

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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.

Keywords

Asphyxia neonatorum; Birth asphyxia; Intrapartum-related neonatal deaths; Low-income countries; Neonatal; Neonatal encephalopathy; Neonatal resuscitation; Newborn resuscitation; Perinatal; Hypothermia

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.

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

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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 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].

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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.

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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.

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 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

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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: still-births 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 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).

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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

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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 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 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 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].

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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.

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 Desawere 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.

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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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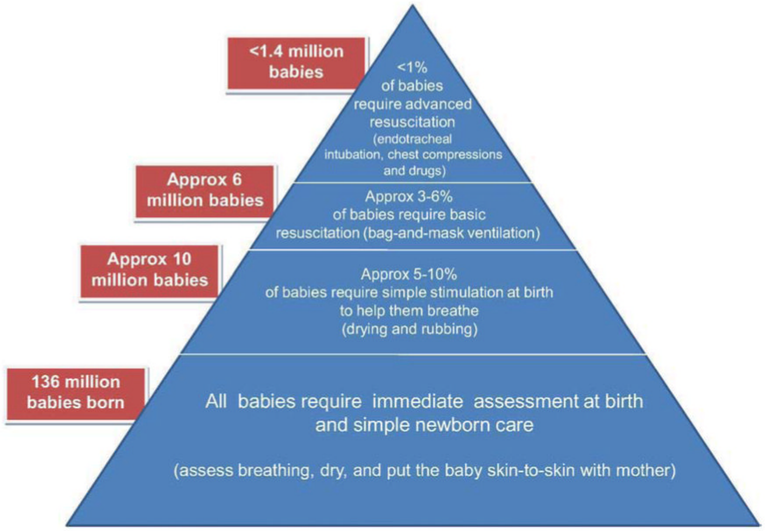

Fig. 1.

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

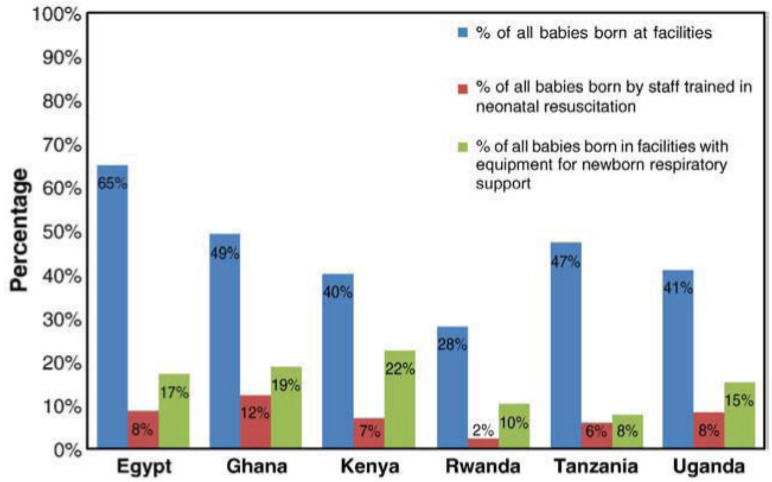

Fig. 2.

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.

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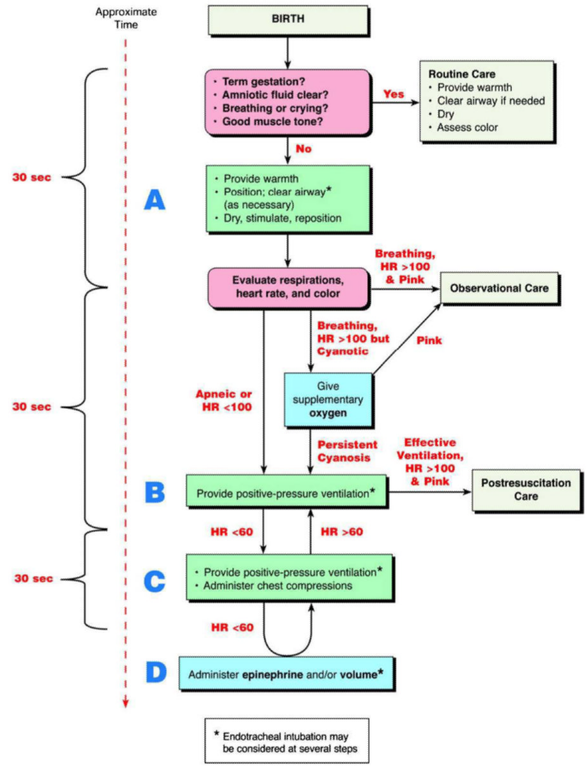

Fig. 3.

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].

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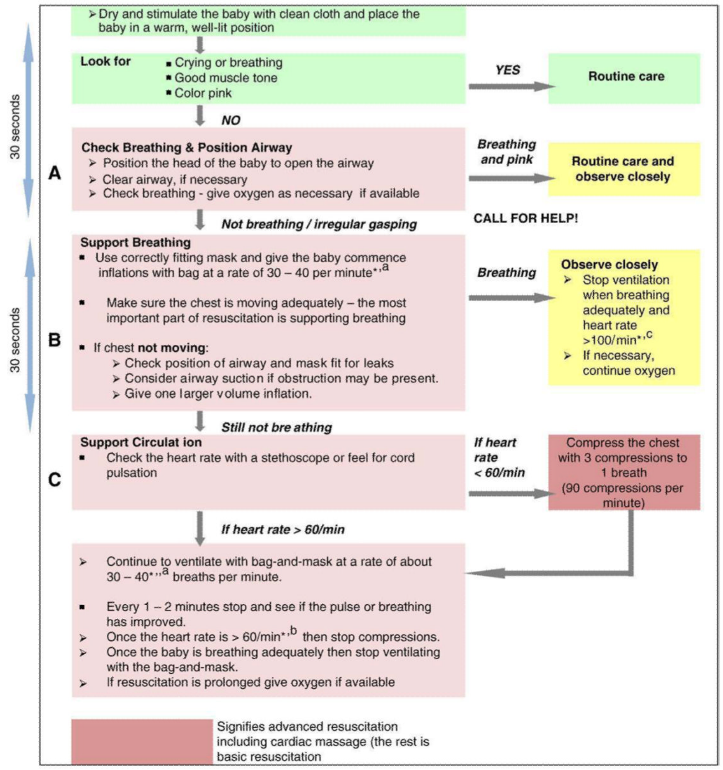

Fig. 4.

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).

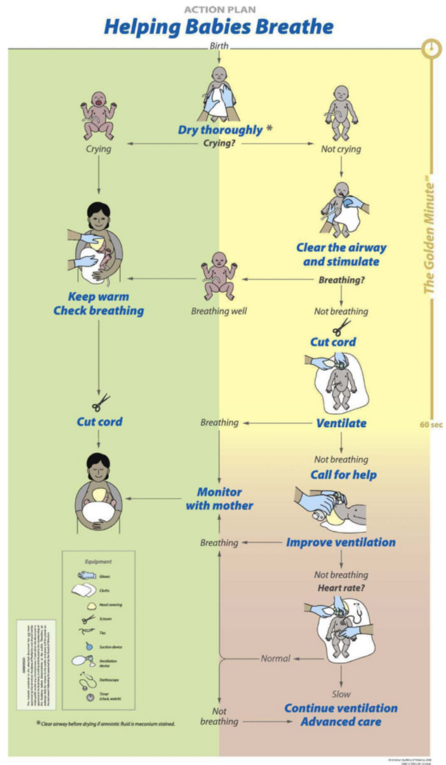

Fig. 5.

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

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.

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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.

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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 IPR-NMR 5.1 PMR 21	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.

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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.				

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**
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.

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