Beyond basic resuscitation: What are the next steps to improve the outcomes of resuscitation at birth when resources are limited?

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Abstract

Implementation of basic neonatal resuscitation in low- and middle-income settings consistently saves lives on the day of birth. What can be done to extend these gains and further improve the outcomes of infants who require resuscitation at birth when resources are limited? This review considers how resuscitation and post-resuscitation care can advance to help meet the survival goals of the Every Newborn Action Plan for 2030. A brief summary of the evidence for benefit from basic neonatal resuscitation training in low- and middle-income countries highlights key aspects of training, low-dose high-frequency practice, and implementation with single providers or teams. Reorganization of processes of care, as well as new equipment for training and selected clinical interventions can support further quality improvement in resuscitation. Consideration of the resuscitation algorithm itself focuses on important actions for all babies and special considerations for small babies and those not crying after thorough drying. Finally, an examination of the vital elements of assessment and continued stabilization/care in the health facility draws attention to the opportunities for prevention of intrapartum-related events and the gaps that still exist in postnatal care. Extending and improving implementation of basic resuscitation to make it available to all newborns will assure continued benefit to the largest numbers; once high coverage and quality of basic resuscitation are achieved, health systems with maturing capacity can extend survival gains with improved prevention, more advanced resuscitative interventions, and strengthened postnatal care.

Keywords

Resuscitation, neonatal; low- and middle-income countries; medical education, neonatal mortality, perinatal mortality, stillbirth

Key clinical practice points

- Focusing on basic interventions during training on neonatal resuscitation in low- and middleincome countries has resulted in important reductions in fresh stillbirth and first-day neonatal deaths.
- Low-dose, high-frequency practice facilitates incorporation of new skills into clinical performance and provides a mechanism to sustain and improve skills.
- Utilizing quality improvement cycles in conjunction with basic neonatal resuscitation can identify gaps in prevention of intrapartum-related events and postnatal care.
- Integrating maternal and newborn care and reorganizing processes of care can improve performance and outcomes.

Key research directions

- New adjuncts to training in neonatal resuscitation may facilitate acquisition of skills and foster low-dose, high-frequency practice.
- Improved techniques for monitoring heart rate and ventilation during resuscitation may improve short-term outcomes.
- Implementation research will be necessary to help identify key interventions during labor, resuscitation, and postnatal care to improve long-term newborn survival.

Background

Intrapartum-related events, or birth asphyxia, continue to be one of the leading causes of neonatal death, along with prematurity and severe infection ¹. Furthermore, neonatal death remains the single largest contributor to under-5 child deaths globally; nearly half of under-5 deaths occur in the first 28 days after birth ¹. In order to focus efforts on improving survival in the first 28 days, the Every Newborn Action Plan (ENAP) has set a target for all countries of < 10 neonatal deaths per 1000 live births by 2035 ². ENAP also seeks to end preventable stillbirths, reducing that rate for all countries to < 10 per 1000 total births. Currently, global averages for both neonatal deaths continue at rates > 30 per 1000 live births ^{1.3}. Extending coverage and improving quality of resuscitation clearly play important roles in achieving the ENAP targets. This review summarizes the available evidence for effectiveness of basic neonatal resuscitation in reducing fresh stillbirth and first-day neonatal deaths in low- and middle-income countries (LMIC) and proposes strategies to help achieve ENAP targets.

Impact of neonatal resuscitation on patient outcomes

A meta-analysis of randomized controlled trials of standardized neonatal resuscitation training programs in LMIC concluded that there is moderate-quality evidence that programs such as the Neonatal Resuscitation Program, Newborn Life Support, and adaptations of these decrease early neonatal mortality ⁴. Two cluster-randomized trials involving training of traditional birth attendants in simplified neonatal resuscitation also showed significant decreases in early neonatal mortality ^{5,6}. Helping Babies Breathe (HBB), a basic neonatal resuscitation program implemented in over 80 countries, has produced consistent and significant reductions in fresh stillbirths and first-day neonatal deaths (Table 1) ⁷⁻¹¹. A recent meta-analysis of these non-randomized trials (before/after intervention comparisons) highlights the impact on fresh stillbirths ¹². The HBB algorithm (Figure 1) emphasizes that within the first minute after birth, "The Golden Minute", a baby should breathe or receive positivepressure ventilation ¹³. All babies who do not cry after thorough drying should receive the initial steps of clearing the airway (positioning or suctioning if necessary) and specific stimulation to breathe, followed by positive-pressure ventilation if necessary. Providing the initial steps of resuscitation and ventilation to all babies (with the exception of those with evident maceration) has resulted in successful reversal of primary and secondary apnea and has included many babies who would previously have been misclassified as fresh stillborn and not offered timely intervention ¹⁴. Immediate ECG signal-data at birth, from a rural HBB study site in Tanzania, elucidates that progression to fresh stillbirth or first-day asphyxia-related neonatal death is likely part of the same circulatory end-process ¹⁵. Furthermore, almost 60% of babies classified by the provider as fresh stillborn after attempted resuscitation had heart rate activity around 50-60 beats/minute at cessation of good quality ventilation, demonstrating how difficult it may be to clinically distinguish a severely asphyxiated newborn from a true fresh stillbirth ¹⁵. The structure of training with HBB emphasizes the correct performance of initial steps including ventilation with air and eliminates training in chest compressions, intubation, and medication administration – more advanced interventions that distract attention from the importance of the initial steps both in training and clinical performance. It is still unclear to what extent chest compression

and/or medication would help restore cardiovascular integrity and prevent deaths among newborns with unresponsive bradycardia ¹⁵.

While basic neonatal resuscitation saves lives on the day of birth, very few studies have documented longer-term management and outcomes including mortality at 7 and 28 days. No studies of basic resuscitation have shown increased 7-day or 28-day neonatal mortality, suggesting that those babies who respond to basic resuscitation have generally good outcomes. Studies specifically examining developmental outcome of resuscitated babies also support this trajectory ¹⁶. Nonetheless, studies which have reported mortality through discharge or 28-day neonatal mortality have shown little decrease in overall neonatal mortality after implementation of basic neonatal resuscitation. Recently, a large single-centre implementation trial of HBB with quality improvement cycles in Nepal showed a significant decrease in fresh stillbirth, all-cause mortality within 24 hours of birth, and cause-specific mortality due to intrapartum-related events through discharge or 28 days. However, overall mortality to discharge did not significantly change, remaining around 12 per 1000 live births ¹⁷. Deaths from prematurity were postponed, but rates of survival for prematurity, infection, and congenital anomalies were unchanged. Similar findings from Tanzania point to the challenges in providing adequate thermal protection, nutrition, and protection from infection during inpatient care for small and/or sick newborns ^{18,19}.

Improving performance through training, practice, and quality improvement

Several strategies can be employed to improve the quality and performance of neonatal resuscitation, including training with content most appropriate to clinical responsibilities, low-dose high frequency practice, and system-level supports for sustainability and quality improvement.

Several training resources based upon the common scientific framework of the ILCOR Consensus on Science and Treatment Recommendations incorporate content and educational strategies for a range of learners²⁰. HBB (hbs.aap.org) is designed specifically for midwives and other birth attendants responsible for both the mother and baby at birth. The program focuses on initial steps during The Golden Minute and building skills in bag and mask ventilation. The Neonatal Resuscitation Program (NRP) shares the same scientific basis provided by the ILCOR Consensus on Science but includes advanced interventions of supplemental oxygen use, chest compressions, tracheal intubation, and medication administration²¹. While appropriate for physicians (e.g. paediatricians and anaesthesiologists) responsible for advanced neonatal resuscitation, the curriculum is often modified to meet the needs of midwives and nurses. Although nurses and midwives show significant improvement in knowledge and skills, their overall mastery remains less when presented with interventions not within the scope of their usual practice ²². Analysis of video recordings of actual resuscitations performed by midwives in a central hospital after NRP training with regular refresher training showed overall low scores for initial steps, bag-mask ventilation and chest compressions ²³. Video recordings and observations in other settings suggest that over-reliance on suctioning, chest compressions and other activities frequently delay and interrupt ventilation during neonatal resuscitation ^{14,24}. This may reflect prior training or experience with adult resuscitation, availability of suction devices and/or uncertainties related to ongoing ventilation ^{25 26}. Recent editions of NRP and the HBB curriculum de-emphasize the use of suctioning and more strongly emphasize techniques for achieving effective ventilation.

After initial training, low-dose high frequency practice facilitates incorporation of newly acquired skills into performance and provides a mechanism to sustain and improve them. Despite successful acquisition of knowledge and skills in training workshops, actual change in practice may not occur ²⁷. Skills decline more rapidly than knowledge following initial training ²⁸. However, implementation of HBB using subsequent deliberate and periodic practice has shown positive change in behaviour and

resuscitation outcomes across diverse settings ^{10,11,29-33}. A high level of coverage with initial training lays the groundwork for frequent refresher training to allow individual providers to correct and improve performance and build a shared model of action. Self-reflection, feedback from peers or near-peers, and debriefing of a team (where that exists) carry techniques used in the initial training into the practice setting, where they are necessary to overcome social and structural barriers to implementation. Pairing deliberate practice with quality-improvement cycles can address gaps in performance in a systematic way within a facility ³⁴. When conducted at the district level and supported by national Ministries of Health, such a system of continuous, brief practice and quality improvement can become a sustainable plan for improving patient outcomes ^{22,35}.

New devices and adjunctive methods for training in resuscitation show potential for building skills and improving clinical performance. Practice scenarios incorporating action steps for care of both the mother and newborn allow midwives to integrate skills that may have been taught separately into a single clinical pathway ³⁶. Video resources from a number of sites (hbs.aap.org, globalhealthmedia.org, medicalaidfilms.org, mpoweringhealth.org) can be used to focus on correct technique of individual steps, overall pacing, teamwork, or subsequent essential newborn care. Devices to give feedback on tidal volume, leak, and rate of ventilation during training have shown promise in helping providers achieve adequate ventilation more quickly. Such devices are currently under development for the commercial market (augmentedinfantresuscitator.com) ³⁷. Mobile applications under development address correct real-time decision-making during the resuscitation sequence (NeoTap <u>www.Tap4Life.org</u>, NRP Prompt <u>https://www.youtube.com/watch?v=26QB7tZToA8</u>) and ultimately may link to recording interventions in the clinical record and/or health information management system.

Examining the resuscitation algorithm for opportunities to improve processes of care

Reorganization for improved processes of care can improve the quality and effectiveness of resuscitation, whether basic or advanced. Offering more than basic resuscitative interventions requires the presence of additional trained personnel at birth, additional equipment, agreement on a more comprehensive resuscitation algorithm, and the capacity to support or refer resuscitated infants after immediate stabilization.

Decisions and actions for all babies

Thoughtful consideration of several basic action steps can improve the quality of resuscitation for all babies - those who require minimal stabilization and those who require actual resuscitation at birth. The steps in preparation for birth offer many opportunities for integration of efforts to improve both maternal and newborn survival as well as reorganization and improvement of processes of care ^{25 26}. When identifying a helper and reviewing the emergency plan, it is essential to articulate the actual steps to be performed by the helper and confirm the capacity to carry out those steps ³⁸. Many areas for delivery benefit from reorganization of space to provide privacy (e.g. hanging curtains between beds) and accommodate support persons in labour (e.g. a chair at the bedside) as well as access to soap and water or hand cleaner for both staff and patients/birth companions. The area for resuscitation may be either adjacent to the mother (e.g. on a dry surface at the foot of the bed by the perineum) if positive-pressure ventilation is provided with intact umbilical circulation or at a separate location if there are sufficient personnel to clamp and cut the cord without delaying the initiation of ventilation beyond one minute. Reprocessing and storage of neonatal resuscitation equipment to maintain high-level disinfection is a common gap in LMIC facilities that may expose vulnerable infants to potential sources of infection or damage resuscitation devices ³⁹.

The most recent ILCOR Consensus on Science, WHO Basic Newborn Resuscitation Guidelines, and the teaching materials for NRP and HBB Second Edition all recommend delayed umbilical cord clamping and

expectant management of infants with meconium-stained amniotic fluid. However, these recommendations have relatively limited uptake and at a minimum require deliberate introduction at the facility level and in some cases revision of national guidelines at the level of national Ministries of Health. A recent meta-analysis of randomized controlled trials from both developed and developing country settings concluded that delayed umbilical cord clamping as compared to immediate cord clamping for preterm infants reduced neonatal mortality to discharge ⁴⁰. An observational study from rural Tanzania including more than 15,500 spontaneously breathing infants showed a 20% decreased risk of death/admission for every 10-second delay in umbilical cord clamping after start of spontaneous respirations⁴¹. However, among the non-breathing infants in need of ventilation, the risk of death/admission was not associated with initiation of ventilation before versus after cord clamping, but time to start of ventilation; i.e. the risk for death/admission increased by 12% for every 30-second delay from birth to start of ventilation ⁴². Recent recommendations to eliminate routine tracheal suctioning for depressed infants with meconium-stained fluid further align basic and advanced neonatal resuscitation algorithms ²⁰. Helping Babies Breathe Second Edition reserves oropharyngeal suctioning for babies with meconium-stained amniotic fluid who are not breathing and need positive-pressure ventilation or those with secretions obstructing the airway. Despite this, video recordings and quality improvement observations from many sites confirm that excessive suctioning of the airway – whether with meconium-stained or clear amniotic fluid – is still common practice and leads to unnecessary respiratory depression, bradycardia or injury and subsequent need for increased intervention and support ^{24,30,43}.

Special considerations for preterm and small babies

Special considerations for the resuscitation of preterm and small babies focus on thermal and respiratory support. A decision to care for babies born preterm should signify that conditions have been met for safe administration of antenatal corticosteroids ⁴⁴. Operational guidelines should specify which

babies can receive initial stabilization skin-to-skin and how small babies will be kept warm during delayed umbilical cord clamping and initial stabilization. In addition to pre-warmed linen and radiant warmers, increased environmental temperature, plastic wrap and caps, as well as warming mattresses can be used in this setting ²⁰. Ventilation devices which provide PEEP during positive-pressure ventilation (bags with PEEP valves, T-piece devices) offer the theoretical advantage of avoiding de-recruitment of immature alveoli. T-piece devices further permit early initiation of CPAP with blended oxygen in the delivery setting and facilitate transport to the ultimate site of continued care ⁴⁵. High-flow nasal cannulae offer an alternative for early initiation of distending airway pressure and support after extubation ^{46,47}; however, rigorous evaluation of this method is in progress and the availability of a blender to achieve targeted oxygen saturations is essential to avoid increased risk of retinopathy of prematurity. Finally, the importance of contact between mother and baby at birth is now recognized to include later mental-health consequences for mothers as well as developmental consequences for the newborns ⁴⁸.

Special considerations for babies who fail to breathe spontaneously

For babies who fail to cry after thorough drying and the initial steps and require positive-pressure ventilation, the availability of more advanced interventions may permit immediate survival; however, the ability to provide long-term supportive care and the potential to inflict unintended harm must be addressed simultaneously. Implementation of the HBB algorithm in low-resources settings suggests that thorough drying and elimination of unnecessary interventions (suctioning, 100% oxygen administration) results in more newborns who cry spontaneously and require only routine care ^{10,30}. In low resource settings, of those who fail to cry or breathe spontaneously after drying (approximately 22%), about two-thirds will respond to specific stimulation to breathe and clearing the airway as needed (Figure 2) ^{14,15,49}. Approximately 7% will go on to receive bag-mask ventilation and among those, roughly 30% will require special newborn care and approximately 7% will be classified as fresh stillbirths or die within 30 minutes

after birth^{14,15,49}. Early heart rate guidance with ECG using a dry electrode contact is being explored for its potential to increase successful resuscitation ⁵⁰. A recent observational study demonstrates the relationship between delivered ventilation volumes and changes in heart rate. The most effective delivered tidal volume to produce the largest increase in heartrate was 9.3 ml/kg ⁵¹. A recent clinical trial of a new upright vs. conventional bag showed delivered higher tidal volume, mean airway pressure, peak inspiratory pressure and early expired CO₂ as well as improved clinical outcome immediately post-delivery with the upright device ⁵². Monitoring of exhaled CO₂ provides a relatively low-cost method for monitoring adequacy of ventilation ⁵³. Introduction of supplemental oxygen for resuscitation requires availability of pulse oximetry and blended oxygen/air as specified both by ILCOR and by WHO ^{20 44}.

If babies fail to respond to positive-pressure ventilation with bag and mask, advanced interventions can be provided according to the ILCOR resuscitation algorithm or specific guidelines of regional resuscitation councils (e.g. American Heart Association/Emergency Cardiovascular Care Guidelines in the U.S., Australia/New Zealand Guidelines, European Resuscitation Council.). However, key interventions such as tracheal intubation may be unavailable due to lack of skilled personnel or equipment. The laryngeal mask airway may prove to be a useful alternative to intubation when face mask ventilation is ineffective; recent mannequin and clinical trials suggest that training in insertion and use are feasible in resource-limited settings ^{54,55}. Modified algorithms for advanced resuscitation have been proposed for selected circumstances, for example specialized teams responding to humanitarian emergencies or disasters ⁵⁶. The ultimate utility of modified algorithms remains to be proven by field trials that include immediate and long-term clinical outcomes. Training with more advanced algorithms may distract from high-quality performance of initial steps and diminish their effectiveness. Furthermore, the infrastructure and resources for post-resuscitation care must be more robust and the local health

system must have capacity to support survivors with special health needs as they return to the community.

Strengthening post-resuscitation care to improve survival

In the drive to improve long-term neonatal survival, it may first be necessary to improve supportive care after resuscitation in order to sustain the gains achieved by basic resuscitation before introducing more advanced resuscitative interventions. Respiratory support with supplemental oxygen and distending airway pressure, thermal support with kangaroo mother care, nasogastric feeding of breastmilk, and heightened infection prevention/treatment for more vulnerable infants are core functions that can improve survival without full neonatal intensive care ⁵⁷. However, specialized newborn care also carries risks of unintended harm: lung injury and retinopathy of prematurity from inadequately regulated oxygen use, hyperthermia/hypothermia from lack of continuous temperature monitoring with radiant warmers or incubators, inadequate nutrition or unsafe substitutes for breastmilk, and nosocomial infection from crowding and insufficient hygiene ⁵⁸. These gaps in care result not only in morbidity, but also mortality – especially from prematurity/low birth weight and infection in the first week and month after birth ¹⁷.

Neonatal resuscitation is only the initial component of the package of essential newborn care, which addresses the key elements of thermal protection, breastfeeding, infection prevention, recognition of danger signs and treatment of presumed infection. Much as basic neonatal resuscitation can save lives on the day of birth, essential newborn care is necessary to preserve the gains in survival through the first days and weeks of life. All babies need assessment (weight, temperature, physical exam) concurrent with stabilization after resuscitation to make a plan for either routine care or special support

⁵⁷. Table 2 summarizes a number of gaps and potential solutions in providing essential newborn care and basic special inpatient care.

Prevention and treatment of intrapartum-related conditions and sequelae

Basic neonatal resuscitation focuses on secondary prevention of hypoxic-ischemic injury by immediate stabilization and reversal of pathophysiology in a non-breathing baby. Further reduction of adverse perinatal outcomes requires primary prevention of the intrapartum-related event and/or tertiary prevention of complications in the baby through specially directed postnatal therapy. Ideally, the implementation of a successful program of neonatal resuscitation results in examination of cases with adverse outcomes and analysis for potential underlying gaps in care. Detection of abnormal fetal heart rate (< 120 or > 160 beats/min) is highly associated with delivery of bag/mask resuscitation, early neonatal death, and stillbirth ⁵⁹. However, adequate fetal monitoring, correct use of the partogram, and timely obstetric interventions have proven complex, labour-intensive, and elusive to achieve with high coverage ^{60,61}. Interest in tertiary prevention of hypoxic-ischemic injury with postnatal therapeutic hypothermia in LMIC has grown with the success of this intervention in preventing sequelae of moderate encephalopathy in the technologically developed setting. Evaluation of evidence in LMIC provides support for therapeutic hypothermia only under clearly defined protocols in facilities with the capability for multidisciplinary care including IV therapy, respiratory support, antibiotics, anticonvulsants, and laboratory testing ²⁰. Two small studies have shown that babies with moderate to severe neonatal encephalopathy in hospital facility settings undergoing basic thermal care, experience "natural cooling" during the first 24 hours after birth 62,63. Although widely observed, it is unclear whether this natural cooling response to intrapartum hypoxia-ischemia is protective. The role of natural or passive cooling during referral to a centre equipped and staffed to provide therapeutic hypothermia

has yet to be investigated; however, unintentional hypothermia is strongly associated with increasing risk of death following a dose-response relationship ²⁰. When considering any tertiary preventive approach, the trade-off against devoting resources to primary prevention deserves consideration.

Conclusion

Reaching the ENAP goals for 2030 will require continued emphasis on basic neonatal resuscitation and

essential newborn care to achieve a high level of coverage and quality in all facilities ⁶⁴. Recent data

suggest that nearly half of all neonatal deaths occur within 24 hours of birth and in rural areas nearly

one-third occur within 6 hours ⁶⁵. Surveys of resuscitation protocols and equipment continue to show

important gaps in middle-income countries as well as low-resource areas ^{66,67}. Providing more advanced

resuscitation support becomes advantageous when prenatal prevention has been maximized and

postnatal care is provided with adequate numbers of trained staff, appropriate equipment and physical

infrastructure, health benefits which allow patient access to advanced care, regional transport/referral,

and health data and quality systems to track and respond to patient outcomes.

References

1. Liu L, Oza S, Hogan D, et al. Global, regional, and national causes of under-5 mortality in 2000-15: an updated systematic analysis with implications for the Sustainable Development Goals. Lancet 2016;388:3027-35.

2. World Health Organization. Every Newborn: An Action Plan to End Preventable Deaths. Geneva: World Health Organization; 2014.

3. Blencowe H, Cousens S, Jassir FB, et al. National, regional, and worldwide estimates of stillbirth rates in 2015, with trends from 2000: a systematic analysis.[Erratum appears in Lancet Glob Health. 2016 Mar;4(3):e164]. The Lancet Global Health 2016;4:e98-e108.

4. Pammi M, Dempsey EM, Ryan CA, Barrington KJ. Newborn resuscitation training programmes reduce early neonatal mortality. Neonatology 2016;110:210-24.

5. Gill CJ, Phiri-Mazala G, Guerina NG, et al. Effect of training traditional birth attendants on neonatal mortality (Lufwanyama Neonatal Survival Project): randomised controlled study. BMJ 2011;342:d346.

6. Carlo WA, Goudar SS, Jehan I, et al. Newborn-care training and perinatal mortality in developing countries. New England Journal of Medicine 2010;362:614-23.

7. Msemo G, Massawe A, Mmbando D, et al. Newborn mortality and fresh stillbirth rates in Tanzania after helping babies breathe training. Pediatrics 2013;131:e353-e60.

8. Goudar SS, Somannavar MS, Clark R, et al. Stillbirth and newborn mortality in India after Helping Babies Breathe training. Pediatrics 2013;131:e344-e52.

9. Bellad RM, Bang A, Carlo WA, et al. A pre-post study of a multi-country scale up of resuscitation training of facility birth attendants: does Helping Babies Breathe training save lives? BMC Pregnancy & Childbirth 2016;16:222.

10. KC A, Wrammert J, Clark RB, et al. Reducing perinatal mortality in Nepal using Helping Babies Breathe. Pediatrics 2016;137.

11. Arabi AME, Ibrahim SA, Manar AR, et al. Perinatal outcomes following Helping Babies Breathe training and regular peer-peer skills practice among village midwives in Sudan. Archives of Disease in Childhood 2018;103:24-7.

12. KC A, Ewald U, Niermeyer S, et al. Impact of Helping Babies Breathe program on perinatal outcomes in low- and middle-income countries: a systematic review and meta-analysis. Pediatr 2018; in review.

13. American Academy of Pediatrics. Helping Babies Breathe, Second Edition. Elk Grove Village, IL: American Academy of Pediatrics; 2016.

14. Ersdal HL, Mduma E, Svensen E, Perlman JM. Early initiation of basic resuscitation interventions including face mask ventilation may reduce birth asphysia related mortality in low-income countries. A prospective descriptive observational study. Resuscitation 2012;83:869-73.

15. Ersdal HL, Eilevstjonn J, Linde JE, et al. Fresh stillborn and severely asphyxiated neonates share a common hypoxic-ischemic pathway. International Journal of Gynaecology & Obstetrics 2017;17:17.

16. Carlo WA, Goudar SS, Pasha O, et al. Neurodevelopmental outcomes in infants requiring resuscitation in developing countries. Journal of Pediatrics 2012;160:781-5.e1.

17. Wrammert J, KC A, Ewald U, Malqvist M. Improved postnatal care is needed to maintain gains in neonatal survival after the implementation of the Helping Babies Breathe initiative. Acta Paediatrica 2017;106:1280-5.

18. Ersdal HL, Mduma E, Perlman JM. Helping Babies Breathe training is associated with decreased 24-hour neonatal mortality, and unchanged neonatal mortality beyond 24 hours. Pediatric Academic Societies; 2013.

19. Massawe A, Kidanto H, Moshiro R, et al. A care bundle including antenatal corticosteroids reduces premature infant mortality in Tanzania, a low-resource country. PLoS ONE 2018;in press.

20. Perlman JM, Wyllie J, Kattwinkel J, et al. Part 7: Neonatal Resuscitation: 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. Circulation 2015;132 (suppl 1):S204-S41.

21. Weiner G, ed. Textbook of Neonatal Resuscitation, 7th Edition. Elk Grove Village, IL: American Academy of Pediatrics; 2016.

22. Enweronu-Laryea C, Engmann C, Osafo A, Bose C. Evaluating the effectiveness of a strategy for teaching neonatal resuscitation in West Africa. Resuscitation 2009;80:1308-11.

23. Cavicchiolo ME, Cavallin F, Bertuola F, et al. Continuous refresher training on neonatal resuscitation improves intervention times in a low-resource setting. Archives of Disease in Childhood Fetal & Neonatal Edition 2017;in press.

24. Lindback C, KC A, Wrammert J, Vitrakoti R, Ewald U, Malqvist M. Poor adherence to neonatal resuscitation guidelines exposed; an observational study using camera surveillance at a tertiary hospital in Nepal. BMC Pediatrics 2014;14:233.

25. Moshiro R, Ersdal H, Kidanto H, Mdoe P, Mbekenga C. Factors affecting effective ventilation during newborn resuscitation: A qualitative study among midwives in rural Tanzania. Global Health Action 2017;in press.

26. Isangula KG, Kassick ME, Kairuki AK, et al. Provider experience with the large-scale "Helping Babies Breathe" programme in Tanzania. Paediatrics & International Child Health 2016;Sep 29:1-7.

27. Ersdal HL, Vossius C, Bayo E, et al. A one-day "Helping Babies Breathe" course improves simulated performance but not clinical management of neonates. Resuscitation 2013.

28. Bang A, Patel A, Bellad R, et al. Helping Babies Breathe (HBB) training: What happens to knowledge and skills over time? BMC Pregnancy & Childbirth 2016;16:364.

29. Mduma E, Ersdal H, Svensen E, Kidanto HL, Auestad B, Perlman J. Frequent brief on-site simulation training and reduction in 24-h neonatal mortality - An educational intervention study. Resuscitation 2015;93:1-7.

30. Kamath-Rayne BD, Josyula S, Rule ARL, Vasquez JC. Improvements in the delivery of resuscitation and newborn care after Helping Babies Breathe training. Journal of Perinatology 2017;37:1153-60.

31. Rule ARL, Maina E, Cheruiyot D, Mueri P, Simmons JM, Kamath-Rayne BD. Using quality improvement to decrease birth asphyxia rates after 'Helping Babies Breathe' training in Kenya. Acta Paediatrica 2017;106:1666-73.

32. Mduma E, Ersdal H, Kvaloy JT, et al. Using statistical process control methods to trace small changes in perinatal mortality after implementation of training program in a low-resource setting. International Journal for Quality in Health Care 2017;in press.

33. Arabi AM, Ibrahim SA, Ahmed SE, et al. Skills retention in Sudanese village midwives 1 year following Helping Babies Breathe training. Archives of Disease in Childhood 2016;101:439-42.

34. Theilen U, Fraser L, Jones P, Leonard P, Simpson D. Regular in-situ simulation training of paediatric Medical Emergency Team leads to sustained improvements in hospital response to deteriorating patients, improved outcomes in intensive care and financial savings. Resuscitation 2017;115:61-7.

35. Charafeddine L, Badran M, Nakad P, Ammar W, Yunis K. Strategic assessment of implementation of neonatal resuscitation training at a national level. Pediatrics International 2016;58:595-600.

36. Evans CL, Bazant E, Atukunda I, et al. Peer assisted learning to sustain provider performance after onsite, low-dose, high-frequency training and practice to prevent and treat postpartum hemorrhage and neonatal asphyxia: A pragmatic cluster randomized trial in Uganda. PLoS ONE 2017; in press.

37. Bennett DJ, Itagaki T, Chenelle CT, Bittner EA, Kacmarek RM. Evaluation of the Augmented Infant Resuscitator: A monitoring device for neonatal bag-valve-mask resuscitation. Anesthesia & Analgesia 2017;31:31.

38. Wrammert J, Sapkota S, Baral K, KC A, Malqvist M, Larsson M. Teamwork among midwives during neonatal resuscitation at a maternity hospital in Nepal. Women & Birth: Journal of the Australian College of Midwives 2017;30:262-9.

39. Eslami P, Bucher S, Mungai R. Improper reprocessing of neonatal resuscitation equipment in rural Kenya compromises function: Recommendations for more effective implementation of Helping Babies Breathe. Resuscitation 2015;91:e5-6.

40. Fogarty M, Osborn DA, Askie L, et al. Delayed vs early umbilical cord clamping for preterm infants: a systematic review and meta-analysis. American Journal of Obstetrics & Gynecology 2017;30:30.

41. Ersdal HL, Linde J, Mduma E, Auestad B, Perlman J. Neonatal outcome following cord clamping after onset of spontaneous respiration. Pediatrics 2014;134:265-72.

42. Ersdal HL, Linde J, Auestad B, et al. Timing of cord clamping in relation to start of breathing or ventilation among depressed neonates-an observational study. BJOG: An International Journal of Obstetrics & Gynaecology 2016;123:1370-7.

43. Wrammert J, Zetterlund C, KC A, Ewald U, Malqvist M. Resuscitation practices of low and normal birth weight infants in Nepal: an observational study using video camera recordings. Glob Health Action 2017;10:1322372.

44. World Health Organization. WHO recommendations on interventions to improve preterm birth outcomes. Geneva: World Health Organization; 2015.

45. Guinsburg R, de Almeida MFB, de Castro JS, et al. T-piece versus self-inflating bag ventilation in preterm neonates at birth. Archives of Disease in Childhood Fetal & Neonatal Edition 2018;103:F49-F55.

46. Lavizzari A, Colnaghi M, Ciuffini F, et al. Heated, humidified high-flow nasal cannula vs nasal continuous positive airway pressure for respiratory distress syndrome of prematurity: A randomized clinical noninferiority trial. JAMA pediatrics 2016;08:08.

47. Garg BD, Bajaj N, Sharma D. To compare the efficacy of heated humidified high-flow nasal cannula and continuous positive airway pressure in post-extubation period in VLBW infants. Journal of Tropical Pediatrics 2017;08:08.

48. Latva R, Korja R, Salmelin RK, Lehtonen L, Tamminen T. How is maternal recollection of the birth experience related to the behavioral and emotional outcome of preterm infants? Early Human Development 2008;84:587-94.

49. Linde JE, Schulz J, Perlman JM, et al. Normal newborn heart rate in the first five minutes of life assessed by dry-electrode electrocardiography. Neonatology 2016;110:231-7.

50. Linde JE, Eilevstjonn J, Oymar K, Ersdal HL. Feasibility of a prototype newborn resuscitation monitor to study transition at birth, measuring heart rate and ventilator parameters, an animal experimental study. BMC Research Notes 2017;10:235.

51. Linde JE, Schulz J, Perlman JM, et al. The relation between given volume and heart rate during newborn resuscitation. Resuscitation 2017;117:80-6.

52. Thallinger M, Ersdal HL, Francis F, et al. Born not breathing: A randomised trial comparing two self-inflating bag-masks during newborn resuscitation in Tanzania. Resuscitation 2017;116:66-72.

53. Blank D, Rich W, Leone T, Garey D, Finer N. Pedi-cap color change precedes a significant increase in heart rate during neonatal resuscitation. Resuscitation 2014;85:1568-72.

54. Pejovic NJ, Trevisanuto D, Nankunda J, Tylleskar T. Pilot manikin study showed that a supraglottic airway device improved simulated neonatal ventilation in a low-resource setting. Acta Paediatrica 2016;105:1440-3.

55. Pejovic NJ, Trevisanuto D, Lubulwa C, et al. Neonatal resuscitation using a laryngeal mask airway: a randomised trial in Uganda. Archives of Disease in Childhood 2017;14:14.

56. Umphrey L, Breindahl M, Brown A, et al. When Helping Babies Breathe is not enough: Designing a novel midlevel Médecins Sans Frontières neonatal resuscitation algorithm for low resource hospital settings. Neonatology 2017;in press.

57. Niermeyer S. Global gains after Helping Babies Breathe. Acta Paediatrica 2017;106:1550-1.

58. United States Agency for International Development. Do No Harm Technical Briefs2017.

59. Langli Ersdal H, Mduma E, Svensen E, Sundby J, Perlman J. Intermittent detection of fetal heart rate abnormalities identify infants at greatest risk for fresh stillbirths, birth asphyxia, neonatal resuscitation, and early neonatal deaths in a limited-resource setting: a prospective descriptive observational study at Haydom Lutheran Hospital. Neonatology 2012;102:235-42.

60. Kidanto HL, Mogren I, van Roosmalen J, et al. Introduction of a qualitative perinatal audit at Muhimbili National Hospital, Dar es Salaam, Tanzania. BMC Pregnancy & Childbirth 2009;9:45.

61. Semrau KEA, Hirschhorn LR, Marx Delaney M, et al. Outcomes of a coaching-based WHO Safe Childbirth Checklist program in India. New England Journal of Medicine 2017;377:2313-24.

62. Robertson NJ, Nakakeeto M, Hagmann C, et al. Therapeutic hypothermia for birth asphyxia in low-resource settings: a pilot randomised controlled trial. Lancet 2008;372:801-3.

63. Martinello K, Enweronu-Laryea C, Rose M, et al. Temperature profile of infants with moderate to severe encephalopathy undergoing standard temperature management at a Ghanian hospital: a pilot study. Neonatal Society UK; 2017.

64. de Graft-Johnson J, Vesel L, Rosen HE, et al. Cross-sectional observational assessment of quality of newborn care immediately after birth in health facilities across six sub-Saharan African countries. BMJ Open 2017;7:e014680.

65. Baqui AH, Mitra DK, Begum N, et al. Neonatal mortality within 24 hours of birth in six low- and lower-middle-income countries. Bulletin of the World Health Organization 2016;94:752-8B.

66. Trevisanuto D, Cavallin F, Arnolda G, et al. Equipment for neonatal resuscitation in a middleincome country: a national survey in Vietnam. BMC Pediatrics 2016;16:139.

67. Trevisanuto D, Marchetto L, Arnolda G, et al. Neonatal resuscitation in Vietnam: a national survey of a middle-income country. Acta Paediatrica 2015;104:e255-62.

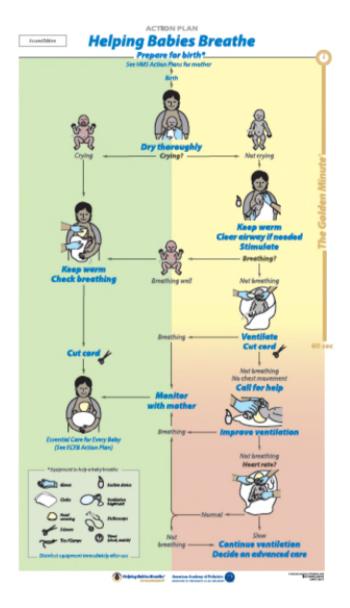


Figure 1. The Helping Babies Breathe Action Plan, an algorithm for basic newborn resuscitation. Reprinted from Helping Babies Breathe, Second Edition, Copyright 2016, with permission from the American Academy of Pediatrics (*request pending*).

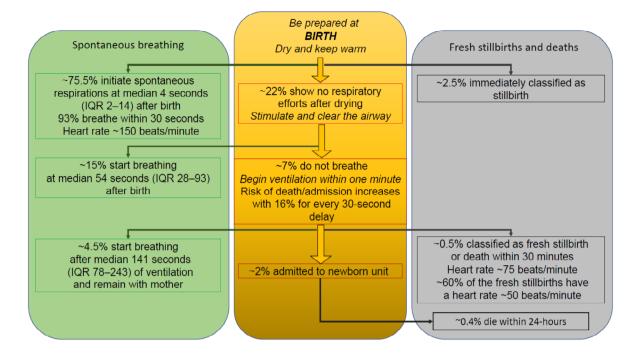


Figure 2. Observed response rates to basic neonatal resuscitation performed by midwives in a rural referral hospital in sub-Saharan Africa ^{14,15,49} More than three-quarters of babies breathe spontaneously after thorough drying and more than 90% are breathing after additional stimulation and clearing the airway as needed. Approximately 7% need ventilation with bag and mask. Of those babies receiving ventilation, the majority start breathing spontaneously and the remainder either require admission to a newborn unit or are classified as fresh stillbirth or immediate neonatal death.

Author/year	Setting	Outcomes	Change in rates	Measure of
				effect
Msemo 2013 ⁷	Tanzania	Fresh stillbirth	Reduction from 19	RR 0.76, 95% CI
	8 high-volume		to 14/1000 births	0.64, 0.98
	hospitals	Deaths in first 24	Reduction from	
		hours	13.4 to 7.1/1000	RR 0.53, 95% CI
			live births	0.43, 0.65
Goudar 2013 ⁸	India (Karnataka)	Fresh stillbirth	Reduction from 17	OR 0.54, 95%
	12 primary health		to 9/1000 births	CI 0.37, 0.78
	center, rural district			
	hospitals and urban	Pre-discharge	Unchanged at	
	hospitals	mortality	0.1%	
Bellad 2016 ⁹	India	Stillbirth	No significant	
	2 semi-urban and	Perinatal deaths	change	
	rural clusters in			
	Belgaum and Nagpur			
	Kenya	Stillbirth	Reduction from	MD 11.71, 95%
	Rural communities		25.7 to 16.4/1000	CI 0.95, 21.59
			live births	

		Perinatal death	Reduction from	MD 11.71, 95%
			38.5 to 28.2/1000	CI 0.39, 23.03
			births	
KC 2016 ¹⁰	Nepal	Fresh stillbirth	Reduction from 9	aOR 0.46, 95%
	High-volume, urban		to 3.2/1000 births	CI 0.32, 0.66
	maternity hospital	Deaths in first 24	Reduction from	aOR 0.51, 05%
		hours	5.2 to 1.9/1000	CI 0.31, 0.83
			live births	
		Intrapartum-		aOR 0.47, 95%
		related deaths		CI 0.35, 0.63
		through		
		discharge/28days		
Arabi 2018 ¹¹	Sudan	Fresh stillbirth	Reduction from 10	Pearson χ2
	Village midwives		to 3/1000 births	p=0.003
		Early neonatal	Reduction from 13	p<0.001
		deaths	to 4/1000 live	
			births	

Table 1. Implementation trials of Helping Babies Breathe showing consistent reductions in fresh stillbirth

and very early neonatal deaths.

Gaps in care	Potential solutions			
Thermal support				
Separation of mother and infant after	Criteria for immediate skin-to-skin care after			
resuscitation	resuscitation			
Use of mechanical warming devices without	Availability of temperature probes and use of			
adequate temperature control – hypothermia	servo-control of temperature			
and hyperthermia	Increased availability of kangaroo mother care			
Recognition of hypoxic-eschemic encephalopathy	Criteria for passive cooling and referral			
(HIE) and safe use of therapeutic hypothermia	Safer and more effective anticonvulsants for HIE			
Respiratory support				
Delivery of supplemental oxygen	Availability of pulse oximetry monitoring and			
	blenders for neonatal delivery systems for oxygen			
	administration			
Support with distending airway pressure	Early CPAP initiation after resuscitation			
	Appropriate patient interfaces for delivery of			
	CPAP and high-flow nasal cannula oxygen			
Breastfeeding	1			
Separation of mother and infant after	Criteria for immediate skin-to-skin care after			
resuscitation	resuscitation			

	Expression of colostrum within first hour after	
	birth	
	Presence of mothers in special care units and	
	participation in feeding	
Infection prevention/treatment		
Inadequate reprocessing/storage of neonatal	Guidelines for reprocessing (high-level	
resuscitation equipment	disinfection) and facility routines	
Overcrowding in special care areas	Appropriate use of kangaroo mother care and	
	sufficient staff/equipment	
Lack of handwashing facilities or hand cleaner for	Hand cleaner at each patient bedside and	
staff, families, and visitors	social/behavioural change communication	

Table 2. Common gaps in post-natal care in facilities and potential solutions