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Ending Preventable Neonatal Deaths: Multicountry Evidence to Inform Accelerated Progress to the Sustainable Development Goal by 2030

Joy E. Lawn[a, b] Zulfiqar A. Bhutta[c, d] Chinyere Ezeaka[e]
Ola Didrik Saugstad[f, g, h]

[a]MARCH Centre, London School of Hygiene and Tropical Medicine, London, UK; [b]NEST360 alliance, Rice University, Houston, TX, USA; [c]Centre for Global Child Health, The Hospital for Sick Children, Toronto, ON, Canada; [d]Center of Excellence in Women and Child Health, The Aga Khan University, Karachi, Pakistan; [e]College of Medicine, University of Lagos, Lagos, Nigeria; [f]Department of Pediatric Research, University of Oslo, Oslo, Norway; [g]Oslo University Hospital, Oslo, Norway; [h]Ann and Robert H. Lurie Children's Hospital of Chicago, Northwestern University Feinberg School of Medicine, Chicago, IL, USA

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Abstract
Introduction: The Sustainable Development Goal (SDG) 3.2 aims for every country to reach a neonatal mortality rate (NMR) of ≤12/1,000 live births by 2030. More than 60 countries are off track, and 2.3 million newborns still die each year. Urgent action is needed, but varies by context, notably mortality level. ***Methods:*** We applied a five-phase NMR transition model based on national analyses for 195 UN member states: I (NMR >45), II (30–<45), III (15–<30), IV (5–<15), and V (<5). We analyzed data over the last century from selected countries to inform strategies to reach SDG3.2. We also undertook impact analyses for packages of care using the Lives Saved Tool software. ***Results:*** An NMR of <15/1,000 requires firstly wide-scale access to maternity care and hospital care for small and sick newborns, including skilled nurses and doctors, safe oxygen use, and respiratory support, such as CPAP. Neonatal mortality could be reduced to the SDG target of ≤12/1,000 with further scale-up of small and sick newborn care. To reduce neonatal mortality further, more investment is required in infrastructure, device bundles (e.g., phototherapy, ventilation), and careful attention to infection prevention. To reach phase V (NMR <5), which is closer to ending preventable newborn deaths, additional technologies and therapies such as mechanical ventilation and surfactant replacement therapy are needed, as well as higher staffing ratios. ***Conclusions:*** Learning from high-income country is important, including what not to do. Introduction of new technologies should be according to the country's phase. Early focus on disability-free survival and family involvement is also crucial.

karger@karger.com
www.karger.com/neo

Correspondence to:
Ola Didrik Saugstad, o.d.saugstad@medisin.uio.no

Introduction

Global child mortality has been substantially reduced over the last three decades. As part of the Millennium Development Goals, there was political will to reduce child mortality from the baseline of 1990 by two thirds for the year 2015, and substantial mortality reductions of more than 60% were achieved [1]. Neonatal mortality requires distinct interventions but had less attention and progressed much less. Hence, almost half of under-five deaths occur now in the neonatal period – first 28 days after birth – still totaling 2.3 million neonatal deaths annually [2–5]. Additionally, stillbirths after 28 weeks gestation were an estimated almost 2 million annually in 2020, almost half of which were intrapartum [6]. Importantly, most of this annual toll of 4.5 million newborn deaths and stillbirths are preventable [5, 7–11].

In the Sustainable Development Goals (SDGs), for the first time, global goals included a specific target to end preventable newborn deaths. SDG number 3 is directly related to health, and target 3.2 is for every country to reduce neonatal mortality rate (NMR) to 12 or fewer deaths per 1,000 live births by 2030 [12, 13]. This target was based on analyses and wide consultation [10]. The "Every Newborn Action Plan" also included a stillbirth target, was endorsed by all UN member states in 2014 [9], and is being actively implemented by >90 countries. However, at least 50 countries are considered off track to meet the NMR target. A reduction from the present neonatal mortality of 18/1,000 to 12/1,000 could save almost 1 million newborn lives every year. A further reduction to 5/1,000 may prevent loss of another close to 1 million newborn lives annually.

Hence, the opportunity for impact is major. The three leading causes of global neonatal mortality are eminently addressable: prematurity, infections, and intrapartum related events ("birth asphyxia"). Congenital anomalies are fourth on the list globally [2, 14]. An estimated 20 million low-birthweight infants are born each year, and 15 million newborns are born preterm [15]. Among the 2.3 million neonatal deaths each year, over 80% are low birthweight, and more than half of these are preterm [11]. In addition to millions of deaths per year, there are also survivors with disability or lost development potential and millions of adults at increased risk of noncommunicable diseases after being born preterm or low birthweight or affected by other preventable neonatal conditions such as infections, intrapartum complications, or jaundice [11].

Ten suggestions to reduce global neonatal mortality were proposed in 2010 [16], the first being to "learn from the experience of improvements by other countries." Classification of care levels and regionalization represents an important factor in neonatal mortality reduction [16–18]. It is estimated based on current progress that some countries may not reach the SDG 3.2 target of 12 until 100 years later [10]. What strategies could help more rapid progress? The aim of this article is to inform accelerated reduction, in NMR to reach 12/1,000, fulfilling the SDG, especially in high-burden countries.

Methods

We use data from two different sources:

1. Historical data from selected countries that have reached the SDG target
2. Lives Saved modeling for 90 countries using national cause-of-death data and comparing impact over time to 2030 of increased national coverage for various packages and interventions.

Analyses 1: What Can We Learn from Historical Data?

We adapted an NMR transition model previously published based on national data for 195 UN member states, analyzing NMR by cause-specific mortality structure and associations with health service coverage such as facility birth rates [19, 20]. The previous five-phase neonatal mortality transition model has been widely used including for planning services based on context. The phases include I (NMR >45), II (30–<45), III (15–<30), IV (5–<15), and V (≤5) [14, 19–21].

We used this same 5-phase model to examine NMR trends and interventions over the last century and applied historical data from selected countries that have reached the SDG target. Included countries were those for which we had national data trends since 1900 (UK, USA) and also added Norway, Turkiye, and China with more recent decades (Fig. 1). We then examined published and unpublished literature from these countries to understand which strategies were applied in each country, with a focus on phases III and IV as this is where many countries are now and could change trajectories to reach the SDG by 2030 [5, 20].

The USA and UK reached the SDG target of NMR ≤12/1,000 live births in the 1970s (Fig. 1). The reduction from around 30 to 12/1,000 took over three decades, and the more rapid changes in the 1970s were in the early phase of neonatal care, just as the first neonatal doctors were being appointed, ventilatory support was being scaled up, and the care systems were being developed [22, 23]. Antenatal corticosteroids (ACS) were also introduced about this time, although initially coverage was low. Surfactant was not widely used in the UK until the late 1980s, or early 1990s, by which stage NMR was already under 5 per 1,000.

Norway reached the target of 12/1,000 in the 1960s, during the early days of neonatal care medicine (Fig. 1). Between 1970 and 2020, neonatal mortality in Norway dropped further from 10 to less than 2/1,000 [4]. We identified 3-4 interventions responsible for 50% of this later reduction: respiratory support/continuous positive airway pressure (CPAP), ACS, and then adding surfactant replacement therapy, which was included in neonatal care after the NMR was already below 5 per 1,000 [24].

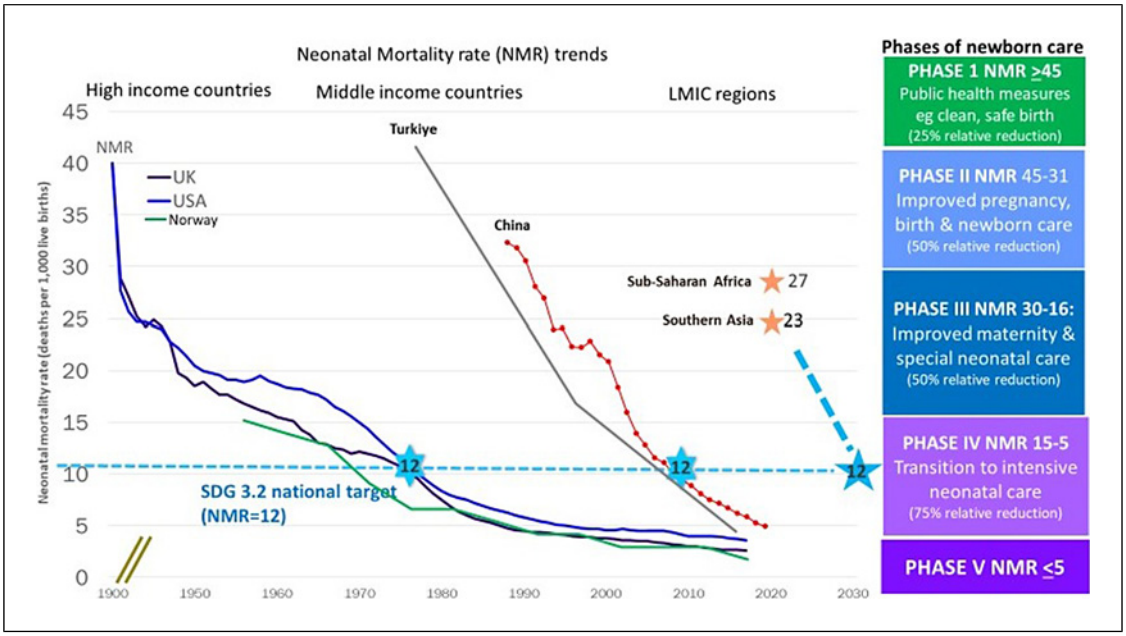


Fig. 1. Phases of neonatal mortality transition for the UK. Norway and USA from 1900 to 2020, China and Turkiye from 1980 to 2020, and sub Saharan Africa and Southern Asia 2000–2020, with estimated trends to 2030. Stars indicate when SDG 3.2 for an NMR of 12 per 1,000 live births was reached. Figure adapted and updated from reference [19] and reference [53]. Data sources: UK and US data: CDC, NIH, UK Office for National Statistics, 2012. China data from reference [25]. Norway and Turkiye data from reference [3, 4]. Regional estimates from reference [5].

China reached the target by 2007. What high-income countries (HICs) achieved during 40 years between 1930 and 1970, China did much more quickly [2–4] with very rapid reported NMR progress in phases III and IV, taking less than a decade to get from ~26 (current NMR for sub-Saharan Africa and South Asia) to 12/1,000 in about 2007, and is now surpassing the SDG target, reaching phase V (NMR ≤5) by 2020 [2–4]. In China, building on deliberate investment in basic primary care, there was intentional scale up of maternity and neonatal care and then policies and investment to reduce inequities including ensuring access to skilled personnel in rural area [25].

Turkiye also achieved more rapid progress than the historical trends in the USA, UK, and Norway [18]. In 1960, NMR in Turkiye was 63/1,000 dropping slowly to 33/1,000 in 1990. However, between 1990 and 2020 there was a 50% reduction per decade reaching the SDG of NMR of 12/1,000 in around 2007 and a further reduction to 5/1,000 in 2020. Turkiye needed 30 years from 1960 to move from phase I to III. From there to reach phase IV took 20 years and another 10 years to reach phase V. The basis for the Turkish success was introduction of a central health plan, shift of births into facilities, and scale up of special newborn care, with ventilation, trained personnel, and free medicine to every child if needed [18]. Based on these and other literature, we outline some common principles regarding strategies across this five-phase neonatal mortality transition model:

- Phase I (NMR >45) has no countries in this band of NMR now, with several having moved to phase II recently, most of which have had long-term humanitarian crises (Table 1). However, in 1990 most low- and middle-income countries (LMICs) were at this level of NMR, and some have since demonstrated impressive reductions, mostly since the year 2000, yet most are still above the SDG target of ≤12/1,000. Typically, most births are still at home, and more than half of neonatal deaths are due to infections.
- Phase II (NMR 30–<45): there are 14 countries still in this band, many of which have context of humanitarian crises, yet some have made remarkable progress (Table 1). Other countries showed more limited mortality progress potentially related to economic or political crises, the HIV epidemic, or a combination. It is important to note that there are data gaps in these countries, notably Yemen, given instability (Table 1) [2].

Births are in these countries moving into facilities, with perhaps half in facility by the end of this phase [20, 21]. Population-level measures may lead to a large absolute reduction (e.g., 45 to 30) and this would be a relative reduction of about one third. Interventions include, for example, clean births, neonatal tetanus immunization, improved breastfeeding practices, and access to antibiotics. Despite Afghanistan's challenges, NMR dropped from 1990–2020 from 74 to 35 per 1,000 [26].

- Phase III (NMR 15–<30): there are 49 countries still in this band as of 2021 (Table 1). Typically, most births are in facilities, with the majority in facility by the end of this phase [20], including improving obstetric care plus scale up of neonatal care with specific rooms or units, dedicated staff, and some equipment. Fewer neonatal deaths are due to infections; there is still an excess mortality risk from intrapartum complications, but still the highest proportion of neonatal deaths are due to preterm birth complications [20], notably respiratory distress syndrome.

Table 1. NMR progress for 200 countries and territories by phase of transition

Phase	NMR	Number of countries in 2021	Fastest progressors based on average annual rate of reduction (%) for NMR 2010–2021
I	≥45	0	–
II	30–<45	14	Above 2.0% per year: Guinea Bissau, Pakistan, Sierra Leone
III	15–<30	49	Above 4.0% per year: Bangladesh, India, Nepal
IV	5–<15	66	Above 6.0% per year: Azerbaijan, Kazakhstan, Sao Tome, Uzbekistan
V	<5	71	All those above 6.0% per year: Belarus, China, Estonia, Latvia, Montenegro, North Macedonia, Russia, Saudi Arabia, Turkiye

Source: analyses based on UN-IGME levels and trends report 2023. Reference [5]: https://data.unicef.org/resources/levels-and-trends-in-child-mortality/.

Importantly, as small, vulnerable newborns are cared for and stay longer in hospitals, there is a risk of hospital-acquired infections and specific prevention and detection/surveillance strategies are needed to address this risk [27].

- Phase IV (NMR 5–<15) now has 66 countries in this group, and almost all births in facilities, with increasing scale up of neonatal care systems, and some countries showing remarkable rates of progress for NMR reduction (Table 1). Yet there is still an excess mortality of preventable neonatal deaths, notably due to preterm birth. For neonatal care, this phase involves large-scale introduction of intensive newborn care (WHO level 3) and achieving an NMR of 12/1,000 for the SDG is unlikely without addressing preterm respiratory distress, with support such as CPAP. ACS can also play a key role. In addition, as neonatal mortality is reduced, the proportion of deaths due to congenital abnormalities becomes relatively more important.

During phase IV, the NMR may have a relative reduction by 75%, noting this is a smaller absolute reduction of 10, from 15 to 5 per 1,000. Based on lessons learned from HIC, an increasing emphasis on disability-free survival is fundamental [28] and a crucial shift to family-centered care related to family demand and patient-centered systems [20]. These shifts are also important in LMICs, not simply expanding neonatal intensive care with limited focus on safety and follow-up.

- Phase V (NMR <5) is based on universal coverage of neonatal intensive care with optimization and incremental quality improvement based on data, improving care systems and devices, introducing additional single therapies like surfactant therapy or therapeutic cooling. There are 71 countries in this band, and 9 countries have an average annual rate of change of >6.0% over the last decade. There are countries that have reached NMRs of under 2/1,000 and these are mainly countries with lower preterm birth rates such as Norway or Singapore which may relate to wider determinants of women's health and empowerment and access to free universal health care. In some countries, under-regulated assisted reproductive technologies may contribute to higher rates of multiple births and there may also be excessive nonmedically indicated caesarean sections, driving up preterm birth rates [29]. Despite major advances in neonatal care, there has been limited success for primary prevention of preterm births. Other countries have shown similar trajectories (Table 1), although we do not have access to their annual NMRs to show in Figure 1.

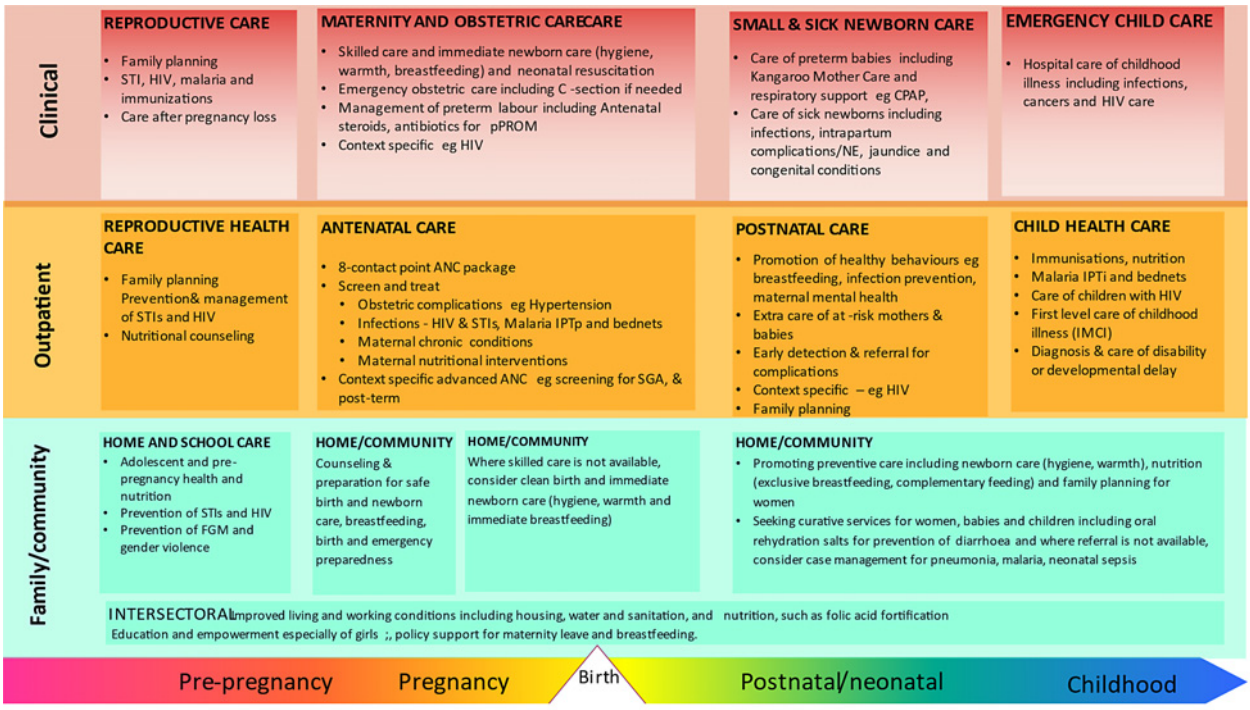
Chile is another example of successful reduction of mortality within phase IV with a 40% reduction of NMR from 9.2 to 5.7/1,000 during the 1990s, surpassing the SDG target, attributed to (1) improved infrastructure and equipment, e.g., warming devices, ventilators, (2) increased staffing with special training, and (3) more advanced respiratory support with later addition of exogenous surfactant therapy [30]. Chile's specific focus on addressing health inequities, 1990–2004, may have contributed to reductions in stillbirth and maternal mortality, as well as NMRs [31]. The Kyrgyz Republic for instance reduced NMR from 16.9 in 2010 to 11.7 in 2020, while scaling up neonatal care [32].

Analyses 2: What Can We Learn from Lives Saved Modeling?

Packages to prevent neonatal deaths across the continuum of care shown in Figure 2 include (1) antenatal care, (2) birth care, (3) postnatal care, and (4) newborn care in hospital [33] (Fig. 2). These packages each include a range of evidence-based interventions shown in the figure and as recommended by WHO. To inform the Every Newborn Action Plan (ENAP) strategies, the Lives Saved Tool (LiST) was used to undertake analyses for 90 countries based on national data for cause of death, coverage, and applying impact of these known interventions in packages. Based on this LiST analysis, Bhutta et al. [33] estimated that these packages if provided at wider scale (more than 90% coverage) in 75 high-burden countries could reduce the three most common causes of neonatal mortality – preterm, intrapartum events (asphyxia), and infection-related deaths – by 58%, 79%, and 84%, respectively. Interventions delivered during labor and at birth had the maximum effect on combined stillbirths, and maternal deaths, and important impact on neonatal deaths (Fig. 2a) [34]. However, the highest impact package for neonatal mortality reduction is for hospital care of small and sick newborns estimated at ~750,000 deaths averted per year. We underline that for these to succeed, it is critical to have a foundation of a functioning newborn care unit, with space, staff, and data for quality improvement as recommended by WHO level 2 (Fig. 2b) [35].

Antenatal Care

Figure 2a outlines the WHO recommended content for 8 contacts during pregnancy, with a focus on screening for maternal conditions. ACS are estimated to reduce mortality



a

Level 1 Immediate and essential newborn care	Immediate newborn care (delayed cord clamping, drying, skin to skin etc) Neonatal resuscitation for those who need it Breastfeeding early initiation and support Thermal care including skin to skin Essential newborn care Identification and referral of complications Targeted care as needed eg PMTCT of HIV
Level 2 Special newborn care	Thermal care including KMC Assisted feeding and IV fluids Safe administration of oxygen Detection and management of neonatal sepsis with injection antibiotics Detection and management of neonatal jaundice with phototherapy Detection and management of neonatal encephalopathy Detection and referral/management of congenital abnormalities
Transition to intensive care	CPAP management of preterm respiratory distress Follow up of at-risk newborns Exchange transfusion
Level 3 Intensive newborn care	Mechanical/assisted ventilation Advanced feeding support (eg parenteral nutrition) Paediatric surgery for congenital conditions Screening and treatment for RoP

b

Fig. 2. a Continuum of care showing evidence – based packages for reproductive, maternal, and newborn care. Adapted from reference [34]. **b** Levels of newborn care with interventions according to WHO guidelines. Adapted from reference [35, 53].

among premature neonates by 22% (RR 0.78, 95% CI: 0.70–0.87) [36]. The recent WHO-led ACTION trial in five LMICs showed a similar effect with dexamethasone compared to placebo (RR 0.84, 95% CI: 0.72–0.97) [37]. This study demonstrates that ACS must be used appropriately and in facilities by trained staff. Questions remain regarding the optimal dosing and duration, as noted in WHO updated guidelines [38].

Birth Care

Recommended care at birth by WHO includes a focus on midwifery lead care and a positive birth experience, plus effective interventions, such as timely caesarean section if indicated. Basic neonatal resuscitation is lifesaving [39]. Risks with oxygen have been increasingly recognized and have driven safer oxygen practices. The first multicenter study with air resuscitation found a 5% absolute reduction in mortality in term and near-term newborn infants compared to using 100% oxygen [40]. This is confirmed by a Cochrane review demonstrating a 4.9% absolute reduction of mortality, 16.2% versus 11.3% (RR 0.71, 0.54, 0.94) with number needed to treat (NNT) of 20 [41]. These studies paved the way for resuscitation programs including widely used programs like "Helping Babies Breathe" [42].

Postnatal Care

Postnatal care for mother and baby is important at this time of transition and includes healthy behaviors such as breastfeeding and clean cord care [43] (Fig. 2a).

Neonatal Care

WHO has published norms and standards for small and sick newborn care (SSNC) [44] and for care of the preterm newborn [45], based on levels of care and content detailed in Figure 2b. Immediate kangaroo mother care (KMC) involving continuous skin-to-skin contact reduced nosocomial infections/sepsis (RR 0.35, 95% CI: 0.22–0.54) and increased exclusive breastfeeding at 1–3 months of age (RR 1.20, 95% CI: 1.01–1.43). Furthermore, KMC is associated with lower length of hospital stay, however, with no proven difference in psychomotor development [46]. Immediate KMC, in addition to a full package of SSNC with CPAP, can further reduce mortality in babies weighing 1–1.8 kg in the context of newborn care units already able to provide respiratory support (RR 0.67, 95% CI: 0.48–0.95) [47].

CPAP was described in 1911 and reintroduced and applied to premature infants with respiratory distress in 1971 [48, 49]. Mortality before CPAP was approximately 25% and CPAP almost halved mortality versus oxygen therapy alone (RR 0.53 [0.34–0.83]) with a NNT of 9 [50]. Robust, low-cost methods to provide CPAP are now widely available.

Apnea of prematurity remains a risk, especially in units with low baby-to-nurse ratios. Caffeine citrate is now the drug of choice and reduces bronchopulmonary dysplasia but is not easily available nor affordable in many LMIC, despite that the WHO had included it as a specific drug for neonatal care since 2009 [51, 52] and underlined the value in the latest WHO guidelines [53]. In the CAP trial, treatment with caffeine compared with a placebo significantly improved the rate of survival without neurodevelopmental disability at a corrected age of 18–21 months (OR 0.77; 95% CI: 0.64–0.93; $p = 0.008$), significantly reduced the incidence of cerebral palsy (4.4 vs. 7.3%; OR 0.58; 95% CI: 0.39–0.87; $p = 0.009$) and of cognitive delay (33.8 vs. 38.3%; OR 0.81; 95% CI: 0.66–0.99; $p = 0.04$) [52].

Artificial ventilation before the introduction of CPAP was reported to reduce mortality (RR 0.86 [0.74–1.00], NNT 10) [54]. However, most likely many of those who were treated with artificial ventilation before CPAP was introduced, today would survive with CPAP alone (Figure 2b).

Surfactant therapy could further reduce mortality. Early studies with one dose of natural surfactant in countries with NMR already below 5 per 1,000 (Fig. 1, phase V) showed that mortality was reduced in newborns with birthweight between 700 and 2,000 gram [55]. Typical relative risk for mortality reduction with surfactant is 0.68 (95% CI: 0.57–0.82). The NNT is 11 [56]. The estimated relative risk reduction in mortality by surfactant therapy of 32% is close to the estimated reduction by Das et al. [57] in neonatal mortality by surfactant at RR 0.60 (95% CI: 0.47–0.77) in eight countries already with lower mortality.

Cooling after HIE is recommended in HICs leading to a 25% reduction in cause-specific mortality [58]. However, some studies, including Helix, suggest that other risks may outweigh the gains of cooling in LMIC contexts [59, 60].

Implications

The Every Newborn Action Plan (ENAP) emphasized that for countries to achieve their goals for newborn mortality and stillbirth prevention it is crucial to scale up high-quality antenatal, childbirth, and postnatal care as well as inpatient care for small and sick newborns, with equity [11]. Given the number of countries off track in 2020, four coverage targets were co-developed and agreed to by all countries for 2020–2025 [13]:

Every pregnant woman: four or more antenatal care contacts, which is already close to 80% worldwide, and the target set is a global average of 90%.

Every birth: births attended by skilled health personnel, which is also close to 80% worldwide, and the target set is a global average of 90%.

Every mother and newborn: postnatal care within 2 days, which is slightly lower coverage, with the target set is a global average of 80%.

Every small and sick newborn: this small and sick newborn care (SSNC) is recognized to be a newer focus, with limited availability now in many countries. Indeed, coverage data are lacking, which is a crucial issue to address to better track progress and equity. The target set, based on country consultation, was for "80% of districts (or equivalent subnational unit) have at least one level-2 inpatient unit to care for small and sick newborns, with respiratory support including provision of CPAP.

This coverage target for scale up of SSNC is an ambitious but important step for many countries, now receiving a lot of policy attention. The examples presented in this paper from many countries and all regions convey an important message.

We have demonstrated that evidence-based care may save hundreds of thousands of newborn lives each year. An NMR of <15/1,000 is possible with focus on systematic scale up of SSNC. To reach an NMR <12/1,000, most countries included respiratory support in their newborn care but given recent innovations that can be achievable with CPAP.

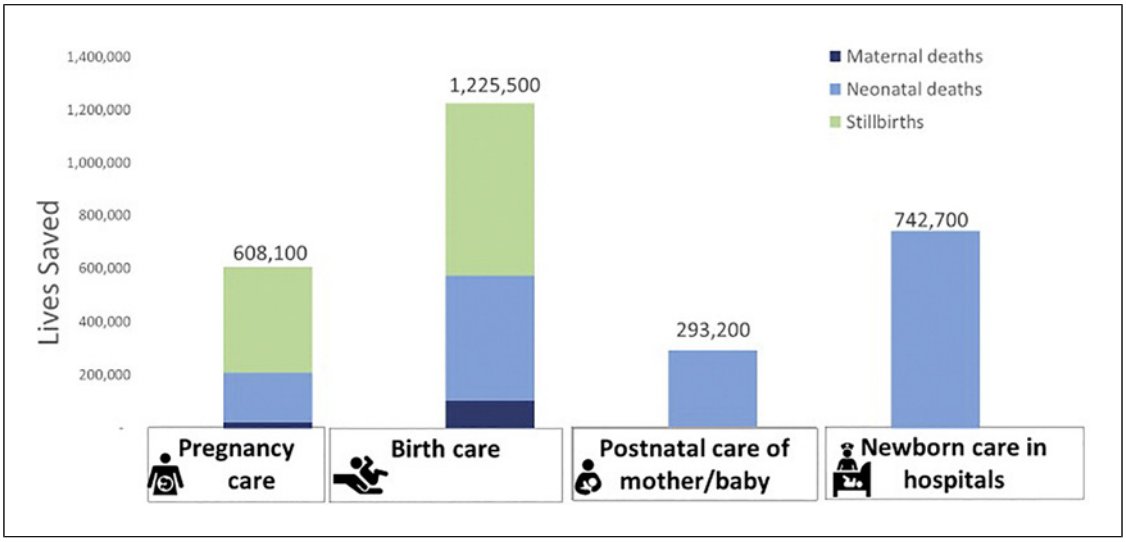


Fig. 3. Lives saved analysis using LiST for annual impact for stillbirths and maternal and neonatal death if 90% coverage of care is achieved by 2030. Adapted from reference [9] and reference [38], Every Newborn Action Plan (see Figure 2a and b for overview of package content).

To reach phase IV, and get to NMR <5, closer to ending preventable newborn deaths, additional therapies such as surfactant, artificial ventilation, and other more complex care such as total parenteral nutrition may be needed. The majority of the world's 135 million births are in LMIC and >80% are in facilities [61]. Most countries are now in phase III or IV. Table 1 shows the current status of 195 UN member states according to phases; some are progressing rapidly and are now potentially on track for SDG3.2. India demonstrated substantial NMR reductions from 85/1,000 in 1970 to 20/1,000 in 2020 [3, 4], and now with over 900 newborn care units built nationwide, admission >1million babies a year, poised for more rapid progress with an ambitious target of "single-digit NMR" by 2030 [2]. In sub-Saharan Africa, one of the fastest NMR progressors is Malawi, where across 27 districts there are 37 hospitals with level 2 SSNC units able to provide CPAP, as part of the Newborn Essential Solutions and Technologies (NEST360) alliance of four African country governments and 17 organizations across Africa [62].

Implementation learning networks and research led by LMIC are important to speed up reduction for neonatal mortality and morbidity [63]. A large open-access online platform Implementation Toolkit for Small and Sick Newborn Care has recently been launched by NEST360 and UNICEF to enable more rapid sharing of tools such as floor plans, and hundreds of LMIC implementers and innovators are already collaborating [62]. Results from randomized trials from HIC cannot be assumed to LMIC contexts given known limitations of human resources and differing contexts [60]. Research initiated from HIC, especially when testing out new technology or interventions, must be careful to apply the highest ethical standards [63]. Equitable collaborations are fundamental for more rapid improvement.

The package of small and sick newborn includes interventions with the potential to prevent almost three-quarters of a million lives each year (Fig. 3) [53]. We have focused mainly on health system packages to accelerate reduction in global newborn mortality, including systems change such as regionalization and classification of care levels, in addition to better organization of maternal and neonatal service provision (Fig. 2a, b). We are therefore not discussing in detail on topics such as need of clean water, use of antibiotics, although these are referred to as part of phases I and II for neonatal mortality reduction. We acknowledge the importance of fundamental human needs such as water and sanitation, noted in phase I.

Empowering women, including educating girls and securing women's rights, is also transformative. Socioeconomic improvement and governance enable sustainable change [64], although we note that there are countries with poor governance indicators and still low gross national income that have made major progress for maternal, newborn, and child health outcomes [65].

Conclusion

Many countries have potential now for more rapid progress for NMR and could reach the SDG of ≤12/1,000 before having full neonatal intensive care. A package of SSNC including KMC and CPAP, with skilled staff, especially more nurses, and effective quality improvement approaches can achieve this target. To reduce NMR lower than 12/1,000, reaching phase V (NMR <5) and getting closer to ending preventable newborn deaths, additional technologies and therapies are needed, as well as higher staffing ratios. Learning from HIC lessons, earlier focus on family-centered care and disability-free survival is crucial. Importantly, reaching further for newborn care requires not just medical interventions but social movements, parents' voices, and political will, more ambitious investment – also giving major returns on that investment, with a healthier start for every newborn.

Acknowledgment

This article is dedicated in honor and memory of Dr. Shereen Zulfiqar Bhutta (1957–2022).

Statement of Ethics

Ethical approval and consent were not required as this study was based on publicly available data.

Conflict of Interest Statement

O.D.S. has received consultancy honorarium from Chiesi Farmaceutici and InfanDx AG.

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Author Contributions

O.D.S. initiated the idea. J.E.L. provided the analyses and figures and drafted the manuscript with O.D.S. Z.B. and C.E. contributed to the ideas, added text, and reviewed final draft.

Data Availability Statement

The datasets generated and/or analyzed during the current study are available in the public domain. All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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