Lancet series: Small Vulnerable Newborns 1

Small vulnerable newborns – big potential for impact

Manuscript version 2023-02-15

Prof. Per Ashorn, MD[1,2], Ulla Ashorn, PhD[1], Yvonne Muthiani, MSc[1], Samira Aboubaker, MD [3], Sufia Askari, MD[4], Rajiv Bahl, PhD[5], Prof. Robert E Black, MD[6], Nita Dalmiya, MPH[7], Prof. Christopher P Duggan, MD[8], Prof. G Justus Hofmeyr, DSc[9], Prof. Stephen H Kennedy, MD[10], Prof. Nigel Klein, MD[11], Prof. Joy E Lawn, PhD[12], Prof. Jeremy Shiffman, PhD[13], Prof. Jonathon Simon, PhD[14], Prof. Marleen Temmerman, PhD[15], UN low birth weight estimate collaborative group

[1] Center for Child, Adolescent and Maternal Health Research, Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland

[2]Department of Paediatrics, Tampere University Hospital, Tampere, Finland

[3]Independent consultant, Geneva, Switzerland

[4]Sight and Life, Kaiseraugst, Switzerland.

[5]Indian Council for Medical Research, New Delhi, India

[6]Department of International Health, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD, USA

[7]United Nations Children's Fund (UNICEF), New York, USA

[8]Center for Nutrition, Division of Gastroenterology, Hepatology and Nutrition, Boston Children's Hospital, Boston, MA, USA

[9]University of Botswana, Gaborone, Botswana; Effective Care Research Unit, University of the Witwatersrand and Walter Sisulu University, East London, South Africa

[10]Nuffield Department of Women's and Reproductive Health, University of Oxford, Oxford, UK

[11]UCL Great Ormond Street Institute of Child Health, University College London, London, UK

[12]Maternal, Adolescent, Reproductive & Child Health (MARCH) Centre, London School of Hygiene & Tropical Medicine, London, UK

[13]Johns Hopkins Bloomberg School of Public Health and Paul H Nitze School of Advanced International Studies, Johns Hopkins University, Baltimore, MD, USA

[14]Independent consultant, Condon, MT, USA

[15]Centre of Excellence in Women and Child Health, Aga Khan University, Nairobi, Kenya

Correspondence to

Prof. Per Ashorn, Center for Child, Adolescent and Maternal Health Research, Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland. per.ashorn@tuni.fi

Manuscript length

3650 words in the main text, 225 in summary

4 figures, 2 tables, 1 supplementary table

3 boxes (815 + 247 + 250 words)

255 references

Key messages

1. Newborns who are preterm, small for gestational age (SGA), or have low birth weight (LBW), account for most neonatal deaths worldwide. These conditions are also associated with stillbirth and life-long health adversities among those who survive their early weeks.

2. Prevention of preterm birth, SGA, and LBW would lead to major advancements in global health and economic and social development. However, there has been little progress in prevention, despite several globally expressed commitments in the past 30 years. This can be explained by the inadequate response of the global community to four challenges, consisting of problem definition, framing of the problem, coalition-building, and governance. Major impact is possible with adequate response to these challenges.

3. To facilitate an improved problem framing and response, we propose a new definition with a conceptual framework, bringing preterm birth, SGA, and LBW together under a broader umbrella term - the “small vulnerable newborn” (SVN).

4. Interventions that focus on the health of women and fetuses, can reduce newborn vulnerability, stillbirth, and maternal ill-health, leading to thriving individuals, families and nations.

Summary

Despite major achievements in child survival, the burden of neonatal mortality has remained high and even increased in some countries. Currently, most neonatal deaths are attributable to being born preterm, small for gestational age (SGA), or with low birth weight (LBW). Besides neonatal mortality, these conditions are associated with stillbirth and multiple morbidities with short- and long-term adverse consequences, in the newborn, their families, and society at-large, resulting in a major loss of human capital. Prevention of preterm birth, SGA, and LBW is thus critical for global child health and broader societal development. Progress has, however, been slow, largely because of the global community's failure to agree on the definition and magnitude of newborn vulnerability and best ways to address it, to frame the problem attractively, and to build a broad coalition of actors and a suitable governance structure to implement a change. We propose a new definition and a conceptual framework, bringing preterm birth, SGA, and LBW together under a broader umbrella term of the "small vulnerable newborn" (SVN). Adoption of the framework and the unified definition can facilitate improved problem definition and better programming for SVN prevention. Interventions aiming at SVN prevention would result in a healthier start for live-born infants, whilst also reducing the number of stillbirths, improving maternal health, and contributing to a positive economic and social development in the society.

The importance of newborn vulnerability

Child health and wellbeing have been a global development priority for decades. Improved child survival was one of the United Nations eight Millennium Development Goals[1], remains an important target in the United Nations Sustainable Development Agenda[2], and is emphasised in many global initiatives such as the United Nations Global Strategy for Women's, Children's and Adolescent's Health. [3] During the period of increased global attention, child survival has improved remarkably.[4] Between 1990 and 2021, the number of deaths of children under 5-years of age worldwide fell by 61%, from 12.8 to 5.0 million per year.[5]

The positive trend in child survival has been documented in all age-groups, but unfortunately not quite evenly; mortality in the neonatal period (in the first 28 days of life) has declined more slowly than that among older children.[6] As a result, neonatal mortality now accounts for almost half of all under-5 mortality in the world.[5] Strikingly, there are countries and regions that in absolute terms experienced even more neonatal deaths in 2021 than in 1990. Neonatal mortality rates (expressed per 1000 live births) have also decreased in these settings, but these reductions have been offset by larger increases in the numbers of births (**Supplemental table 1**).[5,7] This early mortality is seen as a major hindrance to development especially in Sub-Saharan Africa, where health is becoming a priority for future nation building.[8]

Globally, and especially for low and middle income countries (LMICs), most authorities list preterm birth, intrapartum complications (birth asphyxia and birth trauma), and infections as the main direct causes of neonatal deaths.[9] Preterm birth is considered the cause of death when it is associated with respiratory distress syndrome, intracranial haemorrhage or other complications of fetal immaturity.[10] In addition to the directly attributed deaths, preterm birth increases the risk of death due to infections.[11] In many settings, where gestational age at birth

is uncertain, low birth weight (LBW) is listed instead of preterm birth as a major cause of neonatal mortality.[12] Although rarely considered a direct cause, newborns who are smaller than expected for their gestational age (SGA) also have an increased mortality risk.[13] In most cases being born SGA indicates that the infant has experienced harmful intrauterine exposures resulting in fetal growth restriction. In a small minority of individuals, it can indicate constitutional smallness. Together, preterm birth, LBW, and SGA account for most of the early mortality. It has been estimated that as many as 80% of all neonatal deaths in the world occur in LBW infants, of whom two-thirds are likely preterm and one-third SGA.[14]

There are no unified databases on the overlap between different newborn types, but approximately 10% of the world's infants are born preterm and the proportions of newborns with LBW or SGA are estimated to be even higher.[14–16] Besides mortality[13,17], these newborns have an increased risk for undernutrition[18], metabolic disorders[19,20], developmental delay[21], and a multitude of adverse health conditions throughout their lifespan.[22] Prevention of preterm birth and small birth size is therefore critical for global health and well-being and forms the basis for this *Lancet* series. Its article collection builds on and supplements the WHO-UNICEF-Lancet Commission on Child Health[23], the Optimising Child and Adolescent Health and Development series[24], and several other earlier *Lancet* series on maternal and child health.

In the first article of the series, we will review the evolution of constructs for identifying preterm or small newborns. We will demonstrate a considerable overlap in preterm birth, SGA, and LBW, in terms of their determinants and implications for health and survival outcomes. For public health purposes, we propose to merge them under a new holistic term of "small vulnerable newborn" (SVN), recognizing, however, that there are differences in clinical management of the different SVN types, applicable especially in high-resource

settings. Finally, we will identify challenges that will need to be overcome and myths that need to be broken for successful SVN prevention.

To provide a comprehensive description of the magnitude of the SVN problem and to provide the rationale for preventive interventions, the second article in the series will provide novel estimates on SVN prevalence and risks based on large, individually linked datasets[25]. The subsequent two articles will describe the biological basis and expected benefits from preventive interventions, by reviewing pathophysiological mechanisms leading to SVN births[26] and outlining evidence-based interventions within the antenatal care package and estimating their potential impact on health and well-being.[27] In an associated comment, there will be a call for action for promoting women's, maternal and fetal health, minimising newborn vulnerability, and supporting a healthy start for every newborn.[28]

Since there is an urgent implementation gap for SVN prevention, the included articles focus on that and will not discuss prevention of other newborn vulnerabilities, such as hypoxic injury, perinatal infections, or being post-term or term and large for gestational age. These issues as well as the management of the sick and vulnerable newborns are planned to be discussed in detail in another series in *the Lancet*. We will also not discuss strategies which would reduce but are not specific to SVN, such as enhanced contraception services.

Evolution of criteria for identifying high-risk newborns: From LBW to SVN

Currently, there are three main constructs used to define small newborns who have an increased risk of adverse health outcomes: LBW, preterm birth, and SGA. These definitions have evolved over the past 100 years, as a function of advancing knowledge and technology, and changing evidence and diagnostic priorities among health professionals **(Box 1)**. All three

definitions are being used, but for varying purposes and by different professions. LBW has traditionally been used worldwide in clinical practice, epidemiological research, and in public health comparisons, such as United Nations statistics. The definition of preterm birth is of special interest to obstetricians and midwives who make decisions about the management of individual pregnancies based on the risk of early delivery. Additionally, it is used by paediatricians and neonatologists making care-related decisions based on the estimated "maturity" of the newborn. SGA is utilised by neonatal and paediatric practitioners and researchers, especially in the field of nutrition, and its antenatal correlate fetal growth restriction is used by obstetricians and midwives for antenatal decision-making.

The use of three different dichotomous definitions for newborns who are preterm or small in absolute or relative terms is understandable, given the historical evolution of the terms and fragmentation of the communities who use the data. However, there are also major disadvantages to this practice. First, the definitions convey different types of information: preterm birth and SGA indicate processes that lead to newborn vulnerability, whereas LBW indicates only small birth size, with no reference to its determinants. Importantly, the use of multiple definitions makes it difficult to determine the total burden of the small newborn problem, since each definition is incomplete. In a recent dataset including over 18 million births from Brazil between 2011 and 2018, the prevalence of preterm birth was 9.4%, SGA 9.2%, and LBW 9.6%. However, 18.0% of the newborns were included in at least one of the categories, indicating that the use of any one of the individual definitions would underestimate the number of all at-risk newborns by approximately 50%.[29]

In addition to providing an incomplete estimate, the use of several different criteria obscures that the same newborn can belong to more than one group. When combined, the LBW, preterm, and SGA cut-offs define a total of seven possible newborn types, of which six

indicate a special vulnerability and only one is "non-risk".[30] For simplicity, and based on mortality risk analyses[25], vulnerable newborns can be categorised into three main groups: preterm newborns, those who are SGA (most of whom were subject to fetal growth restriction), and those who are both preterm and SGA. Of these, the preterm-SGA newborns have the highest risk of neonatal death, followed by preterm but not SGA infants.[13,29] An analogous risk gradient has been shown for post-neonatal infant mortality[29,31] and child mortality[29] and may also apply to other adverse health sequelae.

Although the exact mechanisms leading to preterm birth, SGA, and LBW and the clinical management of the affected newborns are different[26] they share many risk factors, aetiologies and consequences. All these newborns are also "small" in some respect: either in the duration of their fetal life (preterm infant), absolute size (LBW), or size relative to the duration of pregnancy (SGA). For public health purposes, we therefore propose a new unifying concept of "Small Vulnerable Newborn" (SVN), encompassing all newborns who are preterm or SGA, or have LBW (**Box 2**). Because of its inclusiveness, adopting this concept will improve estimates of the global burden and facilitate better public health programming and monitoring of progress.

Conceptual framework of SVN: Multiple causes, three types, wide adverse consequences

Our conceptual framework is structured similarly to the one WHO used for childhood stunting.[32] It assumes that there are contextual factors (root causes) that predispose mothers and fetuses to adverse exposures (immediate causes), leading to fetal growth restriction, preterm birth, or both. These two mechanistic pathways can result in three main SVN types. Under very adverse conditions, the same pathways can lead to fetal death, i.e., a miscarriage

or stillbirth. For the liveborn SVN, mother, family, and wider society, there are multiple short and long-term adverse consequences (**Figure 2**).

The contextual factors include broad social determinants of health, such as poverty[33], armed conflict[34], and political instability.[35] High food prices[36,37] and poor food security[36,38,39] make women susceptible to undernutrition and problems with water, sanitation and hygiene also to infections.[40] Environmental pollution and climate change can reduce newborn size through multiple mechanisms, including undernutrition and physiological changes in the mother, or trans-placental exposure of the fetus to harmful environmental compounds.[41] Poor maternal education may reduce maternal socioeconomic status and access to antenatal care and other health services[42–46] and problems in health systems governance will further limit the availability and quality of services.[47] Finally, cultural beliefs, norms and social support given to a pregnant woman may affect her dietary patterns, macro- and micronutrient intakes, smoking, other health-related behaviours and health care utilisation, ultimately also affecting the duration of pregnancy and newborn size.[48–50]

The most commonly highlighted adverse exposures that initiate or contribute to fetal growth restriction and preterm birth include maternal underweight[51], short stature[52], anaemia[53–55], and infections.[56–60] Another large group includes various environmental exposures, such as air pollution[61–63], intimate partner violence[64,65], physical workload[66], and tobacco[67] or alcohol[68,69] consumption. In total, these three clusters of potentially modifiable risk factors, i.e., maternal nutrition, infections, and environmental exposures, are estimated to account for approximately 50% of spontaneous preterm birth[70] and 39% of SGA in LMICs.[70,71] The relative importance of the risk factors varies by region, infections being associated with the largest fraction of SVN in Sub-Saharan Africa and nutrition being most important in Southern Asia.[70,71]

In addition to these three large risk factor clusters, there are also several other modifiable risk factors, such as maternal depression[72], stress[73], gestational diabetes[74], endometriosis[75], short uterine cervix[76], high or low age maternal age[77,78], high or low parity[79] and short interpregnancy interval.[80,81] Finally, there are risk factors that do not fit into any of the previously mentioned groups, such as multiple pregnancy[82] and residence at high altitude.[83] Most of the stated risk factors have been associated both with fetal growth restriction and preterm birth, some with only one of the pathways.

For a landscape analysis on adverse outcomes associated with preterm birth, SGA and LBW, we conducted a scoping review of English language literature, searching for systematic reviews, meta-analyses, and other research syntheses in Ovid Medline, CINAHL and Embase databases. The results confirmed that SVN types are associated with increased neonatal morbidity and mortality[84,85,86,87,88,89,90,91,92,93], and also with child undernutrition, neurodevelopmental impairment, behavioural problems, and excess morbidity and mortality in adolescence and adult life (**Table 1**). Importantly, there are also many adverse social and economic consequences to the newborn's family, such as increased risk of parental stress[94], poor parental sleep quality [95,96], and reduced likelihood of the parents having additional children.[97] For society, there is increased expenditure on health care[98, 99] and loss of human capital, due to excess mortality and lower educational attainment.[100] Many of the studies have used a dichotomised outcome variable (preterm birth, LBW, or SGA), but others have shown that the risk for an adverse outcome rises progressively with extremes of preterm and SGA.

Slow progress in SVN prevention despite increasing global attention on newborn health – why?

So far, there have been few global statistics on trends in SVN prevalence, mostly because of missing or non-standardised data collection on SGA births. However, LBW prevalence trend serves also as a good proxy for all SVN births. **Figure 3** shows the latest United Nations estimates for LBW births in 195 World Health Organization members states from 2000 to 2020.[101] At present, approximately 20 million infants are born with LBW each year, with little decline overall in the past 20 years. In absolute numbers, there has been a small reduction in Southern Asia and an increase in Sub-Saharan Africa – but these changes reflect mostly trends in the numbers of livebirths, rather than changes in LBW prevalence.

The lack of progress in LBW and SVN prevention can be considered surprising, given the plethora of related high-level attention and targets (**Box 3**). To understand this apparent contradiction, we used a published framework that outlines four main challenges which global health networks face in generating attention and resources for the conditions they are concerned about.[102] By networks we refer to webs of individuals and organisations linked by a shared concern for their issue. The four challenges, identified in a research program that examined eight networks engaged in public health, include problem definition, positioning, coalition-building, and governance.[102] According to our subjective analysis, inadequate response of the global community to each of these four challenges has contributed to the persistence of the high SVN prevalence (**Table 2**).

With respect to "problem definition" on SVN prevention, the use of three different definitions (preterm birth, SGA, and LBW) for newborn vulnerability has impeded estimation and appreciation of the full burden and fragmented the clarity on interventions and tractability of prevention. Additionally, although WHO has recently published several recommendations for improving pregnancy outcomes both for the mother and newborn[103–107], there is no internationally agreed document that would concomitantly cover all SVN types and

specifically address prevention. The ENAP identified delivery and postnatal care and management of small and sick newborn as priority package for improving newborn health, with antenatal care as key for prevention of stillbirths. Whilst the importance of preventive interventions was discussed in the background articles, there was less evidence for interventions with high and immediate impact.[108] Because of the confusion on the definition, emphasis on care, and the widespread ambiguity regarding how to address prevention, it has been difficult to mount collective intervention. Therefore, we rate response to the "problem definition" challenge as "contested", i.e., inadequate.

With respect to "positioning" SVN prevention, we also rate this response so far as "contested" (inadequate), as the issue has usually been framed as a purely medical problem. This approach is obvious, but too narrow according to many stakeholders. Other metaphors that global health networks have used for justifying investments include improvement of public health, an act of charity, a fulfilment of human rights or social justice, a tool for foreign policy, an investment into social and economic development, a resolution to a humanitarian crisis, and a safeguard of security.[102,109,110] Of these alternative framings, at least public health, human rights improvement, and investment into societal development fit well to SVN prevention, given the mortality, morbidity and human capital loss associated with being born too soon or too small.

For "coalition-building" we rate the current response as "moderately broad". A joint WHO/UNICEF steering committee, including national government representation, is actively coordinating the ENAP. The original plan was passed as a resolution at the 67th WHA and there will be periodic progress reports until 2030.[111] The countries have also set a new round of targets in 2020-2025 and defined antenatal care as a priority. There are also several large networks of relevance, notably the Partnership for Maternal, Newborn and Child Health

(PMNCH), which operates at head of state level and with inter-sectoral linkage. The Inter-Agency Working Group on Reproductive Health in Crises (IAWG) is especially key for the many countries affected by humanitarian emergencies, and there are also other, smaller networks. However, none of the coalitions focuses solely or predominantly on SVN prevention. Like many other global health networks, they are also mostly technically focused and insular, enlisting like-minded actors in the health sector, but missing broader political alliances such as grassroots civil society actors, heads of government, parliamentarians, and ministers of finance, nor do they involve representatives of affected families – the vulnerable newborns and their parents. Without these stakeholders, major progress will be difficult.

For the fourth challenge, "governance", we rate the current response as "largely cohesive". Both ENAP, PMNCH, and IAWG have clear organisational structures and they do address SVN issues. However, the stakeholders do not have a clear unified structure for collaboration especially on SVN prevention. There are at least three alternatives for this function: a shared network where members interact on a relatively equal basis (a model used by ENAP), a lead organisation-based system where activities are mostly coordinated through a single member, and an administrative model, where a separate entity is set up specifically to govern the network's activities (a model used by PMNCH).[112] Each network is different and needs to make its own decision about the collaborative model. The fact that there are several models for SVN prevention, makes it difficult to agree on a coordinated target, action plan, quality assurance, monitoring framework, or indicators of success.

Management is silver, prevention is gold

The main stakeholders in SVN prevention are women of preconceptional age and dyads that consist of a pregnant woman and her baby. The woman's vulnerabilities need to be addressed

primarily because of their possible adverse impact on her own health. But the woman's vulnerabilities are also carried to her offspring, increasing the risk to be born too soon or too small and suffer from multiple negative consequences throughout the lifespan. Also important, is that the same adverse exposures that result in fetal growth restriction or preterm birth, also contribute to some of the 23 million miscarriages, two million fetal deaths (stillbirths), approximately 350,000 maternal deaths, and a significant amount of maternal morbidity that happen each year.[113–115] Thus, there is a vicious cycle from vulnerable girls and women to vulnerable newborns, continuing to vulnerable adults, families, and societies. Interventions that focus on the health of women and fetuses, can break this cycle and push the balance to thriving individuals, families and nations (**Figure 4).**

Some of the interventions that are necessary for ensuring good pregnancy outcomes can be offered during antenatal care. However, for a maximal impact, it will be critical to address also the social determinants that can negatively impact pregnant women's health and health seeking behaviour. These include the root causes shown in Figure 2, such as poverty, unsafe living environment, lack of education and agency, and the accessibility and quality of antenatal care and other health services that the woman is receiving.

Interventions and policies for maternal and fetal health promotion and SVN prevention will be discussed further in articles 4 and 5 of this series.[27,28] For a successful outcome, it will also be important to tackle two apparent myths that have hampered progress and replace them with views that are based on recent scientific evidence. The first of these is a belief, that the small birth size problem is unpreventable in low-income settings. This misconception probably stems from the fact that most evidence on possible positive effect on prevention comes from single-intervention trials.[116] The limited effect in trials with such a narrow focus is not surprising, given the complexity of the aetiological network: a single-pronged intervention is

unlikely to solve a multifactorial problem. For instance, if undernourished children have concomitant infections, they may lack the ability to respond to dietary supplements.[117] However, if one uses a package of interventions that addresses maternal health, nutrition, and social wellbeing through multiple platforms, both before and during pregnancy, as occurred in the recent WINGS trial in India, the prevalence of LBW can be markedly reduced in just one generation.[118]

The second myth is that it is impossible to produce accurate statistics on SVN since birth weight and gestational age are often measured inaccurately. Ultrasound-based estimation of gestational age is also often seen as expensive, complicated to use, and unreliable for the many women who start antenatal care late. These challenges are real but surmountable. The quality of birth weight data can be improved by increasing the proportion of facility births and providing standardised scales, as well as better training on their use and how to record birth weights[119] and calculate weight for gestational age. Ultrasound technology is becoming less expensive, low-cost devices are easier to use,[120] and women are enrolling in antenatal care much earlier than before, especially in LMICs.[121,122] Moreover, algorithms now exist that allow gestational age to be determined later in pregnancy.[123,124] Further standardization on the gestational age assessment method will be necessary, but already now it is feasible to date all pregnancies reliably also in LMICs, as recommended by WHO. [125,126]

Rapid progress in child survival proves that change is possible with global commitment and local determination and action. Placing more focus on SVN prevention will complement the earlier child health activities and facilitate achievement of the United Nations Sustainable Development Goal 3.2 that calls for neonatal mortality reduction.[2] Importantly, such a focus will likely provide many additional short- and long-term health benefits both to the mother and the newborn and for stillbirth prevention, translating into increased human capital and a

positive development spiral. The time to act is now. Every newborn, family, and society has the right to survive and thrive.

Contributors

PA, UA, SA, REB, JH, NK, JEL, and MT designed the study and planned the data analyses. PA, YM, and UA had access and verified the underlying data and PA conducted the analyses. All authors participated in the conceptualisation and drafting of the original manuscript, reviewed and edited subsequent drafts, and approved the final version of the manuscript. PA made the final decision to submit the manuscript.

Declarations of interest

PA reports a grant from Children's Investment Fund Foundation (CIFF), during the conduct of the study. All other authors declare no competing interests.

The funder had no role in the writing of the manuscript or the decision to submit it for publication.

Acknowledgements

The production of this manuscript was funded by a grant from CIFF to PA (grant number 2004-04635).

References

1 United Nations Millennium Development Goals. https://www.un.org/millenniumgoals/ (accessed Sept 20, 2021).

2 THE 17 GOALS | Sustainable Development. https://sdgs.un.org/goals (accessed Sept 20, 2021).

3 Every Woman Every Child. The global strategy for women's, children's Global Strategy for Women's, Children's and Adolescents' Health (2016–2030). Every Woman Every Child, New York, 2015 https://globalstrategy.everywomaneverychild.org/ (accessed Sept 20, 2021).

4 Wang H, Abajobir AA, Abate KH, *et al.* Global, regional, and national under-5 mortality, adult mortality, age-specific mortality, and life expectancy, 1970–2016: a systematic analysis for the Global Burden of Disease Study 2016. *The Lancet* 2017; 390: 1084–150.

5 United Nations Inter-agency Group for Child Mortality Estimation (UN IGME). Levels and Trends in Child Mortality: Report 2022, Estimates developed by the United Nations Inter-agency Group for Child Mortality Estimation. New York: United Nations Children's Fund, 2023 https://data.unicef.org/resources/levels-and-trends-in-child-mortality/ (accessed Jan 25, 2023).

6 Hug L, Alexander M, You D, Alkema L. National, regional, and global levels and trends in neonatal mortality between 1990 and 2017, with scenario-based projections to 2030: a systematic analysis. *Lancet Glob Health* 2019; 7: e710–20.

7 United Nations Department of Economic and Social Affairs, Population Division (2022). World Population Prospects 2022. Online Edition. 2022 https://population.un.org/wpp/ (accessed Jan 25, 2023).

8 Abubakar I, Dalglish SL, Angell B, *et al.* The Lancet Nigeria Commission: investing in health and the future of the nation. *The Lancet* 2022; 399: 1155–200.

9 Perin J, Mulick A, Yeung D, *et al.* Global, regional, and national causes of under-5 mortality in 2000–19: an updated systematic analysis with implications for the Sustainable Development Goals. *Lancet Child Adolesc Health* 2021; : S2352464221003114.

10 World Health Organization, editor. The ICD-10 classification of mental and behavioural disorders: diagnostic criteria for research. Geneva: World Health Organization, 1993.

11 Shane AL, Sánchez PJ, Stoll BJ. Neonatal sepsis. *The Lancet* 2017; 390: 1770–80.

12 Causes of neonatal and child mortality in India: a nationally representative mortality survey. *The Lancet* 2010; 376: 1853–60.

13 Katz J, Lee ACC, Kozuki N, *et al.* Mortality risk in preterm and small-for-gestational-age infants in low-income and middle-income countries: a pooled country analysis. *Lancet* 2013; 382: 417–25.

14 Blencowe H, Krasevec J, de Onis M, *et al.* National, regional, and worldwide estimates of low birthweight in 2015, with trends from 2000: a systematic analysis. *Lancet Glob Health* 2019; 7: e849–60.

15 Lee AC, Kozuki N, Cousens S, *et al.* Estimates of burden and consequences of infants born small for gestational age in low and middle income countries with INTERGROWTH-21 st standard: analysis of CHERG datasets. *BMJ* 2017; : j3677.

16 Blencowe H, Cousens S, Oestergaard MZ, *et al.* National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. *The Lancet* 2012; 379: 2162–72.

17 Lawn JE, Blencowe H, Oza S, *et al.* Every Newborn: progress, priorities, and potential beyond survival. *The Lancet* 2014; 384: 189–205.

18 Christian P, Lee SE, Donahue Angel M, *et al.* Risk of childhood undernutrition related to small-for-gestational age and preterm birth in low- and middle-income countries. *Int J Epidemiol* 2013; 42: 1340–55.

19 Liao L, Deng Y, Zhao D. Association of Low Birth Weight and Premature Birth With the Risk of Metabolic Syndrome: A Meta-Analysis. *Front Pediatr* 2020; 8: 405.

20 Parkinson JRC, Hyde MJ, Gale C, Santhakumaran S, Modi N. Preterm Birth and the Metabolic Syndrome in Adult Life: A Systematic Review and Meta-analysis. *PEDIATRICS* 2013; 131: e1240–63.

21 Arcangeli T, Thilaganathan B, Hooper R, Khan KS, Bhide A. Neurodevelopmental delay in small babies at term: a systematic review. *Ultrasound Obstet Gynecol* 2012; 40: 267–75.

22 Moster D, Lie RT, Markestad T. Long-Term Medical and Social Consequences of Preterm Birth. *N Engl J Med* 2008; 359: 262–73.

23 Clark H, Coll-Seck AM, Banerjee A, *et al.* A future for the world's children? A WHO–UNICEF–Lancet Commission. *The Lancet* 2020; 395: 605–58.

24 Bhutta ZA, Boerma T, Black MM, Victora CG, Kruk ME, Black RE. Optimising child and adolescent health and development in the post-pandemic world. *The Lancet* 2022; 399: 1759–61.

25 Lawn JE, Ohuma EO, Bradley E, *et al.* Small Vulnerable Newborns 2. Small babies, big risks: Global estimates of prevalence and mortality for vulnerable newborns to accelerate change and improve counting. *The Lancet,* this issue.

26 Hunter PJ, Awoyemi T, Ayede AI, *et al.* Small Vulnerable Newborns 3. Biological mechanisms leading to the birth of a small vulnerable newborn. *The Lancet,* this issue.

27 Hofmeyr JG, Black R, Rogozińska E, *et al.* Small Vulnerable Newborns 4. Evidence-based antenatal interventions to reduce the incidence of small vulnerable newborns and their associated poor outcomes. *The Lancet,* this issue.

28 Mohiddin A, Semrau KE, Simon J, *et al.* Small Vulnerable Newborns 5. The ethical imperative to prevent small and vulnerable newborns and stillbirths: Essential and urgent country actions to improve the global response. *The Lancet,* this issue.

29 Paixao ES, Blencowe H, Falcao IR, *et al.* Risk of mortality for small newborns in Brazil, 2011-2018: A national birth cohort study of 17.6 million records from routine register-based linked data. *Lancet Reg Health - Am* 2021; : 100045.

30 Ashorn P, Black RE, Lawn JE, *et al.* The Lancet Small Vulnerable Newborn Series: science for a healthy start. *The Lancet* 2020; 396: 743–5.

31 Katz J, Lee ACC, Kozuki N, *et al.* Mortality risk in preterm and small-for-gestational-age infants in low-income and middle-income countries: a pooled country analysis. *Lancet* 2013; 382: 417–25.

32 Stewart CP, Iannotti L, Dewey KG, Michaelsen KF, Onyango AW. Contextualising complementary feeding in a broader framework for stunting prevention: Complementary feeding in stunting prevention. *Matern Child Nutr* 2013; 9: 27–45.

33 Blumenshine P, Egerter S, Barclay CJ, Cubbin C, Braveman PA. Socioeconomic Disparities in Adverse Birth Outcomes: A Systematic Review. *Am J Prev Med* 2010; 39: 263–72.

34 Keasley J, Blickwedel J, Quenby S. Adverse effects of exposure to armed conflict on pregnancy: a systematic review. *BMJ Glob Health* 2017; 2: e000377.

35 Rasmussen DN, Unger HW, Bjerregaard-Andersen M, *et al.* Political instability and supply-side barriers undermine the potential for high participation in HIV testing for the prevention of mother-to-child transmission in Guinea-Bissau: A retrospective cross-sectional study. *PLOS ONE* 2018; 13: e0199819.

36 Iqbal S, Ali I. Maternal food insecurity in low-income countries: Revisiting its causes and consequences for maternal and neonatal health. *J Agric Food Res* 2021; 3: 100091.

37 Demétrio F, Teles CA de S, Santos DB dos, Pereira M. Food insecurity in pregnant women is associated with social determinants and nutritional outcomes: a systematic review and meta-analysis. *Ciênc Saúde Coletiva* 2020; 25: 2663–76.

38 Park CY, Eicher-Miller HA. Iron deficiency is associated with food insecurity in pregnant females in the United States: National Health and Nutrition Examination Survey 1999-2010. *J Acad Nutr Diet* 2014; 114: 1967–73.

39 Maitra C. A review of studies examining the link between food insecurity and malnutrition. Rome, Italy: FAO, 2018 http://www.fao.org/publications/card/en/c/CA1447EN/ (accessed Sept 12, 2021).

40 Padhi BK, Baker KK, Dutta A, *et al.* Risk of Adverse Pregnancy Outcomes among Women Practicing Poor Sanitation in Rural India: A Population-Based Prospective Cohort Study. *PLoS Med* 2015; 12: e1001851.

41 Simoncic V, Enaux C, Deguen S, Kihal-Talantikite W. Adverse Birth Outcomes Related to NO2 and PM Exposure: European Systematic Review and Meta-Analysis. *Int J Environ Res Public Health* 2020; 17: 8116.

42 Kuhnt J, Vollmer S. Antenatal care services and its implications for vital and health outcomes of children: evidence from 193 surveys in 69 low-income and middle-income countries. *BMJ Open* 2017; 7: e017122.

43 Gabrysch S, Campbell OM. Still too far to walk: Literature review of the determinants of delivery service use. *BMC Pregnancy Childbirth* 2009; 9: 34.

44 Yaya S, Bishwajit G, Shah V. Wealth, education and urban–rural inequality and maternal healthcare service usage in Malawi. *BMJ Glob Health* 2016; 1: e000085.

45 Ruiz M, Goldblatt P, Morrison J, *et al.* Mother's education and the risk of preterm and small for gestational age birth: a DRIVERS meta-analysis of 12 European cohorts. *J Epidemiol Community Health* 2015; 69: 826–33.

46 Ahmed S, Creanga AA, Gillespie DG, Tsui AO. Economic Status, Education and Empowerment: Implications for Maternal Health Service Utilization in Developing Countries. *PLOS ONE* 2010; 5: e11190.

47 Hamal M, Dieleman M, De Brouwere V, de Cock Buning T. How do accountability problems lead to maternal health inequities? A review of qualitative literature from Indian public sector. *Public Health Rev* 2018; 39: 9.

48 de Diego-Cordero R, Rivilla-Garcia E, Diaz-Jimenez D, Lucchetti G, Badanta B. The role of cultural beliefs on eating patterns and food practices among pregnant women: a systematic review. *Nutr Rev* 2021; 79: 945–63.

49 May S, West R. Do social support interventions ("buddy systems") aid smoking cessation? A review. *Tob Control* 2000; 9: 415–22.

50 Pratley P. Associations between quantitative measures of women's empowerment and access to care and health status for mothers and their children: A systematic review of evidence from the developing world. *Soc Sci Med* 2016; 169: 119–31.

51 Han Z, Mulla S, Beyene J, Liao G, McDonald SD, on behalf of the Knowledge Synthesis Group. Maternal underweight and the risk of preterm birth and low birth weight: a systematic review and meta-analyses. *Int J Epidemiol* 2011; 40: 65–101.

52 Short Maternal Stature Increases Risk of Small-for-Gestational-Age and Preterm Births in Low- and Middle-Income Countries: Individual Participant Data Meta-Analysis and Population Attributable Fraction. *J Nutr* 2015; 145: 2542–50.

53 Figueiredo ACMG, Gomes-Filho IS, Silva RB, *et al.* Maternal Anemia and Low Birth Weight: A Systematic Review and Meta-Analysis. *Nutrients* 2018; 10: 601.

54 Rahmati S, Azami M, Badfar G, Parizad N, Sayehmiri K. The relationship between maternal anemia during pregnancy with preterm birth: a systematic review and meta-analysis. *J Matern Fetal Neonatal Med* 2020; 33: 2679–89.

55 Badfar G, Shohani M, Soleymani A, Azami M. Maternal anemia during pregnancy and small for gestational age: a systematic review and meta-analysis. *J Matern-Fetal Neonatal Med Off J Eur Assoc Perinat Med Fed Asia Ocean Perinat Soc Int Soc Perinat Obstet* 2019; 32: 1728–34.

56 Wedi COO, Kirtley S, Hopewell S, Corrigan R, Kennedy SH, Hemelaar J. Perinatal outcomes associated with maternal HIV infection: a systematic review and meta-analysis. *Lancet HIV* 2016; 3: e33-48.

57 Vallely LM, Egli-Gany D, Wand H, *et al.* Adverse pregnancy and neonatal outcomes associated with Neisseria gonorrhoeae: systematic review and meta-analysis. *Sex Transm Infect* 2021; 97: 104–11.

58 He W, Jin Y, Zhu H, Zheng Y, Qian J. Effect of Chlamydia trachomatis on adverse pregnancy outcomes: a meta-analysis. *Arch Gynecol Obstet* 2020; 302: 553–67.

549 59 Gomez GB, Kamb ML, Newman LM, Mark J, Broutet N, Hawkes SJ. Untreated maternal syphilis
550 and adverse outcomes of pregnancy: a systematic review and meta-analysis. *Bull World Health*
551 *Organ* 2013; 91: 217–26.

552 60 Thompson JM, Eick SM, Dailey C, *et al.* Relationship Between Pregnancy-Associated Malaria and
553 Adverse Pregnancy Outcomes: a Systematic Review and Meta-Analysis. *J Trop Pediatr* 2020; 66:
554 327–38.

555 61 Shah PS, Balkhair T. Air pollution and birth outcomes: A systematic review. *Environ Int* 2011; 37:
556 498–516.

557 62 Lamichhane DK, Leem J-H, Lee J-Y, Kim H-C. A meta-analysis of exposure to particulate matter
558 and adverse birth outcomes. *Environ Health Toxicol* 2015; 30: e2015011.

559 63 Yuan L, Zhang Y, Gao Y, Tian Y. Maternal fine particulate matter (PM2.5) exposure and adverse
560 birth outcomes: an updated systematic review based on cohort studies. *Environ Sci Pollut Res Int*
561 2019; 26: 13963–83.

562 64 Donovan BM, Spracklen CN, Schweizer ML, Ryckman KK, Saftlas AF. Intimate partner violence
563 during pregnancy and the risk for adverse infant outcomes: a systematic review and meta-
564 analysis. *BJOG Int J Obstet Gynaecol* 2016; 123: 1289–99.

565 65 Pastor-Moreno G, Ruiz-Pérez I, Henares-Montiel J, Escribà-Agüir V, Higueras-Callejón C, Ricci-
566 Cabello I. Intimate partner violence and perinatal health: a systematic review. *BJOG Int J Obstet*
567 *Gynaecol* 2020; 127: 537–47.

568 66 Cai C, Vandermeer B, Khurana R, *et al.* The impact of occupational activities during pregnancy on
569 pregnancy outcomes: a systematic review and metaanalysis. *Am J Obstet Gynecol* 2020; 222:
570 224–38.

571 67 Avşar TS, McLeod H, Jackson L. Health outcomes of smoking during pregnancy and the
572 postpartum period: an umbrella review. *BMC Pregnancy Childbirth* 2021; 21: 254.

573 68 Patra J, Bakker R, Irving H, Jaddoe VWV, Malini S, Rehm J. Dose-response relationship between
574 alcohol consumption before and during pregnancy and the risks of low birthweight, preterm
575 birth and small for gestational age (SGA)-a systematic review and meta-analyses. *BJOG Int J*
576 *Obstet Gynaecol* 2011; 118: 1411–21.

577 69 Mamluk L, Edwards HB, Savović J, *et al.* Low alcohol consumption and pregnancy and childhood
578 outcomes: time to change guidelines indicating apparently 'safe' levels of alcohol during
579 pregnancy? A systematic review and meta-analyses. *BMJ Open* 2017; 7: e015410.

580 70 Bryce E, Gurung S, Tong H, *et al.* Population attributable fractions for risk factors for
581 spontaneous preterm births in 81 low- and middle-income countries: A systematic analysis. *J*
582 *Glob Health* 2022; 12: 04013.

583 71 Gurung S, Tong HH, Bryce E, *et al.* A systematic review on estimating population attributable
584 fraction for risk factors for small-for-gestational-age births in 81 low- and middle-income
585 countries. *J Glob Health* 2022; 12: 04024.

586 72 Dadi AF, Miller ER, Mwanri L. Antenatal depression and its association with adverse birth
587 outcomes in low and middle-income countries: A systematic review and meta-analysis. *PLOS*
588 *ONE* 2020; 15: e0227323.

589 73 Traylor CS, Johnson JD, Kimmel MC, Manuck TA. Effects of psychological stress on adverse
590 pregnancy outcomes and nonpharmacologic approaches for reduction: an expert review. *Am J*
591 *Obstet Gynecol MFM* 2020; 2. DOI:10.1016/j.ajogmf.2020.100229.

592 74 Bidhendi Yarandi R, Vaismoradi M, Panahi MH, Gåre Kymre I, Behboudi-Gandevani S. Mild
593 Gestational Diabetes and Adverse Pregnancy Outcome: A Systemic Review and Meta-Analysis.
594 *Front Med* 2021; 8: 993.

595 75 Breintoft K, Pinnerup R, Henriksen TB, *et al.* Endometriosis and Risk of Adverse Pregnancy
596 Outcome: A Systematic Review and Meta-Analysis. *J Clin Med* 2021; 10: 667.

597 76 Bortoletto TG, Silva TV, Borovac-Pinheiro A, *et al.* Cervical length varies considering different
598 populations and gestational outcomes: Results from a systematic review and meta-analysis.
599 *PLOS ONE* 2021; 16: e0245746.

600 77 Pinheiro RL, Areia AL, Mota Pinto A, Donato H. Advanced Maternal Age: Adverse Outcomes of
601 Pregnancy, A Meta-Analysis. *Acta Med Port* 2019; 32: 219–26.

602 78 Gibbs CM, Wendt A, Peters S, Hogue CJ. The Impact of Early Age at First Childbirth on Maternal
603 and Infant Health. *Paediatr Perinat Epidemiol* 2012; 26: 259–84.

604 79 Shah PS. Parity and low birth weight and preterm birth: a systematic review and meta-analyses.
605 *Acta Obstet Gynecol Scand* 2010; 89: 862–75.

606 80 Kozuki N, Lee AC, Silveira MF, *et al.* The associations of birth intervals with small-for-gestational-
607 age, preterm, and neonatal and infant mortality: a meta-analysis. *BMC Public Health* 2013; 13:
608 S3.

609 81 Ahrens KA, Nelson H, Stidd RL, Moskosky S, Hutcheon JA. Short interpregnancy intervals and
610 adverse perinatal outcomes in high-resource settings: An updated systematic review. *Paediatr*
611 *Perinat Epidemiol* 2019; 33: O25–47.

612 82 Vogel JP, Torloni MR, Seuc A, *et al.* Maternal and Perinatal Outcomes of Twin Pregnancy in 23
613 Low- and Middle-Income Countries. *PLOS ONE* 2013; 8: e70549.

614 83 Yang L, Helbich-Poschacher V, Cao C, Klebermass-Schrehof K, Waldhoer T. Maternal altitude and
615 risk of low birthweight: A systematic review and meta-analyses. *Placenta* 2020; 101: 124–31.

616 84 Pels A, Ganzevoort W, Beune IM, van Wassenaer-Leemhuis AG, Limpens J. Early-onset fetal
617 growth restriction: A systematic review on mortality and morbidity. *Acta Obstet Gynecol Scand*
618 2020; 99: 153–66.

619 85 Gladstone M, Oliver C, Van den Broek N. Survival, Morbidity, Growth and Developmental Delay
620 for Babies Born Preterm in Low and Middle Income Countries – A Systematic Review of
621 Outcomes Measured. *PLOS ONE* 2015; 10: e0120566.

622 86 Colin AA, McEvoy C, Castile RG. Respiratory morbidity and lung function in preterm infants of 32
623 to 36 weeks' gestational age. *Pediatrics* 2010; 126: 115–28.

624 87 Isayama T, Lewis-Mikhael A-M, O'Reilly D, Beyene J, McDonald SD. Health Services Use by Late
625 Preterm and Term Infants From Infancy to Adulthood: A Meta-analysis. *Pediatrics* 2017; 140.
626 DOI:10.1542/peds.2017-0266.

627 88 Figueras-Aloy J, Manzoni P, Paes B, *et al.* Defining the Risk and Associated Morbidity and
628 Mortality of Severe Respiratory Syncytial Virus Infection Among Preterm Infants Without Chronic
629 Lung Disease or Congenital Heart Disease. *Infect Dis Ther* 2016; 5: 417–52.

630 89 Siffel C, Kistler KD, Sarda SP. Global incidence of intraventricular hemorrhage among extremely
631 preterm infants: a systematic literature review. *J Perinat Med* 2021.

632 90 Teune MJ, Bakhuizen S, Mol BWJ, *et al.* A systematic review of severe morbidity in infants born
633 late preterm. *Am J Obstet Gynecol* 2011; 205: e1-374.

634 91 Islam N, Thalib L, Alsaied A. Global incidence of Necrotizing Enterocolitis: A systematic review
635 and Meta-analysis. *BMC Pediatr* 2020; 20: 344.

636 92 Sarda SP, Siffel C, Kistler KD, Lewis JFM. Global incidence of bronchopulmonary dysplasia among
637 extremely preterm infants: a systematic literature review. *J Matern Fetal Neonatal Med* 2021;
638 34: 1721–31.

639 93 Pados BF, Hill RR, Yamasaki JT, Litt JS, Lee CS. Prevalence of problematic feeding in young
640 children born prematurely: a meta-analysis. *BMC Pediatr* 2021; 21: 110.

641 94 Schappin R, Wijnroks L, Uniken Venema MMAT, Jongmans MJ. Rethinking stress in parents of
642 preterm infants: a meta-analysis. *PloS One* 2013; 8: e54992.

643 95 Marthinsen GN, Helseth S, Fegran L. Sleep and its relationship to health in parents of preterm
644 infants: a scoping review. *BMC Pediatr* 2018; 18: N.PAG-N.PAG.

645 96 Haddad S, Dennis C-L, Shah PS, Stremler R. Sleep in parents of preterm infants: A systematic
646 review. *Midwifery* 2019; 73: 35–48.

647 97 Alenius S, Kajantie E, Sund R, *et al.* The Missing Siblings of Infants Born Preterm. *Pediatrics* 2018;
648 141. DOI:10.1542/peds.2017-1354.

649 98 Soilly AL, Lejeune C, Quantin C, Bejean S, Gouyon JB. Economic analysis of the costs associated
650 with prematurity from a literature review. *Public Health Elsevier* 2014; 128: 43–62.

651 99 Petrou S, Yiu HH, Kwon J. Economic consequences of preterm birth: A systematic review of the
652 recent literature (2009-2017). *Arch Dis Child* 2019; 104: 456–65.

653 100 Lim SS, Updike RL, Kaldjian AS, *et al.* Measuring human capital: a systematic analysis of 195
654 countries and territories, 1990-2016. *Lancet Lond Engl* 2018; 392: 1217–34.

655 101 Krasevec J, Blencowe H, Coffey C, *et al.* Study protocol for UNICEF and WHO estimates of global,
656 regional, and national low birthweight prevalence for 2000 to 2020. *Gates Open Res* 2022; 6: 80.

657 102 Shiffman J. Four Challenges That Global Health Networks Face. *Int J Health Policy Manag* 2017; 6:
658 183–9.

659 103 World Health Organization. WHO recommendations on antenatal care for a positive pregnancy
660 experience. Geneva: World Health Organization, 2016
661 https://apps.who.int/iris/handle/10665/250796.

104 World Health Organization. WHO recommendations on maternal health: guidelines approved by the WHO Guidelines Review Committee. Geneva: World Health Organization, 2017 https://apps.who.int/iris/handle/10665/259268.

105 World Health Organization. WHO recommendations on interventions to improve preterm birth outcomes. Geneva: World Health Organization, 2015 https://apps.who.int/iris/handle/10665/183037.

106 World Health Organization. Guideline: implementing effective actions for improving adolescent nutrition. Geneva: World Health Organization, 2018 https://apps.who.int/iris/handle/10665/260297 (accessed May 26, 2022).

107 World Health Organization. WHO antenatal care recommendations for a positive pregnancy experience: nutritional interventions update: multiple micronutrient supplements during pregnancy. Geneva: World Health Organization, 2020 https://apps.who.int/iris/handle/10665/333561 (accessed July 6, 2022).

108 Bhutta ZA, Das JK, Bahl R, *et al.* Can available interventions end preventable deaths in mothers, newborn babies, and stillbirths, and at what cost? *Lancet Lond Engl* 2014; 384: 347–70.

109 Stuckler D, McKee M. Five metaphors about global-health policy. *The Lancet* 2008; 372: 95–7.

110 Shiffman J, Shawar YR. Framing and the formation of global health priorities. *The Lancet* 2022; 399: 1977–90.

111 World Health Organization. Every newborn: an action plan to end preventable deaths. Geneva: World Health Organization, 2014 https://apps.who.int/iris/handle/10665/127938 (accessed Dec 21, 2021).

112 Provan KG, Kenis P. Modes of Network Governance: Structure, Management, and Effectiveness. *J Public Adm Res Theory* 2007; 18: 229–52.

113 Hug L, You D, Blencowe H, *et al.* Global, regional, and national estimates and trends in stillbirths from 2000 to 2019: a systematic assessment. *The Lancet* 2021; 398: 772–85.

114 Kassebaum NJ, Barber RM, Bhutta ZA, *et al.* Global, regional, and national levels of maternal mortality, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *The Lancet* 2016; 388: 1775–812.

115 Quenby S, Gallos ID, Dhillon-Smith RK, *et al.* Miscarriage matters: the epidemiological, physical, psychological, and economic costs of early pregnancy loss. *The Lancet* 2021; 397: 1658–67.

116 Koivu A, Haapaniem T, Askari S, *et al.* What more can be done? Prioritizing the most promising antenatal interventions to improve birth weight. *Am J Clin Nutr* In press.

117 Dewey KG, Wessells KR, Arnold CD, *et al.* Characteristics that modify the effect of small-quantity lipid-based nutrient supplementation on child growth: an individual participant data meta-analysis of randomized controlled trials. ; : 28.

118 Taneja S, Chowdhury R, Dhabhai N, *et al.* Impact of a package of health, nutrition, psychosocial support, and WaSH interventions delivered during preconception, pregnancy, and early childhood periods on birth outcomes and on linear growth at 24 months of age: factorial, individually randomised controlled trial. *BMJ* 2022; : e072046.

119 Baye E, Abate FW, Eglovitch M, *et al.* Effect of birthweight measurement quality improvement on low birthweight prevalence in rural Ethiopia. *Popul Health Metr* 2021; 19: 35.

120 Kim ET, Singh K, Moran A, Armbruster D, Kozuki N. Obstetric ultrasound use in low and middle income countries: a narrative review. *Reprod Health* 2018; 15: 129.

121 Jiwani SS, Amouzou-Aguirre A, Carvajal L, *et al.* Timing and number of antenatal care contacts in low and middle-income countries: Analysis in the Countdown to 2030 priority countries. *J Glob Health* 2020; 10: 010502.

122 Hasan MdM, Magalhaes RJS, Fatima Y, Ahmed S, Mamun AA. Levels, Trends, and Inequalities in Using Institutional Delivery Services in Low- and Middle-Income Countries: A Stratified Analysis by Facility Type. *Glob Health Sci Pract* 2021; 9: 78–88.

123 Deb S, Mohammed MS, Dhingra U, *et al.* Performance of late pregnancy biometry for gestational age dating in low-income and middle-income countries: a prospective, multicountry, population-based cohort study from the WHO Alliance for Maternal and Newborn Health Improvement (AMANHI) Study Group. *Lancet Glob Health* 2020; 8: e545–54.

124 Fung R, Villar J, Dashti A, *et al.* Achieving accurate estimates of fetal gestational age and personalised predictions of fetal growth based on data from an international prospective cohort study: a population-based machine learning study. *Lancet Digit Health* 2020; 2: e368–75.

125 World Health Organization. WHO recommendations on antenatal care for a positive pregnancy experience. Geneva: World Health Organization, 2016 https://apps.who.int/iris/handle/10665/250796 (accessed Sept 21, 2021).

126 Hofmeyr GJ. Routine ultrasound examination in early pregnancy: is it worthwhile in low-income countries? *Ultrasound Obstet Gynecol* 2009; 34: 367–70.

127 Ylppö A. Pathologisch-anatomische Studien bei Frühgeborenen. *Z Für Kinderheilkd* 1919; 20: 212–431.

128 Clifford SH. A Consideration of the Obstetrical Management of Premature Labor. *N Engl J Med* 1934; 210: 570–5.

129 Hughes MM, Black RE, Katz J. 2500-g Low Birth Weight Cutoff: History and Implications for Future Research and Policy. *Matern Child Health J* 2017; 21: 283–9.

130 World Health Organization. Manual of the international statistical classification of diseases, injuries, and causes of death : sixth revision of the International lists of diseases and causes of death, adopted 1948. *Man Classem Stat Int Mal Traumatismes Causes Décès Six Révis Nomencl Int Mal Causes Décès Adopt En 1948* 1948. https://apps.who.int/iris/handle/10665/42893.

131 WHO Expert Committee on Maternal and Child Health, World Health Organization. Public health aspects of low birth weight : third report of the Expert Committee on Maternal and Child Health [meeting held in Geneva from 21 to 26 November 1960]. 1961. https://apps.who.int/iris/handle/10665/40487.

132 Working party to discuss nomenclature based on gestational age and birthweight. *Arch Dis Child* 1970; 45: 730–730.

133 World Health Organization, Geneva) IC for the NR of the IC of D (1975 : Manual of the international statistical classification of diseases, injuries, and causes of death : based on the recommendations of the ninth revision conference, 1975, and adopted by the Twenty-ninth World Health Assembly. World Health Organization, 1977 https://apps.who.int/iris/handle/10665/40492 (accessed Sept 24, 2021).

134 Goldenberg RL, Gravett MG, Iams J, *et al.* The preterm birth syndrome: issues to consider in creating a classification system. *Am J Obstet Gynecol* 2012; 206: 113–8.

135 ACOG Committee Opinion No 579: Definition of term pregnancy. *Obstet Gynecol* 2013; 122: 1139–40.

136 Lubchenco LO, Hansman C, Dressler M, Boyd E. INTRAUTERINE GROWTH AS ESTIMATED FROM LIVEBORN BIRTH-WEIGHT DATA AT 24 TO 42 WEEKS OF GESTATION. *Pediatrics* 1963; 32: 793–800.

137 Usher R, McLean F. Intrauterine growth of live-born Caucasian infants at sea level: Standards obtained from measurements in 7 dimensions of infants born between 25 and 44 weeks. *J Pediatr* 1969; 74: 901–10.

138 Warkany J. Intrauterine Growth Retardation. *Arch Pediatr Adolesc Med* 1961; 102: 249.

139 American Academy of Pediatrics. Committee on fetus and newborn. Nomenclature for duration of gestation, birth weight and intra-uterine growth. *Pediatrics* 1967; 39: 935–9.

140 de Onis M, Habicht JP. Anthropometric reference data for international use: recommendations from a World Health Organization Expert Committee. *Am J Clin Nutr* 1996; 64: 650–8.

141 Alexander G, Himes J, Kaufman R, Mor J, Kogan M. A united states national reference for fetal growth. *Obstet Gynecol* 1996; 87: 163–8.

142 Clayton PE, Cianfarani S, Czernichow P, Johannsson G, Rapaport R, Rogol A. Management of the child born small for gestational age through to adulthood: a consensus statement of the International Societies of Pediatric Endocrinology and the Growth Hormone Research Society. *J Clin Endocrinol Metab* 2007; 92: 804–10.

143 WHO MULTICENTRE GROWTH REFERENCE STUDY GROUP, Onis M. WHO Child Growth Standards based on length/height, weight and age: WHO Child Growth Standards. *Acta Paediatr* 2007; 95: 76–85.

144 Villar J, Cheikh Ismail L, Victora CG, *et al.* International standards for newborn weight, length, and head circumference by gestational age and sex: the Newborn Cross-Sectional Study of the INTERGROWTH-21st Project. *Lancet Lond Engl* 2014; 384: 857–68.

145 Villar J, Giuliani F, Fenton TR, Ohuma EO, Ismail LC, Kennedy SH. INTERGROWTH-21st very preterm size at birth reference charts. *The Lancet* 2016; 387: 844–5.

146 Choi SKY, Gordon A, Hilder L, *et al.* Performance of six birth-weight and estimated-fetal-weight standards for predicting adverse perinatal outcome: a 10-year nationwide population-based study. *Ultrasound Obstet Gynecol* 2021; 58: 264–77.

776 147 Marien M, Perron S, Bergeron A-M, Singbo N, Demers S. Comparison of the Accuracy of
777 INTERGROWTH-21 and Hadlock Ultrasound Formulae for Fetal Weight Prediction. *J Obstet*
778 *Gynaecol Can* 2021; 43: 1254–9.

779 148 Fay E, Hugh O, Francis A, *et al.* Customized GROW vs INTERGROWTH-21st birthweight standards
780 to identify small for gestational age associated perinatal outcomes at term. *Am J Obstet Gynecol*
781 *MFM* 2022; 4: 100545.

782 149 World Health Assembly. Resolution WHA65.6. Comprehensive implementation plan on maternal,
783 infant and young child nutrition. Sixty-fifth World Health Assembly Geneva, May 21–26, 2012.
784 Geneva: World Health Organization, 2012.

785 150 World Health Assembly. Maternal, infant and young child nutrition: comprehensive
786 implementation plan on maternal, infant and young child nutrition: biennial report: report by the
787 Director-General. World Health Organization. 2018.

788 151 United Nations. World Declaration on the Survival, Protection and Development of Children and
789 Plan of Action for Implementing the World Declaration on the Survival, Protection and
790 Development of Children in the 1990s :World Summit for Children. New York : UN, 1990.

791 152 World Health Organization. Born too soon: the global action report on preterm birth. 2012; :
792 112.

793 153 Black RE, Victora CG, Walker SP, *et al.* Maternal and child undernutrition and overweight in low-
794 income and middle-income countries. *Lancet Lond Engl* 2013; 382: 427–51.

795 154 Samarasekera U, Horton R. The world we want for every newborn child. *The Lancet* 2014; 384:
796 107–9.

797 155 Berkley S, Dybul M, Godal T, Lake A. Integration and innovation to advance newborn survival.
798 *The Lancet* 2014; 384: e22–3.

799 156 Starrs AM. Survival convergence: bringing maternal and newborn health together for 2015 and
800 beyond. *The Lancet* 2014; 384: 211–3.

801 157 Dong Y, Chen S, Yu J. A systematic review and meta-analysis of long-term development of early
802 term infants. *Neonatology* 2012; 102: 212–21.

803 158 Li W, Peng A, Deng S, *et al.* Do premature and postterm birth increase the risk of epilepsy? An
804 updated meta-analysis. *Epilepsy Behav* 2019; 97: 83–91.

805 159 de KIEVIET JF, Zoetebier L, van ELBURG RM, Vermeulen RJ, Oosterlaan J. Brain development of
806 very preterm and very low-birthweight children in childhood and adolescence: a meta-analysis:
807 Review. *Dev Med Child Neurol* 2012; 54: 313–23.

808 160 Been JV, Lugtenberg MJ, Smets E, *et al.* Preterm birth and childhood wheezing disorders: a
809 systematic review and meta-analysis. *PLoS Med* 2014; 11: e1001596.

810 161 den Dekker HT, Sonnenschein-van der Voort AMM, de Jongste JC, *et al.* Early growth
811 characteristics and the risk of reduced lung function and asthma: A meta-analysis of 25,000
812 children. *J Allergy Clin Immunol* 2016; 137: 1026–35.

162 Sonnenschein-van der Voort AMM, Arends LR, de Jongste JC, *et al.* Preterm birth, infant weight gain, and childhood asthma risk: A meta-analysis of 147,000 European children. *J Allergy Clin Immunol* 2014; 133: 1317–29.

163 Jaakkola J, Ahmed P, Ieromnimon A, *et al.* Preterm delivery and asthma: A systematic review and meta-analysis. *J Allergy Clin Immunol* 2006; 118: 823–30.

164 Mebrahtu TF, Feltbower RG, Greenwood DC, Parslow RC. Birth weight and childhood wheezing disorders: a systematic review and meta-analysis. *J Epidemiol Community Health* 2015; 69: 500–8.

165 Mu M, Ye S, Bai M-J, *et al.* Birth weight and subsequent risk of asthma: a systematic review and meta-analysis. *Heart Lung Circ* 2014; 23: 511–9.

166 Kotecha S, Clemm H, Halvorsen T, Kotecha SJ. Bronchial hyper-responsiveness in preterm-born subjects: A systematic review and meta-analysis. *Pediatr Allergy Immunol Off Publ Eur Soc Pediatr Allergy Immunol* 2018; 29: 715–25.

167 Kotecha SJ, Edwards MO, Watkins WJ, *et al.* Effect of preterm birth on later FEV1: a systematic review and meta-analysis. *Thorax* 2013; 68: 760–6.

168 Edwards MO, Kotecha SJ, Lowe J, Watkins WJ, Henderson AJ, Kotecha S. Effect of preterm birth on exercise capacity: A systematic review and meta-analysis. *Pediatr Pulmonol* 2015; 50: 293–301.

169 Telles F, McNamara N, Nanayakkara S, *et al.* Changes in the Preterm Heart From Birth to Young Adulthood: A Meta-analysis. *Pediatrics* 2020; 146: e20200146.

170 Paquette K, Coltin H, Boivin A, Amre D, Nuyt A-M, Luu TM. Cancer risk in children and young adults born preterm: A systematic review and meta-analysis. *PloS One* 2019; 14: e0210366.

171 Huang Q-T, Gao Y-F, Zhong M, Yu Y-H. Preterm Birth and Subsequent Risk of Acute Childhood Leukemia: a Meta-Analysis of Observational Studies. *Cell Physiol Biochem Int J Exp Cell Physiol Biochem Pharmacol* 2016; 39: 1229–38.

172 Hussain SM, Ackerman IN, Wang Y, Zomer E, Cicuttini FM. Could low birth weight and preterm birth be associated with significant burden of hip osteoarthritis? A systematic review. *Arthritis Res Ther* 2018; 20: 121.

173 Paulsson L, Bondemark L, Soderfeldt B. A systematic review of the consequences of premature birth on palatal morphology, dental occlusion, tooth-crown dimensions, and tooth maturity and eruption. *Angle Orthod* 2004; 74: 269–79.

174 Bensi C, Costacurta M, Belli S, Paradiso D, Docimo R. Relationship between preterm birth and developmental defects of enamel: A systematic review and meta-analysis. *Int J Paediatr Dent* 2020; 30: 676–86.

175 Jacobsen PE, Haubek D, Henriksen TB, Ostergaard JR, Poulsen S. Developmental enamel defects in children born preterm: a systematic review. *Eur J Oral Sci* 2014; 122: 7–14.

176 Moore GP, Lemyre B, Daboval T, Barrowman N. Neurodevelopmental outcomes at 4 to 8 years of children born at 22 to 25 weeks' gestational age: A meta-analysis. *JAMA Pediatr* 2013; 167: 967–74.

177 Pascal A, Govaert P, Oostra A, Naulaers G, Ortibus E, Van den Broeck C. Neurodevelopmental outcome in very preterm and very-low-birthweight infants born over the past decade: a meta-analytic review. *Dev Med Child Neurol* 2018; 60: 342–55.

178 Levine TA, Grunau RE, McAuliffe FM, Pinnamaneni R, Foran A, Alderdice FA. Early Childhood Neurodevelopment After Intrauterine Growth Restriction: A Systematic Review. *Pediatrics* 2015; 135: 126–41.

179 Allotey J, Zamora J, Cheong-See F, *et al.* Cognitive, motor, behavioural and academic performances of children born preterm: a meta-analysis and systematic review involving 64 061 children. *BJOG Int J Obstet Gynaecol* 2018; 125: 16–25.

180 Upadhyay RP, Naik G, Choudhary TS, *et al.* Cognitive and motor outcomes in children born low birth weight: A systematic review and meta-analysis of studies from South Asia. *BMC Pediatr* 2019; 19: 35.

181 Moreira RS, Magalhaes LC, Alves CRL. Effect of preterm birth on motor development, behavior, and school performance of school-age children: a systematic review. *J Pediatr (Rio J)* 2014; 90: 119–34.

182 de Kieviet JF, Piek JP, Aarnoudse-Moens CS, Oosterlaan J. Motor Development in Very Preterm and Very Low-Birth-Weight Children From Birth to Adolescence: A Meta-analysis. *JAMA* 2009; 302: 2235.

183 Edwards J, Berube M, Erlandson K, *et al.* Developmental coordination disorder in school-aged children born very preterm and/or at very low birth weight: a systematic review. *J Dev Behav Pediatr JDBP* 2011; 32: 678–87.

184 FitzGerald TL, Kwong AKL, Cheong JLY, McGinley JL, Doyle LW, Spittle AJ. Body Structure, Function, Activity, and Participation in 3- to 6-Year-Old Children Born Very Preterm: An ICF-Based Systematic Review and Meta-Analysis. *Phys Ther* 2018; 98: 691–704.

185 Williams J, Lee KJ, Anderson PJ. Prevalence of motor-skill impairment in preterm children who do not develop cerebral palsy: a systematic review. *Dev Med Child Neurol* 2010; 52: 232–7.

186 Fuentefria R do N, Silveira RC, Procianoy RS. Motor development of preterm infants assessed by the Alberta Infant Motor Scale: systematic review article. *J Pediatr (Rio J)* 2017; 93: 328–42.

187 Maitra K, Park HY, Eggenberger J, Matthiessen A, Knight E, Ng B. Difficulty in mental, neuromusculoskeletal, and movement-related school functions associated with low birthweight or preterm birth: a meta-analysis. *Am J Occup Ther Off Publ Am Occup Ther Assoc* 2014; 68: 140–8.

188 Arpi E, D'Amico R, Lucaccioni L, Bedetti L, Berardi A, Ferrari F. Worse global intellectual and worse neuropsychological functioning in preterm-born children at preschool age: a meta-analysis. *Acta Paediatr* 2019; 108: 1567–79.

189 Aarnoudse-Moens CSH, Weisglas-Kuperus N, Van Goudoever JB, Oosterlaan J. Meta-analysis of neurobehavioral outcomes in very preterm and/or very low birth weight children. *Pediatrics* 2009; 124: 717–28.

190 Houdt CA van, Oosterlaan J, Wassenaer-Leemhuis AG van, Kaam AH van, Aarnoudse-Moens CSH. Executive function deficits in children born preterm or at low birthweight: a meta-analysis. *Dev Med Child Neurol* 2019; 61: 1015–24.

191 Kerr-Wilson CO, Mackay DF, Smith GCS, Pell JP. Meta-analysis of the association between preterm delivery and intelligence. *J Public Health* 2012; 34: 209–16.

192 Martinez-Nadal S, Bosch L. Cognitive and Learning Outcomes in Late Preterm Infants at School Age: A Systematic Review. *Int J Environ Res Public Health* 2020; 18. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=medl&NEWS=N&AN=33374182.

193 Bhutta AT, Cleves MA, Casey PH, Cradock MM, Anand KJS. Cognitive and behavioral outcomes of school-aged children who were born preterm: A meta-analysis. *J Am Med Assoc* 2002; 288: 728–37.

194 Brydges CR, Landes JK, Reid CL, Campbell C, French N, Anderson M. Cognitive outcomes in children and adolescents born very preterm: a meta-analysis. *Dev Med Child Neurol* 2018; 60: 452–68.

195 Sacchi C, Marino C, Nosarti C, Vieno A, Visentin S, Simonelli A. Association of Intrauterine Growth Restriction and Small for Gestational Age Status With Childhood Cognitive Outcomes: A Systematic Review and Meta-analysis. *JAMA Pediatr* 2020; 174: 772.

196 Chan E, Leong P, Malouf R, Quigley MA. Long-term cognitive and school outcomes of late-preterm and early-term births: a systematic review. *Child Care Health Dev* 2016; 42: 297–312.

197 Chen J, Chen P, Bo T, Luo K. Cognitive and Behavioral Outcomes of Intrauterine Growth Restriction School-Age Children. *Pediatrics* 2016; 137: e20153868.

198 Blencowe H, Lawn JE, Vazquez T, Fielder A, Gilbert C. Preterm-associated visual impairment and estimates of retinopathy of prematurity at regional and global levels for 2010. *Pediatr Res* 2013; 74: 35–49.

199 Fetus, Newborn Committee CPS. Retinopathy of prematurity: A systematic review of the literature. *Paediatr Child Health* 1998; 3: 173–80.

200 Razak A, Faden M. Association of small for gestational age with retinopathy of prematurity: a systematic review and meta-analysis. *Arch Dis Child Fetal Neonatal Ed* 2020; 105: 270–8.

201 Burstein O, Zevin Z, Geva R. Preterm Birth and the Development of Visual Attention During the First 2 Years of Life: A Systematic Review and Meta-analysis. *JAMA Netw Open* 2021; 4: e213687–e213687.

202 Geldof CJA, van Wassenaer AG, de Kieviet JF, Kok JH, Oosterlaan J. Visual perception and visual-motor integration in very preterm and/or very low birth weight children: a meta-analysis. *Res Dev Disabil* 2012; 33: 726–36.

203 Kovachy VN, Adams JN, Tamaresis JS, Feldman HM. Reading abilities in school-aged preterm children: a review and meta-analysis. *Dev Med Child Neurol* 2015; 57: 410–9.

204 Barre N, Morgan A, Doyle LW, Anderson PJ. Language abilities in children who were very preterm and/or very low birth weight: a meta-analysis. *J Pediatr* 2011; 158: 766-774.e1.

928 205 Van Noort-van Der Spek IL, Franken M-CJP, Weisglas-Kuperus N. Language functions in preterm-
929 born children: A systematic review and meta-analysis. *Pediatrics* 2012; 129: 745–54.

930 206 Rechia IC, Oliveira LD, Crestani AH, Biaggio EPV, Souza APR de. Effects of prematurity on
931 language acquisition and auditory maturation: a systematic review. *Efeitos Prematuridade Na*
932 *Aquis Ling E Na Matur Audit Revisao Sist* 2016; 28: 843–54.

933 207 Reynolds V, Meldrum S, Simmer K, Vijayasekaran S, French N. Dysphonia in very preterm
934 children: a review of the evidence. *Neonatology* 2014; 106: 69–73.

935 208 McBryde M, Fitzallen GC, Liley HG, Taylor HG, Bora S. Academic Outcomes of School-Aged
936 Children Born Preterm: A Systematic Review and Meta-analysis. *JAMA Netw Open* 2020; 3:
937 e202027.

938 209 Twilhaar ES, de Kieviet JF, Aarnoudse-Moens CS, van Elburg RM, Oosterlaan J. Academic
939 performance of children born preterm: a meta-analysis and meta-regression. *Arch Dis Child -*
940 *Fetal Neonatal Ed* 2018; 103: F322–30.

941 210 McGowan JE, Alderdice FA, Holmes VA, Johnston L. Early childhood development of late-preterm
942 infants: A systematic review. *Pediatrics* 2011; 127: 1111–24.

943 211 Rodrigues MCC de, Mello RR, Fonseca S, ra C. Learning difficulties in schoolchildren born with
944 very low birth weight. *J Pediatr (Rio J)* 2006; 82: 6–14.

945 212 Cassiano RGM, Gaspardo CM, Linhares MBM. Prematurity, neonatal health status, and later child
946 behavioral/emotional problems: a systematic review. *Infant Ment Health J* 2016; 37: 274–88.

947 213 Mathewson KJ, Pope EI, Schmidt LA, Chow CHT, Dobson KG, Van Lieshout RJ. Mental health of
948 extremely low birth weight survivors: A systematic review and meta-analysis. *Psychol Bull* 2017;
949 143: 347–83.

950 214 Agrawal S, Rao SC, Bulsara MK, Patole SK. Prevalence of Autism Spectrum Disorder in Preterm
951 Infants: A Meta-analysis. *Pediatrics* 2018; 142: 1–14.

952 215 Jenabi E, Bashirian S, Asali Z, Seyedi M. Association between small for gestational age and risk of
953 autism spectrum disorders: a meta-analysis. *Clin Exp Pediatr* 2021.
954 http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=medp&NEWS=N&AN=33539699.

955 216 Fitzallen GC, Sagar YK, Taylor HG, Bora S. Anxiety and Depressive Disorders in Children Born
956 Preterm: A Meta-Analysis. *J Dev Behav Pediatr JDBP* 2021; 42: 154–62.

957 217 Wojcik W, Lee W, Colman I, Hardy R, Hotopf M. Foetal origins of depression? A systematic
958 review and meta-analysis of low birth weight and later depression. *Psychol Med* 2013; 43: 1–12.

959 218 Cassiano RGM, Provenzi L, Linhares MBM, Gaspardo CM, Montirosso R. Does preterm birth
960 affect child temperament? A meta-analytic study. *Infant Behav Dev* 2020; 58: N.PAG-N.PAG.

961 219 Zwicker JG, Harris SR. Quality of life of formerly preterm and very low birth weight infants from
962 preschool age to adulthood: a systematic review. *Pediatrics* 2008; 121: e366-76.

963 220 Norman M. Low birth weight and the developing vascular tree: a systematic review. *Acta*
964 *Paediatr Oslo Nor 1992* 2008; 97: 1165–72.

965 221 Andraweera PH, Condon B, Collett G, Gentilcore S, Lassi ZS. Cardiovascular risk factors in those
966 born preterm - systematic review and meta-analysis. *J Dev Orig Health Dis* 2020; : 1–16.

967 222 Kormos CE, Wilkinson AJ, Davey CJ, Cunningham AJ. Low birth weight and intelligence in
968 adolescence and early adulthood: a meta-analysis. *J Public Health* 2014; 36: 213–24.

969 223 Su Y, D'Arcy C, Meng X. Research Review: Developmental origins of depression - a systematic
970 review and meta-analysis. *J Child Psychol Psychiatry* 2020.
971 http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=medp&NEWS=N&AN=33259072.

972 224 Burnett AC, Anderson PJ, Cheong J, Doyle LW, Davey CG, Wood SJ. Prevalence of psychiatric
973 diagnoses in preterm and full-term children, adolescents and young adults: a meta-analysis.
974 *Psychol Med* 2011; 41: 2463–74.

975 225 Sømhovd MJ, Hansen BM, Brok J, Esbjørn BH, Greisen G. Anxiety in adolescents born preterm or
976 with very low birthweight: a meta-analysis of case-control studies. *Dev Med Child Neurol* 2012;
977 54: 988–94.

978 226 Day KL, Van Lieshout RJ, Vaillancourt T, Schmidt LA. Peer victimization in survivors of premature
979 birth and low birth weight: Review and recommendations. *Aggress Violent Behav* 2015; 25: 259–
980 65.

981 227 de Jong M, Verhoeven M, van Baar AL. School outcome, cognitive functioning, and behaviour
982 problems in moderate and late preterm children and adults: A review. *Semin Fetal Neonatal Med*
983 2012; 17: 163–9.

984 228 Raju TNK, Buist AS, Blaisdell CJ, Moxey-Mims M, Saigal S. Adults born preterm: a review of
985 general health and system-specific outcomes. *Acta Paediatr Int J Paediatr* 2017; 106: 1409–37.

986 229 Visser SSM, van Diemen WJM, Kervezee L, *et al.* The relationship between preterm birth and
987 sleep in children at school age: A systematic review. *Sleep Med Rev* 2021; 57: 101447.

988 230 Gogou M, Haidopoulou K, Pavlou E. Sleep and prematurity: sleep outcomes in preterm children
989 and influencing factors. *World J Pediatr* 2019; 15: 209–18.

990 231 Petrou S, Krabuanrat N, Khan K. Preference-Based Health-Related Quality of Life Outcomes
991 Associated with Preterm Birth: A Systematic Review and Meta-analysis. *PharmacoEconomics*
992 2020; 38: 357–73.

993 232 Crump C. Preterm birth and mortality in adulthood: a systematic review. *J Perinatol* 2020; 40:
994 833–43.

995 233 Kajantie E, Strang-Karlsson S, Evensen KAI, Haaramo P. Adult outcomes of being born late
996 preterm or early term – What do we know? *Semin Fetal Neonatal Med* 2019; 24: 66–83.

997 234 Saad NJ, Patel J, Burney P, Minelli C. Birth Weight and Lung Function in Adulthood: A Systematic
998 Review and Meta-analysis. *Ann Am Thorac Soc* 2017; 14: 994–1004.

999 235 Das SK, Mannan M, Faruque ASG, Ahmed T, McIntyre HD, Al Mamun A. Effect of birth weight on
1000 adulthood renal function: A bias-adjusted meta-analytic approach. *Nephrol Carlton Vic* 2016; 21:
1001 547–65.

1002 236 Senra JC, Carvalho MA, Rodrigues AS, *et al.* An unfavorable intrauterine environment may
1003 determine renal functional capacity in adulthood: a meta-analysis. *Clin Sao Paulo Braz* 2018; 73:
1004 e401.

1005 237 White SL, Perkovic V, Cass A, *et al.* Is low birth weight an antecedent of CKD in later life? A
1006 systematic review of observational studies. *Am J Kidney Dis* 2009; 54: 248–61.

1007 238 Heo JS, Lee JM. The long-term effect of preterm birth on renal function: A meta-analysis. *Int J*
1008 *Environ Res Public Health* 2021; 18: 1–18.

1009 239 de Mendonça ELSS, de Lima Macêna M, Bueno NB, de Oliveira ACM, Mello CS. Premature birth,
1010 low birth weight, small for gestational age and chronic non-communicable diseases in adult life:
1011 A systematic review with meta-analysis. *Early Hum Dev* 2020; 149: 105154.

1012 240 Liao L, Deng Y, Zhao D. Association of Low Birth Weight and Premature Birth With the Risk of
1013 Metabolic Syndrome: A Meta-Analysis. *Front Pediatr* 2020; 8: 405.

1014 241 Li S, Zhang M, Tian H, Liu Z, Yin X, Xi B. Preterm birth and risk of type 1 and type 2 diabetes:
1015 systematic review and meta-analysis. *Obes Rev Off J Int Assoc Study Obes* 2014; 15: 804–11.

1016 242 Harder T, Plagemann A, Harder A. Birth weight and subsequent risk of childhood primary brain
1017 tumors: a meta-analysis. *Am J Epidemiol* 2008; 168: 366–73.

1018 243 Mi D, Fang H, Zhao Y, Zhong L. Birth weight and type 2 diabetes: A meta-analysis. *Exp Ther Med*
1019 2017; 14: 5313–20.

1020 244 Markopoulou P, Papanikolaou E, Analytis A, Zoumakis E, Siahanidou T. Preterm Birth as a Risk
1021 Factor for Metabolic Syndrome and Cardiovascular Disease in Adult Life: A Systematic Review
1022 and Meta-Analysis. *J Pediatr* 2019; 210: 69-80.e5.

1023 245 Mu M, Wang S-F, Sheng J, *et al.* Birth weight and subsequent blood pressure: a meta-analysis.
1024 *Arch Cardiovasc Dis* 2012; 105: 99–113.

1025 246 de Jong F, Monuteaux MC, van Elburg RM, *et al.* Systematic review and meta-analysis of preterm
1026 birth and later systolic blood pressure. *Hypertens 0194911X* 2012; 59: 226–34.

1027 247 Mohseni R, Mohammed SH, Safabakhsh M, *et al.* Birth Weight and Risk of Cardiovascular Disease
1028 Incidence in Adulthood: a Dose-Response Meta-analysis. *Curr Atheroscler Rep* 2020; 22: 12.

1029 248 Wang SF, Shu L, Sheng J, *et al.* Birth weight and risk of coronary heart disease in adults: a meta-
1030 analysis of prospective cohort studies. *J Dev Orig Health Dis* 2014; 5: 408–19.

1031 249 Michos A, Xue F, Michels KB. Birth weight and the risk of testicular cancer: a meta-analysis. *Int J*
1032 *Cancer* 2007; 121: 1123–31.

1033 250 Loret de Mola C, de Franca GVA, Quevedo L de A, Horta BL. Low birth weight, preterm birth and
1034 small for gestational age association with adult depression: systematic review and meta-analysis.
1035 *Br J Psychiatry J Ment Sci* 2014; 205: 340–7.

1036 251 Pyhälä R, Wolford E, Kautiainen H, *et al.* Self-Reported Mental Health Problems Among Adults
1037 Born Preterm: A Meta-analysis. *Pediatrics* 2017; 139: e20162690.

252 Dahan-Oliel N, Mazer B, Majnemer A. Preterm birth and leisure participation: a synthesis of the literature. *Res Dev Disabil* 2012; 33: 1211–20.

253 Robinson R, Lahti-Pulkkinen M, Schnitzlein D, *et al.* Mental health outcomes of adults born very preterm or with very low birth weight: A systematic review. *Semin Fetal Neonatal Med* 2020; 25: 101113.

254 Bilgin A, Mendonca M, Wolke D. Preterm Birth/Low Birth Weight and Markers Reflective of Wealth in Adulthood: A Meta-analysis. *Pediatrics* 2018; 142: e20173625.

255 Mendonca M, Bilgin A, Wolke D. Association of Preterm Birth and Low Birth Weight with Romantic Partnership, Sexual Intercourse, and Parenthood in Adulthood: A Systematic Review and Meta-analysis. *JAMA Netw Open* 2019. https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2737900.

Box 1. Evolution of criteria for identifying high-risk newborns

LBW was the first definition to be formalised for a small, at-risk newborn. The currently used cut-off of 2500 g was initially published approximately 100 years ago by Dr. Arvo Ylppö, a Finnish paediatrician working in Germany.[127] The 2500 g cut-off did not have a biological justification, and it seems to have been selected as a round figure that encompassed approximately 5% of newborns. This assumption is supported by the fact that authors in the United States suggested another round cut-off using the imperial measurement system (5 lb., i.e., 2270 g).[128] The American Academy of Pediatrics, other professional organisations and the World Health Organization (WHO) codified the 2500 g cut-off as an indication of "prematurity" between 1935 and 1948.[129,130] A 1961 report by a WHO Expert Committee on Maternal and Child Health highlighted the difference between preterm infants and term but small infants and suggested changing the term from "premature babies" to "babies with low birth weight".[131]

Although the first criterion for a small newborn was birth weight, the definition itself seemed to refer more to a short pregnancy duration. The German-language term that Dr. Ylppö used for small infants was "frühgeborenen", meaning "early born" and the term used in respective US studies was "premature". In the 1948 International Classification of Diseases (ICD), in which WHO adopted the 2500 g cut-off, the condition was called "immaturity". Interestingly, the text noted that "*if birth weight is not available, a liveborn infant with a period of gestation of less than 37 weeks or specified as "premature" may be considered as the equivalent of an immature infant*.[130] With the development and spread of obstetric ultrasound technology there was increasing interest in a more specific definition for a birth that occurred early. In 1970 a working group of obstetricians and paediatricians at the Second European Congress of

Perinatal Medicine set the boundary between "preterm" and "term" birth at 37 completed weeks of gestation.[132]

As with LBW, there was no justification given to the cut-off selected for preterm birth. Alternative possibilities were apparently discussed, but eventually 37 weeks was chosen because it had already appeared in the 1948 ICD. The 37-week cut-off and the expression "preterm birth" were officially adopted by WHO in its International Classification of Diseases in 1977.[133] Several authors and organisations have subsequently suggested a later cut-off of 39 weeks' gestation, because it would better coincide with functional maturity.[134] So far, 37 weeks' gestation has persisted as the most widely accepted cut-off for preterm birth. However, to account for the stated concerns and to allow a more stratified risk assessment, the American College of Obstetricians and Gynecologists recommends term deliveries to be sub-classified into early term (37.0 - 38.9 weeks), full-term (39.0 – 40.9 weeks), late term (41.0 – 41.9 weeks), and post term (42.0 weeks or more) categories.[135]

The third category used for small newborns stemmed from the concern of health professionals having to define small but term infants "premature" as suggested by the 1948 ICD. Several publications in the 1950s and 1960s highlighted the fact that, in addition to preterm birth, LBW results from what was originally called "intrauterine growth retardation".[136–139] The process of impaired fetal growth has since been renamed fetal growth restriction, and infants who are born with a birth weight that is below an agreed cut-off for their sex and gestational age as SGA.

A WHO Expert Committee adopted the concept of SGA and recommended the use of a US-based, multiracial "Williams" reference in 1995.[140] This was soon replaced by another US-based "Alexander" reference, that classified newborns below its 10th centile as SGA.[141] In 2007, the International Society of Pediatric Endocrinology and the Growth Hormone

Research Society suggested that a cut-off of -2 standard deviations from the mean would be more appropriate than the 10th centile, as it would identify only 2.3% and not 10% of newborns as SGA.[142] Between 2014-2016, the INTERGROWTH-21st Consortium published new sex and gestational age specific birth size standards for term, preterm and very preterm newborns, based on the same prescriptive approach that produced the WHO Child Growth Standards.[143] Because of its multinational cohort, the INTERGROWTH-21st standards were designed to have better global validity than a purely US-based reference.[144145] Many recently published scientific manuscripts use the INTERGROWTH-21st birth weight standard and a cut-off below the 10th centile to define SGA, but there is no official consensus on its use and the discussion about the correct reference and cut-off to use continues.[146–148]

Figure 1 summarises the key milestones in the development of the small newborn definitions. For all these definitions, there is a corollary indicative of a large birth size or long duration of pregnancy, i.e., high birth weight, post-term birth, and large for gestational age. Whilst these states also confer an increased health risk for the newborn, their global health impact has been less studied, and they will not be covered in the current *Lancet* series.

Box 2. Definition of a Small Vulnerable Newborn

Our definition of Small Vulnerable Newborn includes all live newborns who are preterm (born before 37 completed weeks of gestation), are small for gestational age at birth (birthweight below the 10th centile of the recommended international, sex-specific birthweight for gestational age standard) or have low birth weight (<2500g).

In principle the definition could be based only on preterm and SGA, encompassing practically the full set of small newborns who have an increased risk of mortality and other adverse outcomes.[25] Preterm and SGA represent the driving pathways for vulnerability, i.e., duration of pregnancy and fetal growth restriction, and therefore guide the prioritization of preventive interventions and clinical management, whereas LBW does not give this important information. Therefore, we focus on preterm, SGA, and preterm-SGA that are the causes of LBW and are associated with increased risk of mortality and other vulnerabilities both in newborns who do or do not have LBW. However, birth weight is still more commonly measured than pregnancy duration or SGA and easily understood by parents. As opposed to SGA and preterm birth, there is also a global target for reducing LBW prevalence.[149,150] Hence having LBW in the definition will facilitate continuation of monitoring of current targets and identification of vulnerable newborns even in contexts where antenatal services are most limited. In the future, once pregnancy dating and SGA monitoring have become the norm worldwide, the inclusion of LBW in the SVN definition may become less important.

Box 3. Examples of high-level attention to LBW and SVN prevention, 1990 - 2020

The reduction of LBW prevalence to less than 10% was defined as a key nutritional goal already in the 1990 World Summit for Children.[151] In 2012, WHO, supported by many other organisations, published a "*Born Too Soon*" report that had high political resonance and lots of attention, calling for primary prevention of preterm births and better care for preterm infants.[152] Soon afterwards, the World Health Assembly (WHA) set the reduction of LBW prevalence by 30% between 2010 and 2025 (later extended to 2030) as a global nutrition target[149,150] and an article series on maternal and child nutrition in *The Lancet* called attention to the large number of neonatal deaths attributable to SGA.[153] In 2014, the *Every Newborn* series in *The Lancet* led to the WHO and UNICEF facilitated "*Every Newborn Action Plan*" (ENAP), with a World Health Assembly Resolution and the first Sustainable Development Goal (SDG) target for newborn survival.[111] Both the *Born Too Soon* report and the ENAP underlined the impact of small birth size on mortality and disability, calling for emphasis and investments in small and sick newborn care but also for primary prevention through the maternal and child life course.[154–156] The publication of ENAP led to an ongoing active partnership of more than 100 organisations, co-chaired by WHO and UNICEF. As part of this process, more than 90 countries have set specific targets for newborn survival and are regularly reporting on progress.

Figure 1. Key milestones in the evolution of vulnerable newborn terminology. Yellow boxes denote the development of the low birth definition, orange box marks the adoption of the preterm birth definition, blue boxes refer to the definition of small for gestational age and the green box refers to an umbrella term combining the former three definitions. Frühgeborenen born early, AAP American Academy of Pediatrics, ICD International Classification of Diseases, adopted by the World Health Assembly, WHO the World Health Organization, gw gestation weeks, SGA small for gestational age

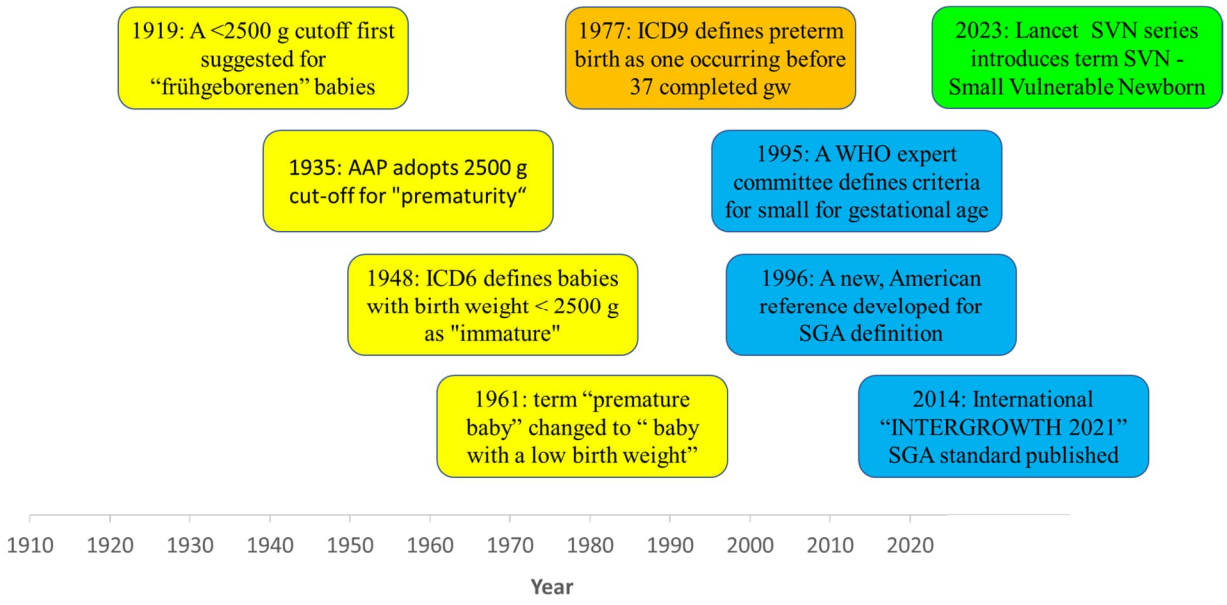


Figure 2. Conceptual framework for the causes and consequences of being born small. Dev development, prob problems, Sdr. syndrome, T2D type 2 diabetes, SGA small for gestational age, SB stillbirth, BMI body mass index, HIV human immunodeficiency virus infection, STI sexually transmitted infections, UTI urinary tract infection, BV bacterial vaginosis, GBS group B streptococcus

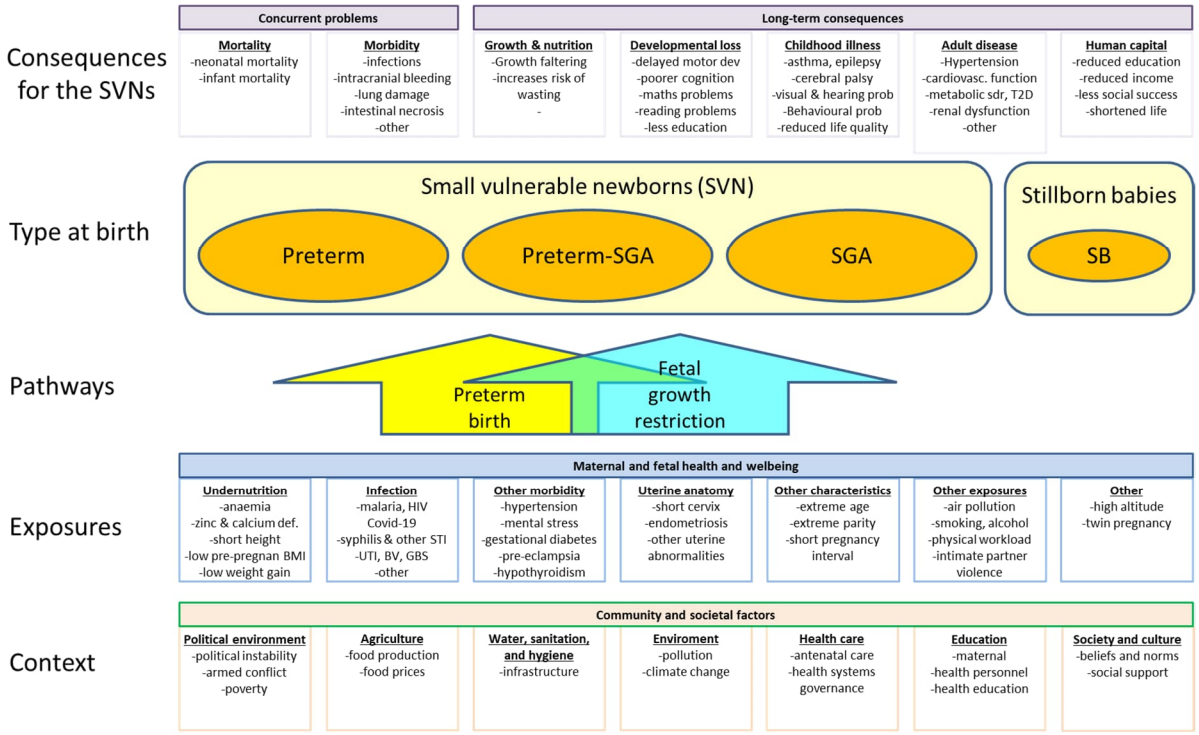
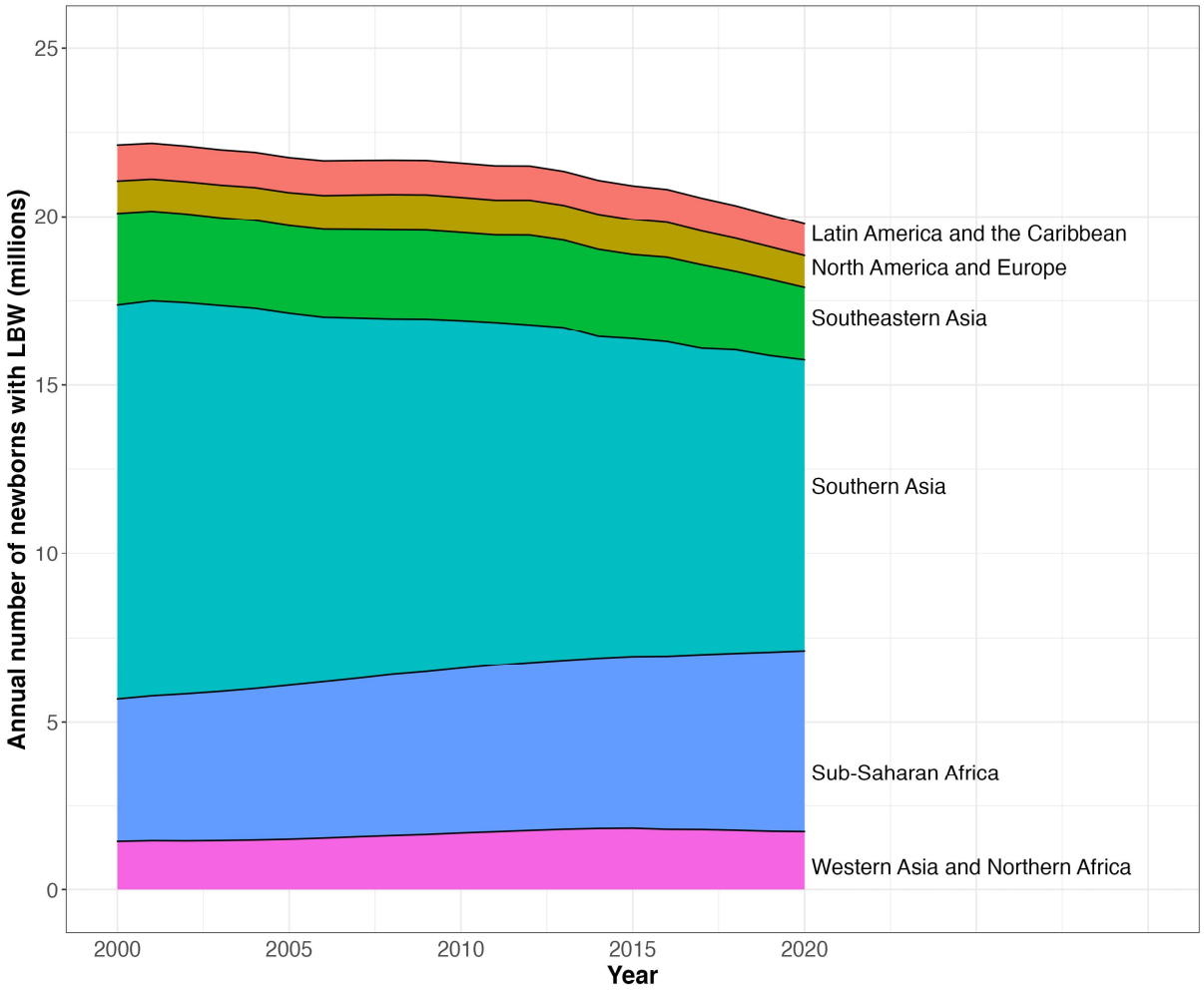
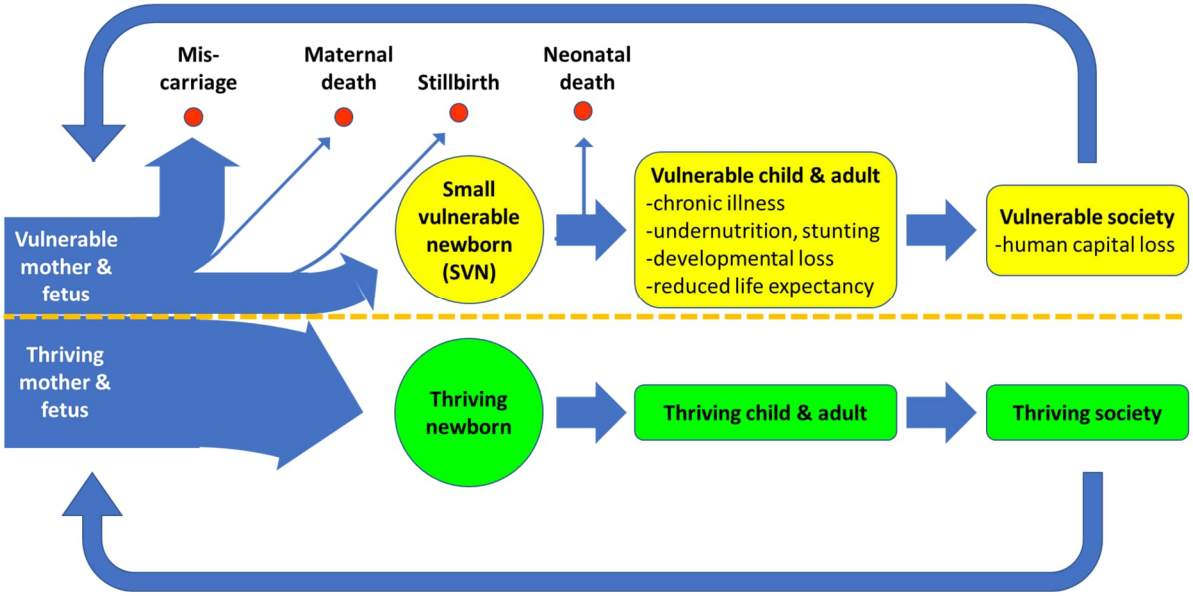


Figure 3. Annual numbers of newborns with LBW between 2000 and 2020, by region.
Estimates by UNICEF and WHO for 195 countries from 2000 to 2020. National annual LBW rates with smoothing applied to national live births per year, as described earlier.[101] LBW low birth weight



1184 Figure 4. The vicious cycle between vulnerable newborns and vulnerable societies

1185



1186

1187
1188
1189

Table 1. Adverse outcomes associated with SVN in systematic reviews and meta-analyses

Childhood

Increased risk of mortality, stunting, and wasting (PT, SGA)[13,18]
Increased risk of cerebral palsy and epilepsy (PT) [157,158]
Reduced brain volume (PT, LBW)[159]
Increased risk of wheezing disorders and asthma (PT, LBW)[160,161,162,163,164,165,166]
Reduced lung function and exercise capacity (PT, SGA) [161,167,168]
Morphological and functional cardiac impairments (PT)[169]
Increased risk of hepatoblastoma and acute myeloid leukemia (PT)[170,171]
Hip bone shape abnormalities and increased risk of hip osteoarthritis (PT, LBW)[172]
Altered palatal morphology and defects in dental enamel (PT, LBW)[173,174,175]
Increased risk of delay and impairment of neurodevelopment (PT, SGA)[176,177, 21,178]
Problems in motor development (PT, LBW)[179,180 ,181 ,182,183,184,185,186187]
Reduced IQ and cognitive performance (PT, SGA, LBW)[188,179,189,190,191,192,193,194,195,196,180,197]
Blindness and other problems with vision (PT, SGA)[198,199,200,201,202]
Problems in reading, spelling, and mathematics (PT)[179, 189,203]
Reduced language abilities and increased risk of dysphonia (PT, LBW)[204,205,206,207]
Impaired school and academic performance (PT, LBW)[157,179,181,192,196, 208, 209, 210 ,211]
Increased risk of ADHD and autism spectrum disorders (PT, LBW,SGA)[193,212,213,214,215]
Increased risk of mental disorders & social problems (PT, LBW)[216,217,181,213,212,218]
Reduced self-rated quality of life (LBW, PT)[219]

Adolescence

Increased risk of asthma and poor lung function (LBW, PT) [164,166,167, 168]
Cardiac and vascular problems and increased blood pressure (PT, LBW)[169,220,221]
Reduced IQ and cognitive performance (LBW, PT) [179,222]
Increased risk of depression, anxiety, and being bullied (SGA, PT, LBW)[223,224,225226]
Increased frequency of school problems (PT)[227]
Increased risk of social difficulties and behavior problems (LBW, PT) [179,213]
Increased risk of a psychiatric diagnosis and hospitalization (PT)[224,228]
Reduced sleep quality and increased risk of sleep breathing disorders (PT) [229,230]
Reduced self-rated quality of life (LBW, PT)[219,231]

Adulthood

Increased morbidity and mortality (PT)[232,233]
Reduced lung function and increased risk of asthma (LBW)[165,234]
Impaired renal function (LBW, PT)[235,236,237,238]
Increased risk of metabolic syndrome and diabetes (LBW, PT)[239,240,20,241,242,243,241,244]
Increased risk of hypertension, coronary disease and stroke (PT, LBW)[221,239,244 ,245,246,247,248]
Increased risk of testicular cancer (LBW)[249]
Increased risk of hip arthroplasty for osteoarthritis (PT)[172]
Increased risk of depression and anxiety (SGA, PT, LBW) [213,223,250]
Increased risk of shyness, social withdrawal, autism, and physical inactivity (PT)[213,228,251 252]
Increased use of psychotropic medication (PT, LBW)[253]
Decreased likelihood of completing higher education and being employed (PT, LBW)[254]
Decreased likelihood of a romantic partnership and becoming a parent (PT, LBW)[255]
Reduced quality of life (PT)[231]

SVN small vulnerable newborn, PT Preterm birth, LBW Low birth weight, SGA Small for gestational age, ADHD Attention deficit and hyperactivity disorder

Table 2. Success of global response to main challenges in SVN prevention.

Challenge	Meaning	Status for SVN prevention	Description
Problem definition	Generating evidence-informed consensus within the global health network on the definition of, and best ways to address the problem	Contested[1]	The three different definitions for adverse birth outcomes compete with each other and complicate a comprehensive synthesis of the problem. Improved management, but not prevention, is seen as a priority.
Positioning	Framing the issue in a way that moves key actors external to the network to provide resources.	Contested	Preterm birth, SGA, LBW typically positioned individually and only as a medical problem for the newborn. Maternal ill health, miscarriages, and stillborn babies are ignored and the life-long impact of SVN and loss of human capital are largely ignored.
Coalition-building	Recruitment of allies beyond core members of the global health network.	Moderately broad	Every Newborn Action Plan pulled together many partners and lead to the formation of multiple international networks. But they involve mainly organisations from the health and health research sector. National governments and actors are underrepresented, and SVN and their parents have no voice.
Governance	Establishing institutions to facilitate collective action	Largely cohesive	No apparent central guiding forum or institution that brings together primary organisations. Only LBW tracked and with a global target.

[1]Possible categories for "Problem definition and preferred solution" and for "Positioning" include cohesive, relatively cohesive, and contested. Possible categories for "Coalition building" include broad, moderately broad, and narrow and those for "Governance" include cohesive, largely cohesive, and fragmented. Framework adopted from Shiffman[102]. SGA small for gestational age, LBW low birth weight, SVN small vulnerable newborn

Supplemental table 1. Number of births and neonatal deaths in different world regions, 1990 and 2021

	Annual number of births (thousands)			Neonatal mortality rate (deaths per 1,000 live births)			Neonatal deaths (number of deaths) thousands		
World Region	**1990**	**2021**	**Decline (percent)**	**1990**	**2021**	**Decline (percent)**	**1990**	**2021**	**Decline (percent)**
Sub-Saharan Africa	22,086	39,441	-79[1]	46	27	41	1,004	1,067	-6
Northern Africa	4,673	5,928	-27	34	15	54	157	91	42
Southern Asia	39,910	36,086	10	57	22	61	2,288	811	65
Eastern Asia	31,039	12,640	59	28	3	89	853	39	95
South-Eastern Asia	11,963	11,086	7	28	12	58	332	130	61
Western Asia	4,824	5,643	-17	28	11	58	133	65	51
Central Asia	1,594	1,772	-11	28	10	66	44	17	62
Europe	9,235	6,880	26	8	2	70	76	17	78
North America	4,568	4,098	10	6	3	42	26	13	48
Latin America & the Caribbean	12,020	9,709	19	23	9	60	272	87	68
Oceania	540	693	-28	13	10	48	7	7	0
World	142,451	133,975	6	37	15	52	5,191	2,345	55

[1]All percentages calculated from unrounded numbers. Birth data source: World Population Prospects: The 2022 Revision -United Nations Population Division.[7] Neonatal death and mortality data estimates developed by the United Nations Inter-agency Group for Child Mortality Estimation.[5]