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Optimising Child and Adolescent Health and Development

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Optimising child and adolescent health and development in the post-pandemic world

Our Series on optimising child and adolescent health and development follows on almost two decades after the original *Lancet* Series on child survival and its corresponding call for action.[1] With less than 10 years left to meet the 2030 Sustainable Development Goals (SDGs), we are concerned that, once again, the world is failing its children. The evidence is strong and calls for change abound; however, effective actions are few and far between.

The four papers in our Series provide an abundance of scientific evidence in support of a holistic agenda for child health spanning sexual, reproductive, maternal, childhood, and adolescent health, as well as nutrition and development. A major agenda to reduce premature mortality remains unfinished, with 8·6 million deaths globally among children and adolescents (aged 0–20 years), including stillbirths, in 2019.[2] Analysis of long-term birth cohorts shows the detrimental effects of early-life deprivation and toxic stress on health, nutrition, and cognitive development of children, often extending across generations.[3] Despite ample evidence supporting evidence-based interventions,[4] implementation across health, education, and social systems is poor.[5]

Although the SDGs were painstakingly crafted and shaped into a global strategy with strong benefit–cost ratios for investing in women and children,[6] corresponding implementation has been disappointing and disjointed, lacking political commitment and resources. The UN Secretary General abandoned his patronage of the Every Woman Every Child initiative, the much touted efforts by WHO on the Universal Health Coverage framework hardly mention children,[7] and resources at UNICEF for core child health and development programmes have stagnated.[8] At the half-way mark of the SDG period, most countries and global programmes remain in the mode of targeting specific diseases and age bands in childhood, rather than the age continuum and integration of child and adolescent periods.[9–11] Many countries are only beginning to localise the SDGs and develop granular national goals,[12] and few have a comprehensive child and adolescent health strategy.

Furthermore, the COVID-19 pandemic has interrupted progress on the SDGs, through major effects on economies and social systems,[13] as well as on health and nutrition services. These effects include potentially substantial reversals of gains in maternal and child survival and nutrition;[14,15] educational disruptions affecting learning and social relationships needed for child development;[16] increased vulnerability of children and women to violence, abuse,[17] and mental health problems; and disproportionate effects on the poorest children and young people.[18] The limitations in response to the pandemic are reflective of the challenge we face in transforming the agenda for child health globally, as governments (and international agencies) appear to be ill prepared to prioritise needs and respond comprehensively. This situation has been further exacerbated by the failure of the 2021 UN Climate Change Conference to rise to the aspirations of millions of children and young people globally with sufficient actions to address the planet's future.[19] Recent humanitarian disasters in Afghanistan and Tigray, Ethopia, coupled with the Russian invasion of Ukraine, have exposed millions of families and children to enormous additional physical and mental health risks.

We underscore the call for action to make children central to the development agenda[20] and to identify several priority actions. We call on planners and policy

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makers to break the artificial silos across the continuum from the preconception period to age 20 years using the nurturing care framework,[21] and to provide adequate nutrition, social protection, and safe learning environments that begin at home and extend to communities, schools, and national policies. The policy changes to support this transformation should enable seamless planning and coordinated delivery across various platforms to support children, adolescents, and families, including school health and nutrition services, social protection, housing services, and community support. Such evidence-based actions and strategies must reach the most marginalised and hard-to-reach children in diverse settings, such as programmes and safety nets for families living in conflict settings, displaced populations, and urban slums.

We urgently need to apportion sufficient resources to meet this ambitious but crucial agenda. An annual global funding gap of US$33 billion had been identified in 2021[22] and is likely to increase following the COVID-19 pandemic. This investment is small with much greater returns in human health and capacity, and future economic productivity[23] compared with the trillions of dollars that high-income countries have spent for their own citizens in response to COVID-19[24] and the widening wealth gaps globally.[25] Existing mechanisms of funding global health and nutrition needs through the Global Financing Facility, Global Vaccine Alliance, Global Fund, and Power of Nutrition are inadequate, and must change rapidly.

Over three decades since the historic meeting in New York that laid out the importance of human capital,[26] we call for a global summit for children that covers the entire period of preconception, pregnancy, childhood, and adolescence (age <20 years), and is responsive to their current and future needs. This summit should engage global leaders, policy makers, civil society, academia, and, importantly, children and young people to agree on the investments needed to link children's health, wellbeing, and education to development in human capital. One of the key objectives should be to agree on a common accountability framework for country and global oversight, as well as tracking across relevant sectors. Multiple global indicators, global indexes, and dashboards already exist; what we call for is not a new measure, but a rigorous pursuit to fill persistent data gaps, use evidence to overcome bottlenecks, and improve key measures for children and adolescents. A renewed focus on country ownership of monitoring and accountability, supported by a dedicated global and regional mechanism to track and review progress, is needed.

The current crisis not only poses a substantial threat of stagnation and reversal of progress for children and adolescents globally, but also offers enormous opportunities. We seek a revitalised global effort to fully protect, nurture, and support the health and development potential for every child everywhere, from before conception to adulthood.

We declare no competing interests.

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Opportunities in crisis for optimising child health and development

The *Lancet* Series on optimising child and adolescent health and development[1-4] arrives at the right time. For many years, the global health community has known that quality primary health care, including antenatal care, immunisation, and optimal nutrition, help children survive past their fifth birthday and live healthy lives. Child survival has improved because of combined efforts in these areas; but the scale and scope of the global threats to child health and wellbeing, including conflicts, climate crises, and other humanitarian emergencies, all compounded by COVID-19, now put decades of progress at grave risk. Nonetheless, these crises present an opportunity to reinvigorate global commitments to child health, wellbeing, and children's rights, and to equitably scale up evidence-based interventions delivered through resilient primary health care to achieve universal health coverage.

In 2020 the WHO–UNICEF–*Lancet* Commission launched its report, *A Future for the World's Children?*[5] and set out a bold vision for a broader focus on child and adolescent health, wellbeing, and social development, expanding on the impressive gains made in young child survival over the past few decades.[6] The Commission urged policy makers to take a long-term view of child wellbeing, considering evidence that shows early investments in children's health, education, and development have lifelong, intergenerational, and economic benefits for children and societies.[7,8] The Commission recommended that investments should not be restricted to health and education alone, but spread across sectors—in universal health coverage, good nutrition and food security, safe and affordable housing, protected environments with clean water and air, and safe places to play—since all sectors contribute to child wellbeing.

The COVID-19 pandemic has slowed, and in some cases reversed, the gains in child health and survival achieved over the past two decades. The pandemic has also illustrated how underinvestment in health systems, together with inequities in accessing health services and a crisis of trust in public health institutions, has left populations and entire countries at risk from preventable causes of death. The pandemic entrenched inequities and widened societal fault lines, increasing vulnerabilities, and shocking health systems and their abilities to deliver primary health care. At the same time, the response to COVID-19 catalysed unprecedented international solidarity, advancements in medical technology, and the mobilisation of unparalleled resources for global health.[9] But more remains to be done to support vulnerable populations and strengthen health systems globally.

Even before the pandemic, progress towards the 2030

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targets in the Sustainable Development Goals (SDGs) to save the lives of women and children was already behind by about 20%, with millions of children and women unable to access life-saving services.[10] Continuing global crises are placing child health and wellbeing at grave risk.

In 2020, 23 million children missed out on vaccination—the highest number of children since 2009.[11] The number of children that received no vaccinations at all increased from 13·6 million in 2019 to 17·1 million in 2020.[11] In parallel, as a result of the pandemic, the world witnessed simultaneous food and nutrition crises on multiple fronts unmatched by any situation encountered in previous decades. In 2020, millions more people were at risk of food insecurity than the previous year, and an additional 142 million children were living in poverty.[12]

Preventable child deaths are also a concern. In 2020, 5 million children younger than 5 years died—one death every 6 seconds—nearly half of them newborn babies.[13] Infectious diseases, including pneumonia, diarrhoea, and malaria, remained the leading cause of deaths among children younger than 5 years, along with preterm birth and intrapartum-related complications.[14] Additionally, an estimated 810 women died each day from causes related to pregnancy and childbirth.[15] In 2020, the under-5 mortality rate in the 38 countries classified as fragile and conflict-affected[13] increased by three times compared with all other countries. Globally in 2020, 43% of deaths among children younger than 5 years occurred in fragile or conflict-affected countries. For example, in Afghanistan, an estimated 72 000 children died before reaching their fifth birthday in 2020.[13]

Conflict and crisis have also undermined the efforts of countries that had met or were on track to meet the SDG 2030 target for child survival. Before war broke out in February, 2022 Ukraine had met this target for child survival.[13] With as many as 1000 births occurring each day in Ukraine,[16] those gains for maternal, newborn, and child survival are expected to be lost due to health service disruption and violence.

The global community has an opportunity that should not be wasted. On the one hand, the COVID-19 pandemic has put an enormous burden on our children, with health systems and education disrupted, lives lost, and livelihoods damaged. The residual impacts of the past 2 years will not be fully quantified for decades to come. The worst consequences of any crisis will fall disproportionately on the poorest and most vulnerable children and their carers in all countries. On the other hand, the pandemic has offered a glimpse of what is possible when the global community comes together in solidarity and makes investments in health a global political priority. This moment offers an opportunity to build stronger health systems to not only prevent future outbreaks, but also to improve essential and life-saving health services for children and communities to reduce disease and prevent deaths over the long term.

At this especially perilous moment in history, with conflict and fragility around the world, all countries need to prioritise child and adolescent health, and tailor health and multisectoral programmes to meet their needs and risk factors. This is the time for governments, donors, and institutions to come together not only to end the pandemic, but also to prevent future ones, fix long-standing structural deficiencies in fragile health systems, including strengthening the health workforce, and address the social and environmental determinants of health that put children at risk. It is time for solidarity to triumph over politics, for the sake of our children and future generations. Failure to do so could result in close to 21 million children and adolescents aged 5–24 years and 43 million children under-5 years dying before 2030.[13] This prospect is unconscionable and unnecessary, because as seen in this *Lancet* Series, stakeholders know what needs to be done so that every child, everywhere, can survive and thrive.

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Optimising Child and Adolescent Health and Development 1

Health and development from preconception to 20 years of age and human capital

Robert E Black, Li Liu, Fernando P Hartwig, Francisco Villavicencio, Andrea Rodriguez-Martinez, Luis P Vidaletti, Jamie Perin, Maureen M Black, Hannah Blencowe, Danzhen You, Lucia Hug, Bruno Masquelier, Simon Cousens, Amber Gove, Tyler Vaivada, Diana Yeung, Jere Behrman, Reynaldo Martorell, Clive Osmond, Aryeh D Stein, Linda S Adair, Caroline H D Fall, Bernardo Horta, Ana M B Menezes, Manuel Ramirez-Zea, Linda M Richter, George C Patton, Eran Bendavid, Majid Ezzati, Zulfiqar A Bhutta, Joy E Lawn, Cesar G Victora

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This is the first in a **Series** of four papers on Optimising Child and Adolescent Health and Development

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Optimal health and development from preconception to adulthood are crucial for human flourishing and the formation of human capital. The Nurturing Care Framework, as adapted to age 20 years, conceptualises the major influences during periods of development from preconception, through pregnancy, childhood, and adolescence that affect human capital. In addition to mortality in children younger than 5 years, stillbirths and deaths in 5–19-year-olds are important to consider. The global rate of mortality in individuals younger than 20 years has declined substantially since 2000, yet in 2019 an estimated 8·6 million deaths occurred between 28 weeks of gestation and 20 years of age, with more than half of deaths, including stillbirths, occurring before 28 days of age. The 1000 days from conception to 2 years of age are especially influential for human capital. The prevalence of low birthweight is high in sub-Saharan Africa and even higher in south Asia. Growth faltering, especially from birth to 2 years, occurs in most world regions, whereas overweight increases in many regions from the preprimary school period through adolescence. Analyses of cohort data show that growth trajectories in early years of life are strong determinants of nutritional outcomes in adulthood. The accrual of knowledge and skills is affected by health, nutrition, and home resources in early childhood and by educational opportunities in older children and adolescents. Linear growth in the first 2 years of life better predicts intelligence quotients in adults than increases in height in older children and adolescents. Learning-adjusted years of schooling range from about 4 years in sub-Saharan Africa to about 11 years in high-income countries. Human capital depends on children and adolescents surviving, thriving, and learning until adulthood.

Introduction

Children's optimal health and development are the ambition of families everywhere and are central to the formation of human capital. The World Bank's Human Capital Project uses the Human Capital Index, which includes measures of mortality, growth, and education, to assess how countries invest in the capabilities and economic potential of citizens.[1] A broadened conceptualisation of human capital should include health and wellbeing, the knowledge, and interpersonal and socioemotional skills needed to fulfil individual and societal potential. Human capital is formed through intergenerational factors and interactive biological–environmental–behavioural processes; it originates before conception and extends throughout childhood, adolescence, and beyond.[2,3]

The Sustainable Development Goals (SDGs), agreed to by all UN member states, provide a pathway to human flourishing and the development of human capital.[4] During the 25 years of the Millennium Development Goals (MDGs)[5] era, from 1990 to 2015, child mortality was halved, including in many of the world's poorest countries, through societal progress and direct health interventions.[6] Achieving the ambitious SDGs in the 15 year timeframe (2015–30) will require faster progress. The SDGs are broader than the MDGs, with an ambitious agenda. First, they go beyond survival to children thriving,[4] including goals for nutrition, child development,[7] and education;[8] all important for human capital formation.[3] Second, they adopt a life course approach, which extends beyond 5 years, to include school-age children and adolescents.[2] Third, the SDGs are more ambitious than the MDGs and aim for wider transformation in health and educational systems and other changes in multiple sectors that affect health and wellbeing.[4] Finally, the SDGs extend beyond a focus on health and education to include economic and environmental goals, along with the social responsibility necessary to ensure sustainability.

The four papers in this Series on optimising child and adolescent health and development aim to explore the determinants and building blocks of thriving, from preconception through fetal development up to 20 years of age. In this first Series paper, we consider conditions of survival, growth, disability, and education in world regions and evidence from longitudinal studies on the crucial periods in the life-cycle before adulthood that build the foundation for human capital. Subsequent Series papers consider the importance of inequities in the determinants of human capital,[9] interventions that have proven to be of benefit,[10] the important need to improve quality of health services,[11] and the way forward to enhance global and national commitments for the health and development of children and adolescents.[12]

Nurturing care and human capital

The interactive biological–environmental–behavioural processes that determine a child's health and development operate through time-dependent crucial and sensitive periods.[13] Factors preceding conception and exposures in the prenatal and early postnatal periods lay the foundation for future health and wellbeing. Adversities can disrupt the course of development—operating through neurobiological processes, such as inflammation and dysregulation of the hypothalamic–pituitary axis—which undermines human capital accrual by increasing the vulnerability of children's health, development, and learning potential. However, human development operates as a dynamic system with mediators and moderators that can alter the life course by mitigating the negative consequences associated with adversities and promoting adaptive processes through protective factors.[14] A conceptual framework to inform the accrual of human capital should incorporate the biological–environmental–behavioural life course processes, the time-dependent periods, and the dynamic changes resulting from mediating and moderating mechanisms to guide policies and programmes that enable children and adolescents to survive and thrive.

Nurturing care is an evidence-based, dynamic framework that was initially proposed to inform policies that would ensure that young children could reach their full developmental potential.[7,15] Nurturing care is activated through a stable environment and behaviours that ensure good health and nutrition, provides protection from threats, and ensures opportunities for learning through relationships that are emotionally supportive and responsive.[15] As a dynamic framework, nurturing care is responsive to mechanisms that mitigate adversities, enhance resilience, and promote the wellbeing of marginalised groups.[14]

Nurturing care has been adapted to include determinants of human capital accrual, beginning with preparation for conception, and continuing through the provision of health care, nutrition, and learning opportunities in the context of responsive care throughout pregnancy, childhood, and adolescence, with support from the community and family-centred services and policies.[16] Nurturing care is particularly important during the time-dependent crucial and sensitive periods when neural plasticity is high, and opportunities for mitigation of adversities are strong.[17] The benefits of nurturing care continue throughout childhood and adolescence. With supportive parenting, ongoing learning, participation, relationship negotiation, and coping with adversities, children build the crucial components of human capital. In addition to gaining academic skills, children learn to modulate their emotions and behaviour, assume responsibilities for themselves and others, and become increasingly self-efficacious.[7,18] With increasing agency and autonomy, adolescents play more important roles in shaping relationships and developing learning and nutritional environments.[18] Nurturing care is an evidence-based framework that integrates health and nutrition, the focus of this Series paper, along with responsive caregiving, learning, security, and safety to promote equity and build human capital from preconception through adolescence (figure 1).[16] Families play a central role in the process, supported by a comprehensive, multisectoral system of services and opportunities that include nurturing care and support the development of human capital (appendix p 3).

Key messages

- Human capital requires a foundation of health, knowledge, skills, and learning acquired from preconception to 20 years of age; healthy growth and development from conception to the second birthday are crucial
- Mortality rates before 20 years of age are important measures of the survival component of human capital; of the 8·6 million deaths before 20 years of age in 2019, more than half were stillbirths or occurred in the first month after birth
- Regional disparities are large with children in south Asia and sub-Saharan Africa having the worst chance to survive and thrive
- The Nurturing Care Framework, as adapted to extend from preconception through childhood and adolescence, conceptualises influences on the formation of human capital and identifies crucial periods for interventions

Surviving to age 20 years

Globally, an estimated 8·62 million deaths occurred between 28 weeks of gestation and 20 years of age in 2019 (appendix p 4).[19–25] Of these deaths, 1·97 million (22·8%) were stillbirths and 2·44 million (28·3%) were neonatal. 2·75 million (31·9%) individuals who died were 1–59-months-old, 506 000 (5·9%) were 5–9-years-old, 368 000 (4·3%) were 10–14-years-old, and 595 000 (6·9%) were 15–19-years-old (appendix pp 5–6). Globally, mortality rates before age 20 years declined substantially from 2000 to 2019, dropping from 111·43 deaths (90% uncertainty interval [UI] 108·96–112·95) per 1000 pregnancies reaching 28 weeks of gestation in 2000 to 62·02 deaths (60·63–65·60) in 2019 (appendix pp 6–8), a 2·98% (90% UI 2·75–3·19) average annual rate of reduction (AARR). The AARR for stillbirths, neonates, and other age groups are provided in the appendix (p 7).

Regional survival disparities remained large in 2019, with the highest mortality rate in west and central Africa (143·19 deaths [90% UI 133·10–160·59] per 1000 pregnancies reaching 28 weeks of gestation) compared with the lowest in high-income countries (HICs; 10·08 deaths [9·86–10·33] per 1000 pregnancies reaching 28 weeks of gestation; 14-times lower than west and central Africa; appendix pp 8–13; table 1). The

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See Online for appendix

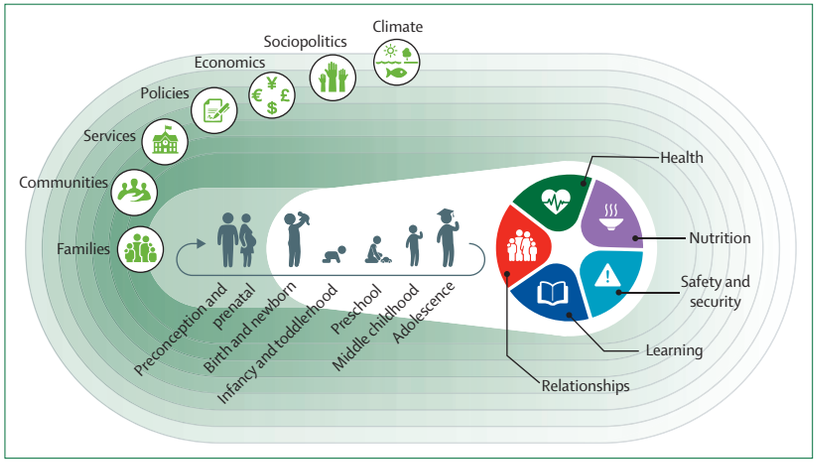

Figure 1: **The Nurturing Care Framework from preconception to adolescence**
Adapted from Black and colleagues.[16]

regional differences were also reflected in the varying age distribution of deaths. For example, the number of neonatal deaths were 30 000 (25·9%) of 115 000 in HICs compared with 882 000 (36·4%) of 2·42 million deaths in south Asia (figure 2; appendix p 4). Fragile and conflict-affected countries have a large number of deaths (3·24 million [90% UI 3·04–3·64]); figure 2; appendix pp 4, 14).[26,27]

Stillbirths are a major contributor to preventable mortality globally, with 1·97 million stillbirths (90% UI 1·92–2·19) in 2019 (figure 2; appendix pp 4, 14).[20,22] Globally, 832 000 (42·3%) stillbirths occurred during labour (intrapartum stillbirths; appendix p 15),[20] but this proportion varied by world region (appendix pp 15–16). The rate of stillbirths was eight-times higher in west and central Africa (22·82 stillbirths [90% UI 19·78–27·67] per 1000 pregnancies) compared with HICs (2·74 stillbirths [2·60–2·91] per 1000 pregnancies; table 1).

The global neonatal mortality rate (NMR) reduced by nearly half from 30·35 (90% UI 29·62–31·17) per 1000 live births in 2000 to 17·48 (16·61–18·97) per 1000 live births in 2019 (appendix pp 5–6).[19,21] However, wide regional disparities remained in 2019. In west and central Africa, the NMR was 30·86 deaths (26·87–36·93) per 1000 live births, more than 11-times higher than in HIC (2·69 [2·57–2·81] per 1000 live births; table 1). Worldwide, the leading causes of neonatal mortality in 2019 were preterm birth complications, intrapartum-related complications, congenital anomalies, lower-respiratory infections, and sepsis (appendix p 15).[25] Preterm birth complications were the predominant causes of neonatal death in all regions (appendix p 17). The proportion of neonates who died from infectious causes or intrapartum events was positively associated with regional NMRs.

There were 20·57 deaths (90% UI 18·93–22·26) before age 5 years per 1000 children who survived to 1 month of age in 2019, a 56·1% decline from the mortality rate in 2000 (46·84 [45·03–46·93]; appendix pp 5–6).[19,21] There were considerable disparities in mortality across regions in this age group in 2019: 1·98 deaths (1·88–2·08) per 1000 1-month-olds were reported in HICs, more than 33-times lower than the highest mortality rate reported in west and central Africa (65·89 [57·44–78·24]; table 1). Globally in 2019, the most common causes of death for children aged 1 to 59 months were lower-respiratory infections, diarrhoea, malaria, injuries, measles, congenital anomalies, and tuberculosis (appendix p 15).[25] The most common direct causes of deaths in west and central Africa were malaria, diarrhoea, and lower-respiratory infections. By contrast in HICs, which reported the lowest mortality, the main causes were congenital anomalies, followed by injuries (appendix p 18).

Globally, mortality rates in 5–9-year-olds were 3·83 (90% UI 3·63–4·02) per 1000 children reaching 5 years of age, 2·90 (2·67–3·57) in children reaching 10 years of age, and 4·89 (4·67–5·24) in adolescents reaching 15 years of age in 2019 (table 1). West and central Africa consistently had the highest mortality rates, whereas HICs had the lowest. Compared with HICs, survival was 28-times lower in 5–9-years-olds and seven-times lower in 15–19-years-olds in west and central Africa (table 1). The age distribution of deaths by age also differed across regions (figure 2; appendix p 4). For example, the number of deaths in 5–9-year-olds were 13 135 (3·9%) of 336 019 deaths from 28 weeks of gestation and 20 years of age in Latin America and the Caribbean and 194 267 (7·1%) of 2·74 million deaths in west and central Africa.

At the global level, the leading causes of death in 2019 were diarrhoea and malaria in 5–9-year-olds; malaria and neoplasms in 10–14-year-olds; self-harm and neoplasms in 15–19-year-old females; and road traffic injuries and interpersonal violence in 15–19-year-old males (appendix p 15).[23] Regionally there are substantial differences in the causes of death that vary by the mortality rate and the presence of endemic diseases, such as malaria (appendix pp 19–22).

In fragile and conflict-affected countries,[27] causes of death were very similar to west and central Africa, where many of these countries are located (figure 2; appendix p 23). These countries have a higher proportion of deaths due to collective violence compared with the global total.[23]

Thriving to age 20 years

Low birthweight

Low birthweight is a substantial global problem, associated with both short-term and long-term health consequences affecting human capital. Low birthweight is defined as birthweight less than 2500 g and can be due to either preterm birth (<37 completed weeks of gestation), growth restriction (measured as small for gestational age [SGA]; ie, less than the tenth percentile of weight for gestational age and sex compared with an international standard for fetal weight[28]), or both. In 2012,

	Stillborn	0–27 days	1–59 months	5–9 years	10–14 years	15–19 years			Risk of death between 28 weeks of gestation and 19 years completed
						Both	Females	Males	
West and central Africa	22·82 (19·78–27·67)	30·86 (26·87–36·93)	65·89 (57·44–78·24)	12·39 (11·24–13·69)	8·25 (6·34–11·42)	11·13 (9·69–13·22)	10·55 (9·24–12·51)	11·69 (10·14–13·93)	143·19 (133·10–160·59)
Eastern and southern Africa	20·52 (18·69–23·61)	23·87 (21·65–27·98)	32·32 (29·06–37·94)	7·33 (6·60–8·00)	4·96 (4·19–7·34)	9·27 (8·40–10·46)	7·51 (6·80–8·46)	11·02 (9·98–12·44)	94·61 (90·49–104·55)
South Asia	18·17 (17·58–22·12)	25·09 (23·02–27·28)	15·51 (13·99–17·04)	3·10 (2·78–3·39)	2·85 (2·09–4·14)	4·69 (4·09–5·37)	4·70 (4·10–5·37)	4·67 (4·09–5·37)	67·63 (65·38–73·42)
Middle East and north Africa	10·43 (9·18–12·42)	12·44 (10·86–14·89)	9·79 (8·15–12·08)	2·26 (2·02–2·49)	2·25 (1·87–3·13)	4·55 (4·24–4·92)	3·15 (2·93–3·43)	5·88 (5·49–6·35)	41·05 (38·28–46·25)
Latin America and the Caribbean	7·95 (7·40–8·75)	9·06 (8·41–10·00)	7·26 (6·60–8·08)	1·26 (1·20–1·34)	1·56 (1·44–1·76)	5·01 (4·84–5·22)	2·54 (2·45–2·66)	7·40 (7·16–7·70)	31·70 (30·70–33·39)
East Asia and the Pacific	7·29 (6·71–8·09)	7·55 (6·86–8·52)	7·46 (6·69–8·36)	1·55 (1·35–1·77)	1·39 (1·06–2·02)	2·51 (2·16–2·96)	1·88 (1·60–2·23)	3·08 (2·66–3·62)	27·45 (26·21–29·50)
Eastern Europe and central Asia	5·03 (4·68–5·56)	6·02 (5·42–6·81)	5·53 (4·94–6·55)	1·01 (1·00–1·03)	1·18 (1·14–1·23)	2·52 (2·47–2·58)	1·78 (1·74–1·83)	3·23 (3·16–3·29)	21·12 (20·38–22·54)
High-income countries*	2·74 (2·60–2·91)	2·69 (2·57–2·81)	1·98 (1·88–2·08)	0·45 (0·44–0·46)	0·55 (0·51–0·59)	1·71 (1·65–1·78)	1·07 (1·03–1·11)	2·32 (2·24–2·41)	10·08 (9·86–10·33)
Global	13·87 (13·55–15·43)	17·48 (16·61–18·97)	20·57 (18·93–22·26)	3·83 (3·63–4·02)	2·90 (2·67–3·57)	4·89 (4·67–5·24)	4·15 (3·94–4·46)	5·59 (5·36–5·97)	62·02 (60·63–65·60)

Data from UN Inter-agency Group for Child Mortality Estimation.[20,21,24] Mortality rates, and the corresponding 90% uncertainty intervals, are expressed in the unit of deaths per 1000 population at the beginning of each age group and who are subject to risk of dying in that group. The mortality rate for the 15–19 age group was disaggregated by sex using the sex ratio in central death rates from the UN WPP2019[76] and standard life table approaches. *High-income countries are listed in the appendix (pp 9–10).

Table 1: **Global and regional all-cause mortality rates by age in 2019**

10·7 million babies were estimated to have been born SGA and had low birthweight, with 11·2 million babies born SGA but with a birthweight of at least 2500 g.[29] Infants who are preterm or have growth-restriction at birth have an increased risk of death (including those who are SGA but weigh ≥2500 g),[19,30] reduced linear growth,[31] and increased risk of poor development.[7]

A 2019 estimate suggests that 20·47 million (90% uncertainty range 17·37–24·02) livebirths were low birthweight in 2015.[32] About half of the world's low birthweight babies were born in south Asia (9·81 million [26·8%] of 37·15 million total births in south Asia had low birthweight). The number of low birthweight babies born in south Asia is almost double the number born in sub-Saharan Africa (5·00 million birth [4·35–6·15]; appendix p 24). Progress in reducing low birthweight rates is too slow to reach the global nutritional target of a 30% reduction by 2025.[33] Between 2000 and 2015 the AARR was 1·2%, but an AARR of 2·7% was required to meet the 30% reduction target.

Regional differences in height and body-mass index (BMI) from birth to 20 years

Globally the prevalence of stunting in children younger than 5 years has declined from 203·6 million (33·1%) of 615·7 million in 2000 to 149·2 million (22·0%) of 677·9 million in 2020.[34] However, regional differences persist with the highest rates occurring in south Asia.

The age patterns in height and BMI in children younger than 5 years were assessed with the latest national Demographic and Health Survey or Multiple Indicator Cluster Survey done since 2010 in low-income and middle-income countries (LMICs). Mean length or height and mean BMI were calculated for each month of age and these results were used to calculate regional means as the average of countries in the region weighted by the population of children younger than 5 years (appendix p 25). Additionally, local polynomial approximations were used to produce smoothed graphs of mean length (appendix pp 26–29) or height and BMI (appendix pp 30–33) by age and sex.[35]

For the **weighted average** see https://www.population.un.org

For 5–19-year-olds (including all individuals up to their 20th birthday) the regional growth trajectories were derived from a pooled analysis of measured height and weight data from 2081 population-based surveys that included a total of 65 million participants.[36] Data were pooled using Bayesian hierarchical models to estimate mean height and BMI by country, year, sex, and single year of age, including weighting by national populations to produce regional averages. The statistical model incorporated non-linear time trends and changes with age to represent the adolescent growth spurts.

Patterns of linear growth from birth to the 20th birthday vary substantially by world region. Mean lengths or heights from birth to 5 years were compared with the international growth standard.[37] For both females and males, the mean length in cm at birth was close to the standard (figure 3), but the mean length-for-age Z scores already showed evidence of growth faltering in early infancy (appendix pp 26–29). From later in infancy until 5 years there was substantial variation in the mean heights by region with the highest linear growth in eastern Europe

For the **Demographic and Health Survey** see https://dhsprogram.com

For the **Multiple Indicator Cluster Survey** see https://mics.unicef.org

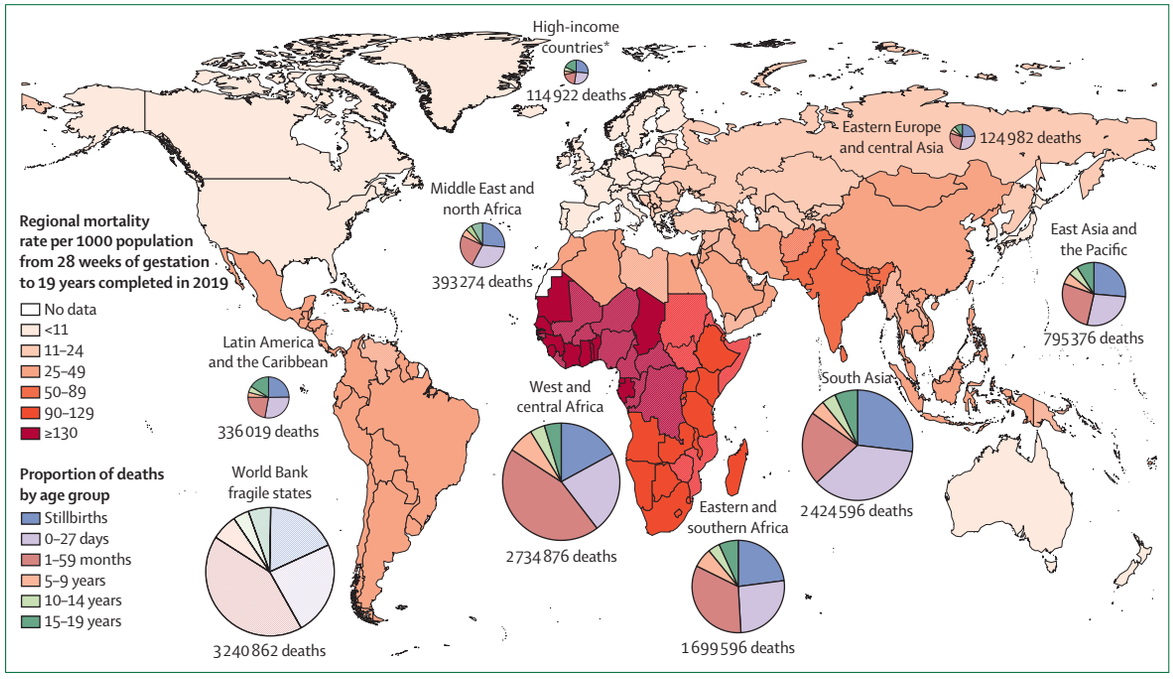

Figure 2: **Regional mortality rates and age-specific proportion of deaths from 28 weeks of gestation to 19 years in 2019**
Data from UN Inter-agency Group for Child Mortality Estimation.[20,21,24] Data to reproduce this figure available in table 1 and the appendix (pp 4, 6). Fragile states are represented by broken colours and identified according to the World Bank definition.[27] *High-income countries are listed in the appendix (pp 9–10).

and central Asia and the lowest in south Asia. Despite the different data sources and analytical methods for the two age ranges, the regional curves were very similar when they come together at 5 years. From 5 years to about 12 years the increases in mean height were largely parallel in all regions, continuing a pattern of growth from the starting points (figure 3). During the pubertal growth period from 13 years there was some regional variation with females and males in eastern Europe and central Asia having accelerated growth resulting in catching up to those in HICs by 19 years. Adolescents in Latin America and the Caribbean have an earlier plateau in height, around the age of 13 years. By 19 years the mean heights of females and males vary substantially by world region and country (appendix pp 34–35). One should note that although growth in utero and during the first 5 years after birth are similar in well nourished populations around the world,[38,39] this has not been shown for growth from 5–19 years.

The BMIs of females and males increased from birth to about 12 months in all regions, but they varied substantially: the highest BMIs were reported in Latin America and the Caribbean and the lowest in south Asia (figure 3). From 12 to 59 months, mean BMI in Latin America and the Caribbean and eastern Europe and central Asia exceeded the WHO standard, whereas mean BMI was far below the WHO standard in south Asia (appendix pp 32–35). From 5 to 19 years, females' BMI increased more than the WHO reference in HICs, Latin America and the Caribbean, and the Middle East and north Africa, whereas females in south Asia continued to have substantially lower average BMI (figure 3). Except for those in south Asia, west and central Africa, and eastern and southern Africa, by 19 years, males in most world regions had a mean BMI that exceeded the WHO reference, reflecting increased adiposity. Mean BMI for 19-year-old females and males varied substantially by region and country (appendix pp 36–37).

Nutritional status of adolescent females is important not only for their own health, but for the health and survival of their offspring. Short stature is associated with small pelvic size and increased risk of intrapartum stillbirths, and underweight is associated with poor fetal growth and low birthweight[40] resulting in intergenerational transmission of undernutrition and poor health outcomes. Conversely, increased adiposity in both females and males increases the risk of nutrition-related non-communicable diseases in adulthood.[41]

Disability in children and adolescents

Disabilities beginning in childhood are a global concern with important effects on human capital; of note, they are not included in the Human Capital Index.[3] Many disabilities can be prevented or their adverse consequences mitigated by environmental adaptation, rehabilitation, corrective services, and supportive families and workplaces. From a nurturing care perspective, providing services to prevent or mitigate the consequences of disabilities advances equity. Underlying differences in the health conditions leading to disabilities and in societal

responses to disabilities result in substantial variation in their prevalence across world regions and consequences for individuals and their societies.

In LMICs the highest rates of years lived with disability for children and adolescents are in Africa and south Asia, and are lower in HICs, although the rates for the older adolescents are more similar across regions.[42] Using broad categories of causes, the largest share of disabilities globally are undernutrition for children and mental disorders and substance use for adolescents.[42] Considering disabilities with long-term impairments (excluding nutritional conditions and infections) in children younger than 20 years, the five most prevalent in 2019 were migraine, injuries, hearing impairment, asthma, and dermatitis.[43]

Educational measures and human capital

Global enrolment in primary schools has improved significantly over the past two decades, with increases in global literacy. However, school enrolment is not a good indicator of learning, and children in LMICs experience challenges in attaining literacy and numeracy.[44] An indicator of the knowledge, skills, and problem-solving abilities obtained through education is often included in human capital indices, measured through test performance or grade attainment.[45] Test performance is an indicator of cumulative learning influenced by environmental context, including school quality. Tests, such as the Programme for International Student Assessment, measure student knowledge and skills.[46] Grades of formal school attained is used as a proxy for learning for the population aged 15 years and older.[47] Attainment of higher grades in adolescents is often interpreted as indicating potential for future national economic growth.[45]

To incorporate both grade attainment and test performance into a single indicator, Filmer and colleagues[48,49] developed the learning-adjusted years of schooling (LAYS) indicator. The LAYS indicator adjusts the average number of grades attained for a given population to reflect the average learning acquired. Using scores on the Programme for International Student Assessment and the Trends in International Mathematics and Science Study, each country is compared with Singapore, a high-performing country. Each country's mean grade attainment by age cohort is then adjusted on the basis of their relative learning performance. For example, the average years of grade attainment for Chile (11·7 grades) is adjusted downwards to 8·1 LAYS.[48]

LAYS are used in the World Bank Human Capital Index to estimate population-level adjusted grades of schooling by sex for countries and world regions (figure 4). However, the information on the distribution of scores within countries, by factors such as geography, income, parental schooling attainment, and language, might be even more important to understanding educational quality and equity. Consistent with the principles of the Nurturing Care Framework, educational attainment can compensate for some factors, such as low socioeconomic status,[50] and the potential for compensation is even higher when school quality is considered, as has been shown in Pakistan[51] and elsewhere. Thus, LAYS might be useful in examining how grade attainment, and investments in school quality, can compensate for individual disparities, including early adversities.[52]

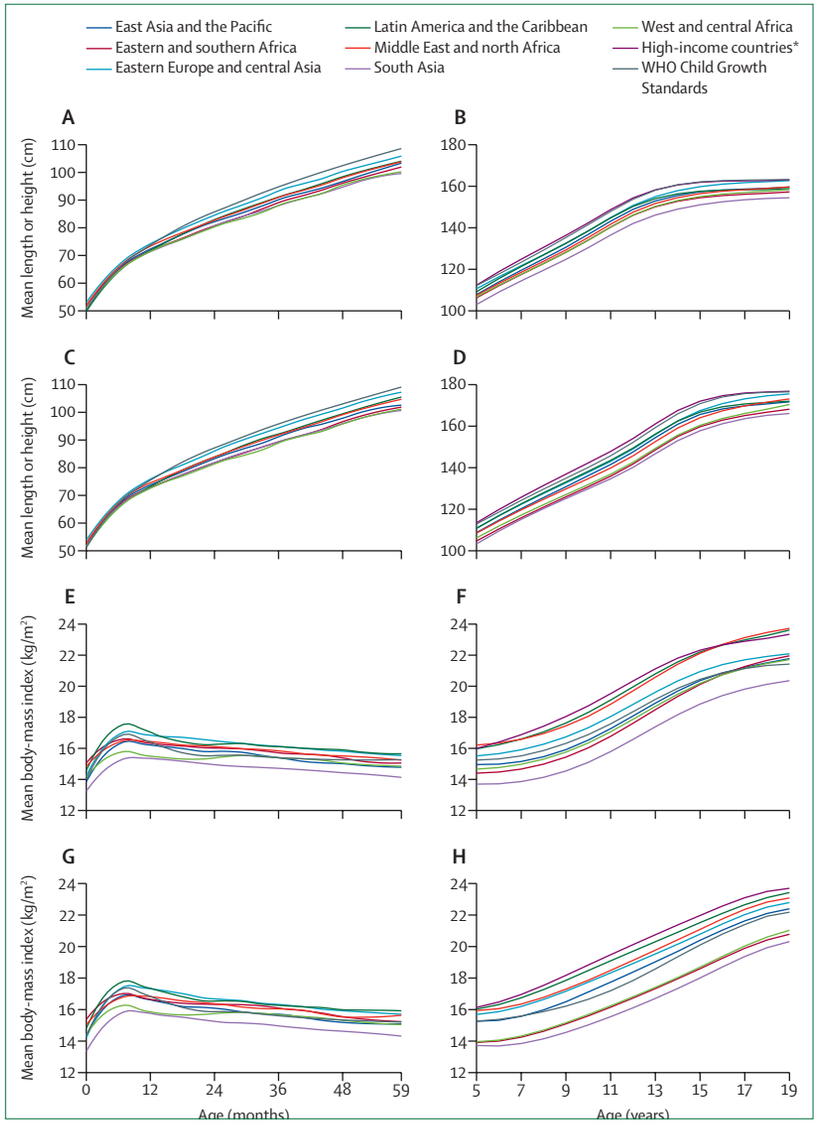

Figure 3: **Mean length or height and body-mass index for females and males from birth to 19 years by world region**

Mean length or height for 0–59-month-old females (A), 5–19-year-old females (B), 0–59-month-old males (C), and 5–19-year-old males (D), and mean body-mass index 0–59-month-old females (E), 5–19-year-old females (F), 0–59-month-old males (G), and 5–19-year-old males (H). Data sources were Demographic and Health Survey, Multiple Indicator Cluster Survey, and the Non-Communicable Disease Risk Factor Collaboration.[36] *High-income countries are listed in the appendix (pp 9–10).

Life course analysis related to human capital

To illustrate the associations of some dimensions of early life to adult human capital, we analysed data from

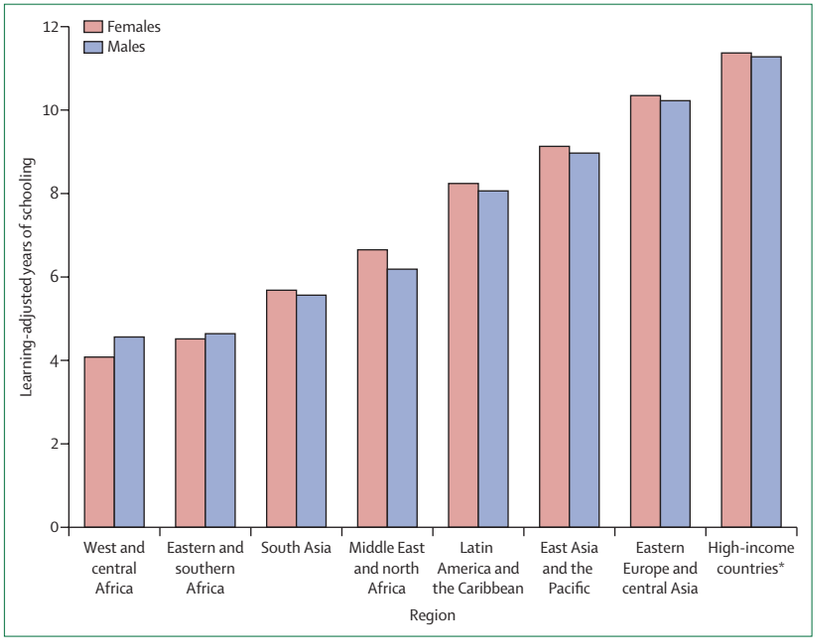

Figure 4: **Learning-adjusted years of schooling by world region**
Adapted from Filmer and colleagues.[49] *High-income countries are listed in the appendix (pp 9–10).

the COHORTS consortium, which includes six LMIC population-based birth cohorts with at least 20 years of follow-up and more than 1000 participants each. Two are from Brazil, and one each are from Guatemala, India, the Philippines, and South Africa.[53] Available human capital outcomes in adulthood included height, completed school grades, intelligence, overweight or obesity, metabolic signs (eg, abdominal adiposity and raised blood pressure), and psychological symptoms (appendix pp 38–41).

The analyses addressed two questions. The first was how important is tracking from birth to adulthood when considering variables in the same domain? These results are highlighted table 2. One Z score increase in birth length was associated with an increase in adult height by 1·7 cm; for conditional length at 2 years (reflecting growth from birth to 2 years) the difference was 3·3 cm; and for height at 4 years (reflecting growth from 2 to 4 years), the corresponding difference was 2·3 cm, consistent with the importance in predictions of the first 1000 days from conception until the second birthday and a smaller predictive role of growth in later childhood (appendix pp 42–44). One Z score higher weight at birth was associated with an adult overweight prevalence ratio of 1·07; one Z score higher BMI at 2 years was associated with an adult overweight prevalence of 1·15; and a one Z score higher BMI at 4 years was associated with an adult overweight prevalence of 1·19 (appendix pp 42, 44). Previous COHORT studies described tracking in height and in adiposity.[54–56] One Z score difference in the developmental quotient at 4 years was associated with 7·3 intelligence quotient (IQ) points in adulthood, consistent with literature from HICs (appendix pp 42, 45).[57,58]

The second question was how well do early growth and development predict a broader range of adult human capital outcomes? The results are adjusted for family early-life socioeconomic position, parental education, and other confounding variables (table 2; appendix pp 38–41). Birth length and weight and conditional length at age 2 years were strongly positively associated with adult intelligence and schooling, but this was not the case for conditional height at 4 years, nor for adult height. These results suggest that linear growth up to the age of 2 years—but not later in childhood or during adolescence—is predictive of schooling and IQ in these cohorts, confirming previous results.[59–62] Cognitive development in childhood was positively associated with schooling. Also consistent with earlier COHORT findings, birthweight was positively associated with adult intelligence and schooling, but this was not the case for relative weights at any age. On the contrary, there were weak inverse associations of conditional relative weights at 2 and 4 years with attained schooling. The strong predictive power for early-life anthropometric measures in the COHORTS studies is also consistent with evidence suggesting that most of the structural and functional development of the brain takes place up to the age of 2 years, and that brain maturation that occurs after this age is much slower.[63] The only long-term randomised trial on the topic found an effect of nutritional supplementation before, but not after, 36 months of age on adult intelligence in both sexes[64] and on income for adult men.[65] Additionally, trials of nutritional interventions suggest a greater benefit on adult cardiometabolic outcomes if they are done in early versus late childhood.[41] Although the COHORTS results reported here and separately[62] are observational, the sum of the available evidence suggests a causal role for good early nutrition on adult outcomes, including human capital.

In addition to being strongly and positively associated with all weight-derived indicators throughout the life course, the prevalence of adult overweight or obesity was positively associated with birth length and conditional length at 4 years. The number of metabolic syndrome signs was positively associated with con-ditional relative weight at 2 years, 4 years, and in adulthood, as earlier analyses had shown.[66] Moreover, consistent with the literature,[67] frequency of mental illness symptoms in adults was inversely associated with cognitive developmental scores in childhood.

Differences between the sexes were examined, but they were observed only for the association of conditional length at 2 years with metabolic syndrome, with a stronger association for males than for females. However, this might be due to multiple testing because only one of 56 interaction tests was statistically significant. Several associations showed heterogeneity across cohorts, but this was mostly in magnitudes rather than the directions of the estimates.

These results are consistent with substantial tracking in linear growth and in intellectual development from early childhood to adulthood. The positive associations of linear growth with intelligence, learning, and schooling are strongest up to the age of 2 years.[62] Analyses of other LMICs cohorts found that growth later in childhood or adolescence also has some predictive power for cognitive function (appendix p 46).[68–71] Our results are also suggestive that early-life adiposity is predictive of adult overweight and of signs of metabolic illnesses. Studies of cohorts in high-income countries, such as New Zealand, show the importance of early-life adiposity and risk of cardiometabolic disease and mortality in adulthood and the association of adversities, such as maltreatment, in early childhood with adult mental health and chronic diseases (appendix pp 47–48).

Conclusions

Human capital encompasses the skills, knowledge, experience, and health of individuals and collectively of populations. The World Bank has highlighted the importance of human capital for global societal and economic development[3] and created the Human Capital Index to monitor national progress.[1] The Human Capital Index includes survival for children to 5 years and for adults from 15 to 60 years, thriving operationalised as healthy growth in the first 5 years of life, and the quantity and quality of education. Others have developed an index of human capital focused on adult mortality, educational attainment, and adult functional health and correlate this with national economic growth.[72] Our analyses, similar to the Human Capital Index, focus on the life course determinants of human capital before adulthood and suggest consideration of loss of life and undernutrition both before birth and for all children and adolescents, along with indicators of overweight and disabilities. We examine how key contributors to human capital differ by world regions and document the key periods of the life course for the optimal development of human capabilities and formation of human capital.

The probability of death from birth to 5 years of age is a commonly used indicator of human capital and the progress of countries. We propose instead the probability of death from the third trimester of pregnancy to the 20th birthday, an age range in which there were 8·6 million deaths in 2019. Regional disparities were large with mortality in west and central Africa 14-times higher than in HICs. These differences were largely due to complications of pregnancy and delivery, and high rates of acute lower-respiratory infections, diarrhoea, malaria, and other infections in the higher mortality regions.[23] Undernutrition is an underlying factor in 45% of deaths in children under 5 years of age, increasing the risk of death from infectious diseases; it also especially effects adolescent mothers through cephalopelvic disproportion and anaemia in childbirth.[73]

	Height (cm)		Intelligence quotient (harmonised units)		Attained schooling (grades attained)		Overweight and obesity (prevalence ratio)		Metabolic syndrome (number of signs)		Mental illness (number of symptoms)	
	Regression coefficient	p value	Regression coefficient	p value	Regression coefficient	p value	Prevalence ratio	p value	Ratio of averages	p value	Regression coefficient	p value
Height												
Birth length	1·68 (1·52 to 1·84)*	<0·0001	0·73 (0·35 to 1·10)	0·0002	0·17 (0·07 to 0·27)†	0·0010	1·05 (1·01 to 1·08)	0·0050	1·00 (0·97 to 1·03)	0·90	−0·06 (−0·29 to 0·17)†	0·60
Conditional length at 2 years	3·34 (3·06 to 3·63)*†	<0·0001	1·52 (0·96 to 2·08)†	<0·0001	0·25 (0·10 to 0·40)†	0·0010	1·01 (0·95 to 1·07)†	0·75	1·05 (0·97 to 1·15)†‡	0·24	−0·01 (−0·16 to 0·13)	0·86
Conditional height at 4 years	2·30 (2·03 to 2·58)*†	<0·0001	0·16 (−0·47 to 0·78)	0·63	0·09 (−0·03 to 0·20)†	0·15	1·05 (1·01 to 1·08)	0·0060	1·03 (0·99 to 1·07)†	0·14	−0·03 (−0·18 to 0·13)	0·75
Conditional height at adulthood	4·19 (3·80 to 4·59)*†	<0·0001	0·05 (−0·91 to 1·00)†	0·94	−0·05 (−0·24 to 0·14)†	0·63	0·90 (0·86 to 0·95)†	<0·0001	0·97 (0·93 to 1·02)	0·31	−0·10 (−0·23 to 0·04)	0·18
Weight												
Birthweight	1·07 (0·95 to 1·19)	<0·0001	0·74 (0·35 to 1·14)	0·0002	0·13 (0·08 to 0·19)	<0·0001	1·07 (1·05 to 1·09)*†	<0·0001	1·00 (0·98 to 1·02)	0·96	−0·04 (−0·14 to 0·06)	0·46
Conditional relative weight at 2 years	−0·14 (−0·44 to 0·15)*†	0·34	−0·26 (−1·21 to 0·69)†	0·59	0·05 (−0·03 to 0·13)	0·23	1·15 (1·12 to 1·18)*†	<0·0001	1·06 (1·02 to 1·11)†	0·0040	−0·05 (−0·59 to 0·48)†	0·84
Conditional relative weight at 4 years	−0·24 (−0·54 to 0·06)*†	0·12	−0·19 (−0·69 to 0·32)	0·47	−0·09 (to 0·18 to −0·01)	0·038	1·19 (1·12 to 1·25)*†	<0·0001	1·08 (1·02 to 1·14)†	0·0080	−0·02 (−0·13 to 0·10)	0·76
Conditional relative weight at adulthood	−0·10 (−0·25 to 0·04)	0·17	0·04 (−0·50 to 0·58)†	0·88	−0·13 (−0·26 to −0·01)†	0·035	1·59 (1·49 to 1·69)*†	<0·0001	1·40 (1·28 to 1·53)†	<0·0001	0·03 (−0·29 to 0·35)†	0·85
Cognitive development (4·0–8·5 years)	0·77 (0·54 to 0·99)	<0·0001	7·30 (5·85 to 8·76)*†	<0·0001	0·82 (0·47 to 1·16)†	<0·0001	1·02 (0·96 to 1·08)	0·58	0·97 (0·91 to 1·03)	0·33	−0·17 (−0·32 to −0·03)	0·021

Data are regression coefficients (95% CI). *Tracking result (results for which the early life variable and the adult outcome are in the same domain [eg, birth length and adult height]) †Significant heterogeneity (ie, Cochran's Q test p<0·05) between cohorts. ‡Significant interaction (ie, interaction test p<0·05) between the sexes.

***Table 2:* Summary of association results between early-life variables and adult outcomes**

Growth and development before adulthood are crucial for human capital, and conditions before conception and in utero are important for a healthy start in life. Low birthweight—a consequence of fetal growth restriction, preterm delivery, or both—is a global problem, but the prevalence of low birthweight in South Asia was nearly double that in sub-Saharan Africa.[32] In the first 5 years after birth, gains in height in LMICs were lower than the WHO growth standard, with the lowest gain in heights reported in south Asia. Between 5 and 12 years, the gains in height were largely parallel across regions, but there was more variation in trajectories between 13 and 19 years. Elevated mean BMI in comparison with the WHO reference began in many regions in the preschool period and continued into adolescence. The highest mean BMI values were in HICs, the Middle East and north Africa, and Latin America and the Caribbean. Conversely, low BMI values through adolescence were found in south Asia. These analyses are based on historical cross-sectional data and might not reflect current growth trajectories if living conditions have changed rapidly.

The analyses of the COHORTS data show that there was strong tracking of size from birth to adolescence. Of the measures of size examined, birth length and growth from birth to 2 years were the strongest predictors of adult height. The association between BMI at 4 years and adult overweight and metabolic disease also suggest the importance of the early childhood in predicting adult health should be considered more strongly in human capital metrics. The importance of nurturing care from preconception through early childhood for human capital formation is shown by the finding that linear growth in the first 2 years of life was a very strong predictor of schooling, learning, and adult IQ.

Nurturing care provides a conceptual framework for our analysis, adopting a life course perspective from preconception through adolescence, highlighting developmental periods that are vulnerable to adversity and sensitive to interventions, and focusing on opportunities that promote equity, resilience, and human capital. Education, beginning during the preprimary school period and extending through secondary school and beyond, plays a crucial role in the accrual of human capital. The absence of quality education is particularly concerning because it most commonly occurs in regions with the highest rates of other early-life adversities (eg, south Asia and sub-Saharan Africa). Consistent with the Nurturing Care Framework, responsive caregiving and learning experiences can mitigate adversities.

Human capital depends on children surviving and thriving throughout their life course, with the first 1000 days following conception especially important, a crucial period of formative development. Investments to promote human capital should begin before conception and support healthy growth and development through adolescence by environments that promote health and nutrition, protect from threats, and provide opportunities for learning and responsive care and relationships.

The SDGs for children are aspirational but resonate with both nations and families. Achieving them, already challenging, will be set back by the COVID-19 pandemic and the resulting economic crisis.[74,75] Achieving the SDGs will need more investment, but would result in a greater return in human capital.

Contributors

REB conceptualised and coordinated the analyses, wrote the first draft of the paper, responded to reviewer comments, and incorporated all revisions until publication. MMB wrote the Nurturing care and human capital section. MMB and AG wrote the section on education. DYo, LH, and BM provided information on stillbirths and mortality. LL, FV, JP, DYe, SC, and REB analysed the UN-Inter-agency Group for Child Mortality Estimation mortality data and contributed the cause-of-death information. FV contributed the map with regional mortality estimates. EB provided the analysis of child mortality in fragile and conflict countries in Africa. HB and JEL contributed on preterm, low birthweight, and stillbirths. LPV and CGV contributed the analyses of height and body-mass index in children younger than 5 years. AR-M and ME contributed the analyses of height and body-mass index in 5–19-year-olds. FPH, CGV, and REB contributed the COHORTS analyses. ADS, RM, and CO advised on statistical analyses. LSA, CHDF, BH, AMBM, MR-Z, and LMR provided the COHORTS data. JB contributed the Young Lives Panel. TV and MMB contributed the Dunedin panel. GP and ZAB provided overall guidance and comments on draft manuscripts. All authors read the final draft and approved submission for publication. REB had full access to all data and final responsibility for the decision to submit for publication.

Declaration of interests

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Optimising Child and Adolescent Health and Development 2

Effects of early-life poverty on health and human capital in children and adolescents: analyses of national surveys and birth cohort studies in LMICs

Cesar G Victora, Fernando P Hartwig, Luis P Vidaletti, Reynaldo Martorell, Clive Osmond, Linda M Richter, Aryeh D Stein, Aluisio J D Barros, Linda S Adair, Fernando C Barros, Santosh K Bhargava, Bernardo L Horta, Maria F Kroker-Lobos, Nanette R Lee, Ana Maria B Menezes, Joseph Murray, Shane A Norris, Harshpal S Sachdev, Alan Stein, Jithin S Varghese, Zulfiqar A Bhutta, Robert E Black

The survival and nutrition of children and, to a lesser extent, adolescents have improved substantially in the past two decades. Improvements have been linked to the delivery of effective biomedical, behavioural, and environmental interventions; however, large disparities exist between and within countries. Using data from 95 national surveys in low-income and middle-income countries (LMICs), we analyse how strongly the health, nutrition, and cognitive development of children and adolescents are related to early-life poverty. Additionally, using data from six large, long-running birth cohorts in LMICs, we show how early-life poverty can have a lasting effect on health and human capital throughout the life course. We emphasise the importance of implementing multisectoral anti-poverty policies and programmes to complement specific health and nutrition interventions delivered at an individual level, particularly at a time when COVID-19 continues to disrupt economic, health, and educational gains achieved in the recent past.

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Introduction

Massive inequalities in the distribution of wealth, both between and within countries, are a key challenge to sustainable development.[1] Despite progress in the alleviation of poverty in most parts of the world over the past three decades, wealth inequalities still exist, and several low-income countries have seen the incomes of the bottom 40% stagnating, or even decreasing.[2,3] In a time trend analysis of 83 countries, the global average Gini index—weighted by national population size—increased from 36·7 in 2000 to 40·8 in 2015. This finding indicates that the average person was living in a country where inequality was on the rise.[4]

Addressing inequality is at the core of the Sustainable Development Goals[5] target of leaving no one behind.[6] Economic inequality is not only important per se, but it is also a major driver of health status, as is emphasised by initiatives aimed at tackling the social determinants of health.[7] In addition to how the poorest communities are at increased risk of illness and malnutrition, inequality affects the health of entire populations. Social gradients in health are ubiquitous, with stepwise increases in illness and mortality down the socioeconomic spectrum.[8]

There is ample literature on the effect of poverty during the life course in high-income societies. Birth cohort analyses, from countries such as the UK, New Zealand, USA, and Norway, point to the lifelong effects of material and psychosocial exposures on health and human capital.[9] By contrast, the literature from low-income and middle-income countries (LMICs) on such topics is scarce. Nevertheless, many (if not most) children currently living in LMICs experience suboptimal nurturing care,[10,11] an innovative concept that encompasses child health, nutrition, learning, relationships, security, and safety. These five components of nurturing care are largely determined by poverty; a "cause of the causes"[12] of poor health and development. Exposure to adversity in early life,[9,13] for which poverty is a proxy measure, is postulated

Search strategy and selection criteria

For analyses of the associations between poverty and health, nutrition, and development outcomes in children and adolescents, we searched the comprehensive Countdown to 2030 survey database, which is also included in WHO's Health Equity Monitor website. The Countdown to 2030 database includes over 450 publicly available demographic and health surveys from over 120 countries. We identified 440 nationally representative surveys with publicly available data from 127 countries, from which we selected all surveys done between 2010 and 2019 with information on household socioeconomic position and the indicators for children and adolescents required for our analyses. 95 countries had these surveys and were included in the analyses.

Analyses of the associations between early-life poverty and outcomes in adulthood were based on collaborative data collection of six birth cohorts from low-income and middle-income countries. In 2006, in preparation for the 2008 *Lancet* Maternal and Child Undernutrition Series, we carried out a systematic search of large long-term, prospective birth cohort studies in LMICs with information on early life and adult variables. We excluded studies with fewer than 1000 subjects or with poor methodological quality. Only five studies qualified for the original pooled analyses. In 2021, a sixth study was included when the 1993 birth cohort study from Pelotas, Brazil, completed 18 years of follow-up. The six studies provided the data for the present analyses.

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Key messages

- Data from low-income and middle-income countries (LMICs) substantiate the negative effects of early-life poverty on the survival, nutrition, and cognitive development of children and adolescents
- Analyses of long-term birth cohorts in LMICs show that early-life poverty is strongly and inversely associated with human capital indicators, such as adult height, achieved schooling, and intelligence
- By contrast, some risk factors for non-communicable diseases, including overweight and signs of metabolic syndrome in adults, are less common in men, but not in women, exposed to early-life poverty than in the rest of the population
- Broad and multisectoral anti-poverty policies and programmes need to be urgently strengthened to offset the impact of COVID-19 on poverty and to promote the health and development of children and adolescents, both in the short term and long term

to be a major driver of adequate nurturing care and of its consequences on human capital.

The first paper in this Series used evidence from longitudinal studies to consider conditions of survival, growth, disability, and education in world regions and their effects on crucial periods in the lifecycle before adulthood that build the foundation for human capital.[11] In this second Series paper, we review data on key conditions related to human capital in children, adolescents, and adults, and analyse how early-life poverty contributes to their enduring prevalence throughout the life course. Using data from 95 national surveys in LMICs, we assess the presence and magnitude of social gradients in the health, nutrition, and cognitive development of children and adolescents, reflecting the accrual of human capital. Additionally, we use data from six large, long-running birth cohorts in LMICs to explore the long-term associations between early-life poverty and health and human capital outcomes in adulthood. In both sets of analyses, we use indicators related to the constructs of nurturing care and of human capital, including survival, health, nutrition, and cognition. We also report on selected conditions that affect an individual's ability to contribute to society, including stunted height[14] and obesity[15] in adulthood, teenage motherhood,[16] and psychological symptoms.[17] This information informs consideration of interventions, intersectoral approaches, and policies, which are addressed in the third[18] and fourth[19] papers of this Series.

An analysis of 95 national surveys

The analyses of national surveys addressed the following five outcomes related to human capital in children and adolescents: mortality rate and prevalence of growth stunting in children younger than 5 years, not being on track for development in children aged 3–5 years (based upon the Early Childhood Development Index),[20] teenage motherhood (the proportion of women aged 20–29 years who had become mothers before age 20 years), and completion of primary school in girls aged 15–19 years. Teenage motherhood was included as a human capital indicator because it is associated with poor linear growth and with attained schooling, in not only mothers but also their children.[21–23]

National surveys with individual-level information on these outcomes and on household-level socioeconomic position, dated 2010 or later, were available for 95 LMICs. These countries included 28 (90%) of 31 low-income countries, 37 (79%) of 49 lower-middle-income countries, and 30 (50%) of 60 upper-middle-income countries. The median date for the surveys was 2014 (IQR 2013–2016). Details on the surveys, indicator definitions, and countries included in the analyses are available in the appendix (pp 1–8).

Table 1 shows the median slope index of inequality (SII) values for each of the five outcomes, comparing across country income groups. Countries were arranged using the World Bank classification at the time of the survey,[24] with all estimates weighted by the number of children younger than 5 years in each country as of 2015.[25] Four of the five outcomes show the highest prevalence in low-income countries and lowest prevalence in upper-middle-income countries, with intermediate prevalence in lower-middle-income countries. The exception is teenage motherhood, which is frequent in some upper-middle-income countries with large populations, such as Mexico, Angola, South Africa, and Iraq. Spearman correlation coefficients for national-level associations with log gross domestic product per capita were negative and highly significant for all five outcomes. The full correlation matrix is available in the appendix (pp 9–109).

Additionally, we investigated the magnitude of inequalities within each country. Stratification by deciles produce more granular results than does breakdown by quintiles, and sample sizes for most national surveys allow for this more detailed analysis.[26] Analyses were done separately for each country (appendix pp 11–13). National results were then aggregated by world regions using the UNICEF classification,[27] with countries weighted by the number of children younger than 5 years or adolescents (aged 10–19 years) in 2015.[25] Results are presented as equiplots, in which each marker corresponds to the value of the outcome in each decile. The SII was calculated for each region; this index represents the slope, or beta statistic, of a regression of the outcome on the household wealth variable. SII might be interpreted as the difference between the richest and poorest extremes of wealth distribution, expressed in deaths per 1000 live births for mortality and in percentage points for the other four outcomes. For

	Mortality rate, deaths per 1000 live births*†	Prevalence of growth stunting, percentage points†	Not-on-track development, percentage points‡	Teenage motherhood, percentage points§	Incomplete primary schooling, percentage points¶
Number of countries with available data	78	86	62	88	94
Country income group					
Low-income					
Median (IQR)	86·7 (75·1–98·3)	36·0 (33·2–38·9)	38·7 (34·8–42·7)	50·4 (45·9–54·8)	18·5 (10·4–26·6)
Number of countries	27	27	20	28	28
Lower-middle-income					
Median (IQR)	57·9 (49·9–65·8)	35·9 (33·4–38·4)	31·9 (26·7–37·1)	34·1 (30·0–38·1)	11·3 (6·4–16·1)
Number of countries	35	34	20	37	37
Upper-middle-income					
Median (IQR)	37·3 (25·4–49·3)	16·3 (12·5–20·2)	18·0 (15·1–20·8)	34·7 (29·7–39·7)	2·3 (0·9–3·6)
Number of countries	16	25	22	23	29
Log per capita GDP					
Correlation coefficient	−0·703	−0·667	−0·778	−0·617	−0·626
p value	<0·0001	<0·0001	<0·0001	<0·0001	<0·0001
Gini index					
Correlation coefficient	−0·148	−0·334	−0·375	−0·411	0·070
p value	0·22	0·0025	0·044	0·0001	0·56

Estimates were weighted by the number of children younger than 5 years in each country, as of 2015. GDP=gross domestic product. *Deaths in the 10 years preceding the date of the survey. †Assessed in children aged <5 years. ‡Assessed in children aged 36–59 months. §Assessed as the proportion of women aged 20–29 years who had become mothers before age 20 years. ¶Assessed in girls aged 15–19 years.

Table 1: **Population-weighted slope index of inequality values for child and adolescent outcomes and Spearman correlation coefficients with national GDP per capita and Gini index for income distribution**

detrimental outcomes, SII values tend to be negative, indicating a decrease with increasing wealth (appendix pp 14–15). The SII is not a simple difference between prevalence or mortality in the wealthiest and poorest deciles, but a regression-based difference between the top and the bottom of the wealth scale.

The national Gini index for income distribution was inversely correlated with the SII for growth stunting, not being on track for development, and teenage motherhood (table 1), indicating that a larger inequality in income was associated with wider inequalities in these three adverse outcomes. Correlations between the Gini index and the mortality rate for children younger than 5 years or incomplete primary schooling were weak and non-significant. The full correlation matrix is shown in the appendix (p 10). Limitations of correlation analyses include potential bias introduced by missing data (although missing data are infrequent in most surveys) and by uncertainty in outcome measures. We opted not to adjust for confounding factors because both independent variables were deemed to be distal determinants of health and human capital outcomes, and we wanted to avoid adjustment for mediating factors.

In relation to inequalities within each country, all SII values were negative, substantiating inverse associations between the five outcomes and family wealth (table 2). For example, the mortality rate for children younger than 5 years in west and central Africa was 85·7 deaths per 1000 live births lower for children at the top of the wealth scale than for those at the bottom, and the corresponding difference in prevalence of growth stunting was 35·9 percentage points. Further details on the SII values and full results are presented in the appendix (pp 8, 14–15).

There were clear gradients in the mortality rate in children younger than 5 years by wealth decile in all regions, with the widest absolute gaps observed in west and central Africa, south Asia, and east Asia and the Pacific (table 2; figure 1). The SII, expressing the difference in the number of deaths per 1000 live births between the upper and lower ends of the wealth spectrum, ranged from −25·3 in Latin America and the Caribbean to −85·7 in west and central Africa (table 2). Comparing across regions, the mortality rates for children younger than 5 years ranged from 9·3 deaths per 1000 live births in the wealthiest decile in eastern Europe and central Asia to 132·0 deaths per 1000 live births in the second poorest decile in west and central Africa, a 14-times difference (appendix p 14). For benchmarking purposes, the mortality rate for children younger than 5 years in western Europe is currently estimated to be four deaths per 1000 live births,[28] which is lower than the rate in even the richest deciles in this analysis.

Gradients in prevalence of growth stunting were present in all regions, with the SII ranging from −6·6 percentage points in eastern Europe and central Asia to −35·9 percentage points in west and central Africa (figure 1). Different inequality patterns were observed in the two regions of sub-Saharan Africa (where

	West and central Africa	Eastern and southern Africa	Middle East and north Africa	Eastern Europe and central Asia	South Asia	East Asia and the Pacific	Latin America and the Caribbean
Mortality rate in children aged <5 years, deaths per live births							
SII	–85·7	–26·2	–25·7	–26·2	–58·6	–54·4	–25·3
p value	<0·0001	<0·0001	<0·0001	<0·0001	<0·0001	<0·0001	<0·0001
Prevalence of growth stunting in children aged <5 years, percentage points							
SII	–35·9	–24·5	–12·3	–6·6	–35·8	–27·3	–25·8
p value	<0·0001	<0·0001	<0·0001	0·0003	<0·0001	<0·0001	<0·0001
Not-on-track development in children aged 36–59 months, percentage points							
SII	–30·6	–21·4	–10·1	–5·4	–23·6	–11·7	–12·2
p value	<0·0001	<0·0001	<0·0001	0·0005	<0·0001	<0·0001	<0·0001
Teenage motherhood, percentage points*							
SII	–47·3	–43·0	–30·1	–13·4	–34·9	–36·2	–42·6
p value	<0·0001	<0·0001	<0·0001	<0·0001	<0·0001	<0·0001	<0·0001
Incomplete primary schooling in girls aged 15–19 years, percentage points							
SII	–41·6	–22·9	–23·7	–0·7	–33·0	–4·7	–3·0
p value	<0·0001	<0·0001	<0·0001	0·0003	<0·0001	0·018	<0·0001

SII=slope index of inequality. *Teenage motherhood was assessed as the proportion of women aged 20–29 years who had become mothers before age 20 years.

Table 2: **Population-weighted SII values for child and adolescent outcomes**

inequality was largely driven by lower prevalence in the wealthiest decile than in the rest of the population), compared with the patterns observed in the regions of east Asia and the Pacific, and in Latin America and the Caribbean (where inequality was mostly driven by higher prevalence in the poorest decile relative to all other deciles). Across regions, stunting prevalence showed a ten-times difference, ranging from 5·5% in the wealthiest decile in Latin America and the Caribbean to 54·4% in the poorest decile in south Asia. In a well nourished population, around 2·5% of children would be classified as having stunted growth based on the normal distribution,[29] a prevalence that is well below those described in table 2 for any decile.

Data on early child development were available for 66 countries (figure 1), with national surveys that applied the Early Childhood Development Index (appendix p 7).[20] There were marked socioeconomic inequalities in most regions, with inverse associations between family wealth and developmental delays. Compared with 19·8% in the wealthiest decile, 48·8% of children in the poorest decile across west and central Africa presented developmental delays, with the SII equalling –30·6 percentage points. In the Middle East and north Africa and in Latin America and the Caribbean, prevalence of these delays did not decrease monotonically with growing wealth; however, inverse associations were significant (SII –10·1 percentage points for the Middle East and north Africa and –5·4 percentage points for Latin America and the Caribbean). Across the world's regions, prevalence of developmental delays ranged from 7·0% in the wealthiest decile in east Asia and the Pacific to 48·8% in the poorest decile in west and central Africa, a seven-times difference.

Four outcome indicators were also analysed by sex. In most regions, boys were more likely to die, have stunted growth, and present developmental delays than were girls. Similar findings on mortality[30] and stunting[31] have been reported previously. Data on schooling for both sexes were available for 56 countries. In south Asia and in west and central Africa, boys were more likely to have completed primary school than were girls; however, this was not the case for the remaining regions (appendix p 16).

In all regions, girls from poor families were the most likely to become teenage mothers (figure 1D). The widest gap was in west and central Africa, where frequency of teenage motherhood in the poorest decile was 67·2% and that in the wealthiest decile was 21·4%. The narrowest gap was observed in eastern Europe and central Asia, where overall frequency of teenage motherhood was the lowest of all regions, ranging from 23·6% in the poorest decile to 9·4% in the wealthiest decile. Across regions, frequency of teenage motherhood ranged from 5·7% in the wealthiest decile in east Asia and the Pacific region to 67·2% in the poorest decile in west and central Africa, a 12-times difference.

Except in regions where primary schooling was universal or nearly so (figure 1)—including eastern Europe and central Asia, Latin America and the Caribbean, and east Asia and the Pacific—there were substantial gaps in education for girls according to wealth. In west and central Africa, the proportion of girls who did not complete primary education ranged from 44·0% in the poorest decile to 5·7% in the wealthiest decile. In south Asia, the corresponding range was 35·0% to 1·9%.

The analyses of national surveys have limitations. First, deciles are relative rather than absolute measures of

socioeconomic position. The poorest decile in a given country might correspond, in terms of absolute wealth, to the third or fourth decile in a low-income country. However, relative poverty is as important in predicting deprivation[32] and health status[33] as is absolute poverty. Second, weighted results are heavily influenced by countries with large populations, such as India; however, unweighted results would give each country (eg, Nigeria and São Tomé and Príncipe) equal weights in the west and central Africa region. Third, there are data gaps in terms of countries that do not have standardised surveys from 2010 onwards, including half of upper-middle-income countries, such as China and Brazil. Finally, although the early indicator for child development used in national surveys is not sufficiently validated, it has proven to be useful for comparing groups of children, as opposed to comparing individual children.[34]

Previous analyses of child mortality,[35] nutritional status,[36,37] and development[34,38] used stratification by wealth quintiles rather than deciles, with the exception of an analysis of growth stunting that included surveys up to 2013.[26] Use of deciles has shown distinctive social gradients in these three outcomes within every region of the world, particularly in the two sub-Saharan Africa regions and in south Asia. By contrast, the narrowest gaps were found in eastern Europe and central Asia, which had the lowest prevalence for all outcomes.

Additionally, use of deciles has allowed us to identify groups at particularly high risk. In east Asia and the Pacific, children in the poorest decile were at substantially higher risk of mortality, growth stunting, and developmental delay than those in the second poorest decile. The same finding was observed for growth stunting in Latin America and the Caribbean. In the two sub-Saharan African regions, children in the poorest four deciles or so had similar levels of risk for most outcomes, indicating that the widespread poverty in this region affects a large proportion of their populations.

Effects of women's empowerment

Early-life poverty is a comprehensive indicator of early child adversity,[13] for which plentiful data are available. Family wealth is used as the main marker for early-life adversity in our analyses; however, there are other important dimensions of adversity, including women's empowerment, which is associated with mortality rates

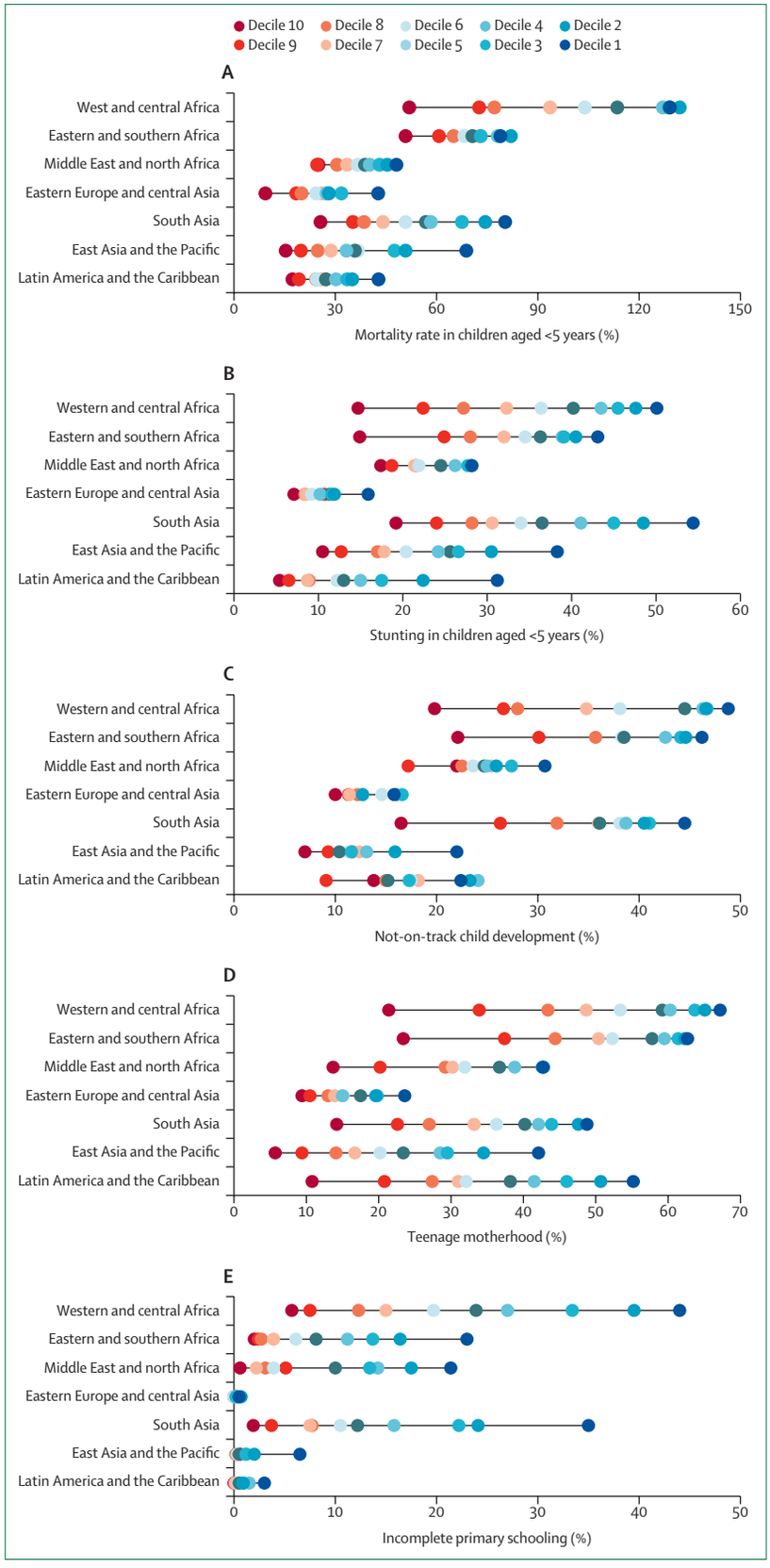

Figure 1: **Child and adolescent indicators according to wealth deciles by world region**

Data taken from 95 national surveys performed between 2010 and 2019. Indicators include mortality rate (A) and prevalence of growth stunting (B) in children younger than 5 years, not-on-track development in children aged 36–59 months (C), teenage motherhood in women aged 20–29 years who had become mothers before age 20 years (D), and incomplete primary schooling among girls aged 15–19 years (E). Wealth by decile is presented in decreasing order from decile 10, representing the wealthiest decile, to decile 1, representing the poorest.

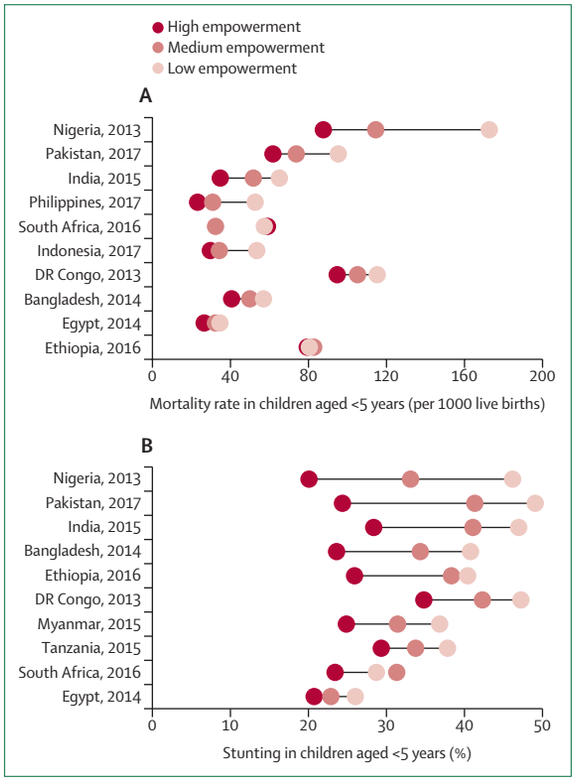

Figure 2: **Associations between women's empowerment and child indicators in the ten most populous countries with available data**
Indicators include the mortality rate (A) and prevalence of growth stunting (B) in children younger than 5 years.

and prevalence of growth stunting in their children younger than 5 years (figure 2).

We used the Survey-based Women's emPowERment (SWPER) global index[39] to categorise women in terciles according to their level of empowerment, and correlated these terciles with mortality and prevalence of growth stunting in their children in the ten most populous countries with available data (figure 2). We opted to use the social independence domain of the SWPER score because it is more closely associated with child health outcomes than are the other two domains—namely, attitudes towards violence and decision making.[39] Growth stunting and mortality in children younger than 5 years were selected as the outcomes because large numbers of countries have data available.

Social independence reflects a woman's level of educational attainment, frequency of reading information (ie, newspapers or magazines), age at first childbirth, and age at first cohabitation, as well as differences in educational attainment and age between a woman and her partner (appendix p 8). In nearly all countries studied, there were stepwise increases in mortality and prevalence of growth stunting in children younger than 5 years as maternal empowerment decreased.

Our findings represent a likely effect of the level of maternal empowerment on mortality in children younger than 5 years, which is consistent with published results on women's empowerment and child mortality in 59 countries.[40] Furthermore, these findings show that similar, if not stronger, associations exist between the level of maternal empowerment and prevalence of growth stunting in offspring. Interventions aimed at empowering women have an important role in improving the health and nutrition of their children.

Analyses of six birth cohort studies

To assess how strongly exposure to early-life poverty predicted adult health and human capital outcomes in LMIC contexts, we reanalysed data from the six longest-running births cohorts in LMICs, the COHORTS consortium, which had at least 1000 participants at recruitment and frequent visits in early life (table 3).[41] All cohorts were population-based, yet socioeconomic inequality was less marked in the urban poor cohort from Soweto, South Africa, and in the rural poor cohort from Guatemala than in the other four settings.

Information on early-life socioeconomic position was based on family income in Cebu, Philippines; Delhi, India; and Pelotas, Brazil, in the 1982 and 1993 cohorts, and on asset indices in Guatemala and Soweto. Quintiles rather than deciles were used in the analyses because of sample size limitations. All analyses were stratified by sex. Details on the samples, variables, and analytical methods are available in the appendix (pp 17–19).

The first step was to verify whether the social patterns for child length and development, which were measured in the 1990s or earlier in each cohort, were consistent with the results from the survey analyses. Length measures were taken during early childhood (age 1·0–2·0 years) and height was measured in middle childhood (age 4·0–8·5 years). Different child development scales were used in each site at age 4·0–8·5 years and were converted into cognitive quotient Z scores, with a mean of 0 (SD 1) in each site (appendix p 18).

The SII was calculated to express the difference in outcome measures between the upper and lower ends of the scale of socioeconomic position (table 3). In all cohorts with data, results were consistent with the national survey analyses, showing important social gradients in child height and development (appendix pp 20–22). The SII values suggest that social gradients were widest in Pelotas and Delhi, intermediate in Cebu and Soweto, and narrowest in Guatemala.

Indicators were selected to cover different components of human capital—namely, health, nutrition, and intelligence, for which data were available for adults from most or all cohorts at ages ranging from 22 years to 57 years (appendix p 17). Outcomes included height, years of schooling, intelligence quotient, teenage motherhood, psychological symptoms (using the Self-Reported Questionnaire scale), prevalence of overweight or obesity (body-mass index ≥25 kg/m²), and the number of signs of

	Men						Women					
	Cebu	Delhi	Guatemala	Pelotas (1982)	Pelotas (1993)	Soweto	Cebu	Delhi	Guatemala	Pelotas (1982)	Pelotas (1993)	Soweto
Desirable outcomes												
Length at age 2 years, Z score												
SII	1·01	1·73	0·53	1·80	1·51	0·81	0·56	1·68	0·47	1·6	1·07	0·66
p value	<0·0001	<0·0001	0·0033	<0·0001	<0·0001	<0·0001	<0·0001	<0·0001	0·0073	<0·0001	<0·0001	<0·0001
Height at age 4 years, Z score												
SII	0·65	1·5	0·35	1·68	1·16	0·71	0·56	1·64	0·44	1·49	0·94	0·36
p value	<0·0001	<0·0001	0·016	<0·0001	<0·0001	<0·0001	<0·0001	<0·0001	0·0022	<0·0001	<0·0001	0·0013
Cognitive quotient at age 4·0–8·5 years, Z score												
SII	0·80	..	0·28	1·24	0·98	0·98	0·58	..	0·28	1·44	1·00	0·43
p value	<0·0001	..	0·057	<0·0001	<0·0001	<0·0001	<0·0001	..	0·036	<0·0001	<0·0001	0·0044
Adult height, cm												
SII	3·1	4·2	4·3	6·8	5·0	2·3	1·9	3·1	1·5	5·4	3·0	-0·9
p value	<0·0001	<0·0001	<0·0001	<0·0001	<0·0001	0·018	0·0021	0·0005	0·0404	<0·0001	<0·0001	0·32
Achieved schooling, years												
SII	3·7	4·7	1·9	6·5	3·6	0·3	1·7	3·7	2·0	8·0	2·9	0·4
p value	<0·0001	<0·0001	0·0005	<0·0001	<0·0001	0·18	<0·0001	<0·0001	<0·0001	<0·0001	<0·0001	0·035
Adult intelligence, intelligence quotient points*												
SII	13·2	..	4·8	22·1	20·5	9·8	6·9	..	4·7	24·8	16·0	6·9
p value	<0·0001	..	0·054	<0·0001	<0·0001	<0·0001	0·0019	..	0·0070	<0·0001	<0·0001	0·0023
Undesirable outcomes												
Teenage motherhood, percentage points												
SII	..	..	..	..	..	..	11·7	6·8	2·4	–39·6	–24·9	..
p value	..	..	..	..	..	..	0·063	0·057	0·72	<0·0001	<0·0001	..
Psychological symptoms, number of symptoms												
SII	–0·4	..	0·5	–1·1	–1·1	0·2	0·8	..	0·6	–2·6	–1·4	0·6
p value	0·28	..	0·31	<0·0001	<0·0001	0·73	0·099	..	0·26	<0·0001	<0·0001	0·40
Prevalence of overweight or obesity, percentage points												
SII	30·4	26·7	5·9	11·6	20·7	14·5	17·3	9·0	–10·4	–16·2	–18·3	1·3
p value	<0·0001	0·0008	0·48	0·0050	<0·0001	0·0092	0·016	0·37	0·060	<0·0001	<0·0001	0·84
Metabolic score, number of signs												
SII	–0·3	0·5	–0·1	0·2	0·1	0·1	0·1	0·2	–0·3	–0·2	-0·4	-0·2
p value	0·10	0·049	0·59	0·0402	0·54	0·29	0·42	0·48	0·078	0·0059	<0·0001	0·24

Values represent the difference in the outcome between the wealthiest and poorest ends of the socioeconomic distribution of households. SII=slope index of inequality.
*Normalised score (mean 100 [SD 15]).

Table 3: **SII values for health, nutrition, and human capital outcomes according to early-life poverty**

metabolic syndrome. More information on definitions and tests used are available in the appendix (p 18).

Positive significant social gradients in height were found in all six cohorts for men and in five cohorts for women, with Soweto as the exception (table 3; figure 3). Similar gradients were observed for attained schooling in the six cohorts for women and in five cohorts for men, again except for Soweto where there was little variability in this indicator (mean 11·7 years [SD 1·5]). Intelligence results were available in all cohorts except for in Delhi, showing positive social gradients in all studies. Of note, the SII value for men from Guatemala had a significance level of p=0·0537.

Social gradients for teenage motherhood, prevalence of overweight or obesity, number of metabolic signs, and number of psychological symptoms were not clear (table 3; appendix pp 23–26). Both cohorts in Pelotas showed inverse social gradients for teenage motherhood, yet results were not significant for the other cohorts. Number of psychological symptoms was inversely related to wealth in men and women from Pelotas, but again not in the other cohorts.

Prevalence of overweight and obesity tended to be directly associated with wealth in men in five cohorts, and metabolic signs showed a similar social patterning in men from the Delhi cohort and the Pelotas 1982 cohort. By contrast, prevalence of overweight and obesity and number of metabolic signs were inversely and significantly associated with wealth in both cohorts of women from Pelotas. In the cohort from Guatemala,

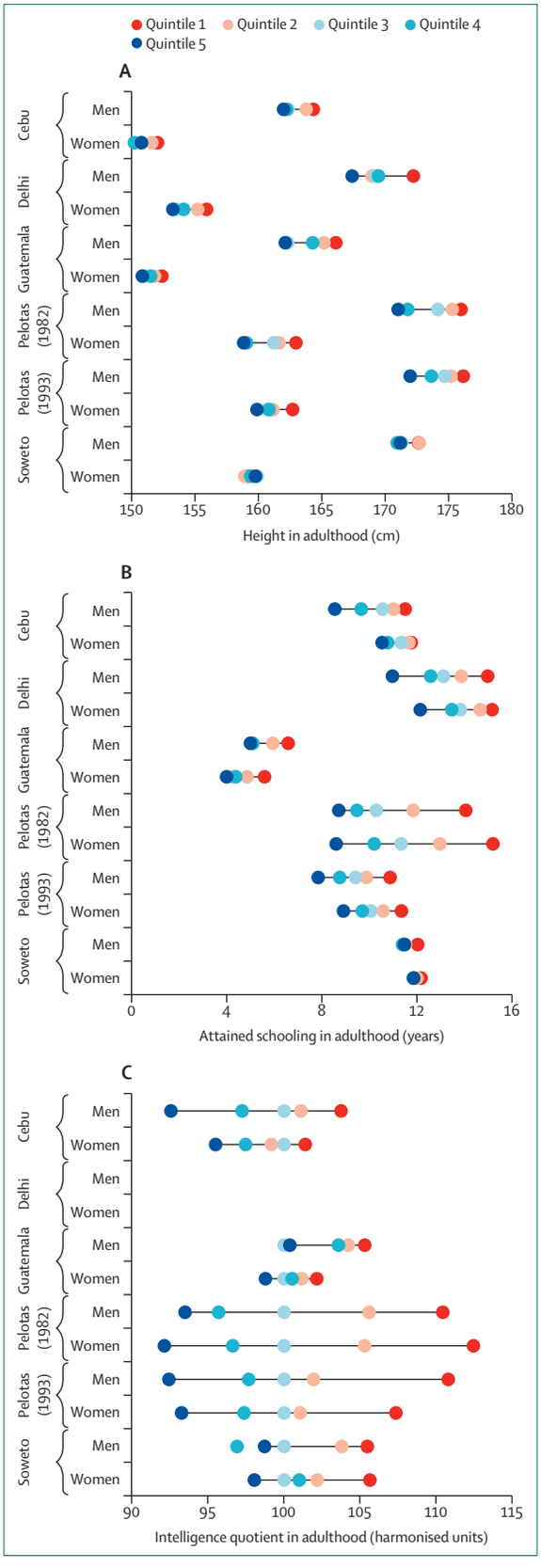

Figure 3: **Distribution of adult indicators by wealth quintile in the six birth cohorts**
Indicators include height (A), attained schooling (B), and intelligence quotients (C) in adulthood in both men and women. Wealth by quintile is presented in increasing order from quintile 1, representing the poorest quintile, to quintile 5, representing the richest.

there were borderline inverse associations with overweight and obesity (p=0·06) and for metabolic signs (p=0·08). In Cebu, prevalence of overweight and obesity was directly associated with wealth in men and women.

Additional evidence on the effects of early-life poverty is provided by the Young Lives study,[42] which included cohorts of children from Ethiopia, India, Peru, and Vietnam recruited at age 6–18 months. A social gradient in growth stunting was present at recruitment and persisted until the final measurement at age 12 years.[43] Similar social gradients were present for the children's vocabulary, from first measurement at age 5 years to final measurement at age 12 years.[43] Trajectory analyses based on measurements at age 1–15 years showed that high wealth quartiles were protective against trajectories of stunting; however, high wealth and urban residence quartiles predicted trajectories of overweight.[44]

A limitation of our analyses is that we used either income or asset indices to measure poverty on the basis of available data from each cohort. Although both indicators are closely related, their constructs are different. For most variables, socioeconomic gaps were wider in the two cohorts from Pelotas than in other sites. These gaps were likely to be due to the remarkable scale of income inequality in Brazilian society and to how both cohorts covered the whole population of a city. In 1982 and 1993, average income in the richest quintile was 12 or more times higher than in the poorest quintile. The larger sample sizes for both Pelotas cohorts also increased the likelihood of obtaining statistically significant differences. The selective nature of some cohort samples was made evident by a comparison of results of national surveys with those from the cohorts in the same country. For example, the survey in Guatemala showed remarkably wide inequality in growth stunting in children (appendix p 11), whereas there was relatively little inequality in the cohort from four rural villages (table 3).

There were instances of heterogeneity in the magnitude and sometimes the direction of associations between early-life poverty and adult outcomes. It is reassuring that for key outcomes, such as height, schooling, and intelligence, results were highly consistent; however, this was not the case for the indicators of morbidity. Like all long-term cohorts, particularly in LMICs, losses to follow-up can be substantial.[41] Of note, the median age of cohort members at the most recent follow-up ranged from 22 years in the 1993 Pelotas cohort to 57 years in Guatemala, a difference that should be taken into account when considering outcomes, such as prevalence of overweight and obesity, number of psychological symptoms, and number of metabolic signs. In addition, metabolic signs included five separate indicators and future analyses are required to reach conclusions on their causes. Furthermore, our analyses on early-life poverty did not consider socioeconomic trajectories, and there is evidence that adult outcomes might differ between individuals whose socioeconomic position

remains the same and those whose socioeconomic position improves over time.[45]

Conclusions and implications

Our analyses provide considerable documentation of pervasive social gradients in the survival, health, nutrition, and cognitive development of children, as well as in teenage motherhood and in girls' education. The analyses of 95 national surveys confirmed the importance of gross domestic product in predicting levels of the five outcomes under study. Within countries, we were able to document consistent, stepwise social gradients in human capital indicators in children and adolescents from LMICs. Of the 35 analyses of five outcomes in seven world regions, 30 (86%) showed at least a doubling of the risk of the detrimental outcome in the poorest decile compared with the richest decile, and in 17 (49%) comparisons, the ratio was more than three times higher. Furthermore, the magnitude of inequality in child mortality, nutrition, and development was positively associated with the degree of economic inequality in each country. These analyses substantiate that children and adolescents are being gravely affected by socioeconomic inequality between and within countries.

Results from six large population-based birth cohorts in five LMICs substantiate that the effects of early-life poverty are—for the most part—persistent, generating wide gaps in health and human capital across the life course. Linear growth and cognitive development in early life showed well defined social gradients in all cohorts. These outcomes, measured between the 1970s and 1990s, support our findings from national surveys. As cohort participants became older, social gradients varied according to the type of outcomes. Indicators related to a narrower definition of human capital, such as the one adopted by the World Bank,[46] including survival, growth, schooling, and intelligence, showed clear positive gradients in virtually all analyses by cohort and sex. Some differences were striking; for example, intelligence quotient was around 20 points higher in individuals at the top of the wealth scale than in those at the bottom in the two cohorts from Pelotas. As reported in the first paper in this Series,[11] and supported by the national survey analyses in this second Series paper, social gradients in cognition are already present in young children (aged <5 years). Although differences in the length and quality of schooling are likely to play a key role, many factors in the environment that disadvantaged children face, starting in gestation, contributes to their underperformance.[10]

By contrast, adult outcomes reflecting a broader definition of human capital, which also incorporates physical and mental health, did not present such clear results. There were inverse social gradients for teenage motherhood and psychological symptoms in the cohorts from Pelotas, but not in the other cohorts. The negative effect of early-life poverty on mental health, at least in some settings, could be an important mechanism for intergenerational transmission of poverty by affecting parental ability to provide nurturing care to their children.[47]

Prevalence of overweight and obesity in men tended to increase with early-life socioeconomic position in most cohorts, and similar patterns were present for metabolic signs in the two cohorts from Pelotas. In our analyses, these outcomes were the only ones that were detrimental in adults, and had the highest prevalence in the wealthiest deciles. By contrast, in women from Pelotas and Guatemala, but not Cebu, the findings for number of metabolic signs and prevalence of overweight and obesity were in the opposite direction. The literature suggests that the social patterns of overweight prevalence change as the nutrition transition progresses.[48] When undernutrition is common, men and women from wealthy deciles tend to show the highest prevalence of overweight and obesity. Over time, this pattern reverses in women, whereas the original pattern remains for men in the same population. Furthermore, when the transition is complete, both men and women show inverse social gradients.[49,50] Our findings suggest that the six cohorts could have been at different stages in the transition, with Cebu showing the traditional pattern of increasing overweight with wealth, Soweto and Delhi in a phase where there was a direct association for men but no social patterning for women, and Guatemala and Pelotas showing a direct association in men and an inverse association in women. None of the cohorts had reached the final stage in the transition when both men and women showed inverse patterns. The Sustainable Development Goals include targets related to both non-communicable diseases and human capital.[51] We have shown that, although early-life poverty is clearly detrimental for human capital, it might be paradoxically associated with a decreased risk of some chronic conditions, at least in men.

Taken together, our findings show clear and positive social gradients in the traditional outcomes of human capital (eg, attained height, intelligence, and attained schooling); mixed results for a broader set of outcomes, including teenage pregnancy and mental health; and increased risk of overweight or obesity and other metabolic conditions in men born to wealthier families. Although early-life poverty has a negative effect on most indicators of adult human capital, the social gradients can be inverted, at least regarding overweight, obesity, and signs of metabolic syndrome in men.

We observed sex differences in several outcomes, which might reflect biological differences and gender norms. In children, boys were more likely to die,[52] have growth stunting,[53] and present developmental delays than were girls,[54] which is probably due to their greater biological frailty.[55] In all but one world region, and in five of the six cohorts, girls had higher schooling than did boys, which is a common finding in many countries and probably reflects gender norms associated with the early

entry of boys in the labour market and possibly with compliance with school discipline.[56] In terms of adult outcomes, as found in studies from many parts of the world, women presented more psychological symptoms than did men in all cohorts. This finding is attributed to a combination of higher levels of stress experienced by women and reluctance to report mental health difficulties in men.[57,58] Furthermore, in five of the cohorts, men in the wealthiest decile had the highest prevalence of overweight and obesity, whereas the reverse was observed in women in three cohorts.

Without a considerable reduction in social disparities, particularly in countries with high poverty and inequality, the world is unlikely to meet the Sustainable Development Goal of ending extreme poverty by 2030. Although global poverty has decreased since 1990,[3] most of the world's population nowadays is likely to live in an economy with higher inequality than they did 25 years ago.[4] In addition, national levels of inequality were more widely variable around the global mean in the past than they are now, as highly unequal countries become more equal, and more egalitarian countries become less so.[4] The health effects of socioeconomic inequality are likely to be felt worldwide.

Our findings should be interpreted in conjunction with the results of the other papers in this Series.[11,18,19] In particular, the third Series paper[18] reviews effective interventions within the health and nutrition sectors aimed at improving human capital. It also reviews broader intersectoral interventions aimed at social determinants, which are supported by the findings presented here showing how early-life poverty shapes the development of human capital. Achieving high and effective coverage with specific interventions is essential, and their effect will be complemented and amplified by broader anti-poverty interventions, including conditional and unconditional cash transfers, minimum wage policies, child benefits, and universal health care. Our analyses are intended to contribute to policies and programmes aimed at reducing poverty and promoting equity through targeting interventions at children and adolescents who are currently being left behind.

Early-life poverty affects children within a context that is increasingly defined by war and conflict,[59] global inequality,[7] climate change,[60] disparities between ethnic groups,[61] and damaging gender norms.[62] On top of such pre-existing threats, interactions between the COVID-19 syndemic and social determinants[63] have resulted in the exacerbation of socioeconomic inequalities, thus threatening recent, albeit modest, progress in the health and education of children and adolescents. The challenges that children of today will confront during their life course are unparalleled. A fair start in life is essential to ensure that all children are optimally enabled to face these global challenges.

Contributors

CGV conceptualised and coordinated the analyses, prepared the first draft of the paper, responded to reviewer comments, and incorporated all revisions until publication. REB, ZAB, ADS, RM, and LMR contributed to the conceptualisation and overall guidance of the analyses and writing of the report. FPH, LPV, AJDB, and CO contributed to the data analyses. The main investigators of the COHORTS consortium—including LSA, FCB, SKB, BLH, MFK-L, NRL, AMBM, JM, SAN, HSS, ADS, AS, and JSV—provided the data. All authors have reviewed and approved the final version of the manuscript. CGV had full access to all the data in the study and final responsibility for the decision to submit for publication.

Declaration of interests

REB serves on the Board of Vitamin Angels, a non-profit charitable organisation supporting maternal and child nutrition services in LMICs. AS and ADS report grants from Bill and Melinda Gates Foundation. AS reports grants from the Wellcome Trust. ZAB reports grants from the International Development Research Centre (reproductive, maternal, newborn, child, and adolescent health in conflict settings: case studies to inform implementation of interventions) and Countdown to 2030–UNICEF. All other authors declare no competing interests.

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Optimising Child and Adolescent Health and Development 3

What can work and how? An overview of evidence-based interventions and delivery strategies to support health and human development from before conception to 20 years

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Progress has been made globally in improving the coverage of key maternal, newborn, and early childhood interventions in low-income and middle-income countries, which has contributed to a decrease in child mortality and morbidity. However, inequities remain, and many children and adolescents are still not covered by life-saving and nurturing care interventions, despite their relatively low costs and high cost-effectiveness. This Series paper builds on a large body of work from the past two decades on evidence-based interventions and packages of care for survival, strategies for delivery, and platforms to reach the most vulnerable. We review the current evidence base on the effectiveness of a variety of essential and emerging interventions that can be delivered from before conception until age 20 years to help children and adolescents not only survive into adulthood, but also to grow and develop optimally, support their wellbeing, and help them reach their full developmental potential. Although scaling up evidence-based interventions in children younger than 5 years might have the greatest effect on reducing child mortality rates, we highlight interventions and evidence gaps for school-age children (5–9 years) and the transition from childhood to adolescence (10–19 years), including interventions to support mental health and positive development, and address unintentional injuries, neglected tropical diseases, and non-communicable diseases.

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Introduction

More than 6 years into the Sustainable Development Goals (SDGs) period, rampant inequalities in newborn, child, and adolescent survival and ill health persist both between and within countries.[1,2] These inequities, coupled with inadequate coverage of essential and high-quality health services,[3] continue to prevent many of the world's children from surviving to adulthood and achieving their full cognitive, social, and economic potential. Although efforts made towards achieving the Millennium Development Goals (MDGs) by scaling up key interventions and strategies to improve maternal and child health and nutrition were successful, progress in many areas seems to have slowed down.[4,5] As the COVID-19 pandemic has shown,[6] many of these gains are tenuous and at great risk of backsliding.[7,8] For countries to achieve their SDGs related to child and adolescent health, concerted action is needed to scale up access to evidence-informed interventions, harness innovative delivery strategies to support older children and adolescents, and reduce inequities in coverage of key interventions.

In the third paper of this Series, a successor to *The Lancet* Child Survival Series,[9] we update and summarise the state of evidence for the effectiveness of interventions across the continuum from preconception through adolescence until the 20th birthday, with a focus on interventions that enhance human capital across the life course. Building on previous evidence syntheses related to younger children and adolescents, this Series paper also describes the repertoire of integrated interventions for gaps in this continuum, especially the missing middle (5–14 year-olds),[10,11] including school-age children and the transition to early adolescence. Such gaps also exist across other risk factors and conditions, such as gender-based violence, mental health, and other non-communicable diseases. We have generally assumed a steady state after the pandemic and do not consider interventions specific to COVID-19 mitigation and treatment.

Review of evidence-based interventions and delivery platforms across the life course

We identified a broad range of existing evidence-based strategies from overviews and systematic reviews of effective reproductive, maternal, newborn, child, and adolescent health interventions spanning preconception and pregnancy to 20 years of age. We focused on interventions with a known effect on four outcomes of interest: mortality, morbidity, growth, and development. Although we focused on evidence from low-income and middle-income countries (LMICs), evidence from relevant high-income countries (HICs) was used when LMIC evidence was scarce or absent. Interventions were selected based on feasibility of implementation in LMICs. We recognise that a large proportion of the direct and indirect gains in health, nutrition, and human capital ensue from investments outside of health and nutrition sectors, such as poverty alleviation, education, environmental health improvements, addressing gender disparities and empowerment, and reducing conflict.[12–14] These key attributes of the inter-connectedness of the SDGs will be considered in the fourth paper of this

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Key messages

- Effective, evidence-based interventions to support survival and development of newborns and children younger than 5 years exist, but need to be scaled up and linked to interventions in school-age children
- A good start is essential; early nurturing care interventions in preconception, pregnancy, childbirth, and early childhood have substantial positive effects on child survival, birth outcomes, reduced morbidity, and improved linear growth and developmental trajectories; multi-sectoral approaches are needed for optimal benefit
- This multisectorial, nurturing care approach for optimising health and wellbeing through nurturing care must continue into later childhood and adolescence; it cannot be neglected if children are to reach their full potential
- Although the evidence base for effective interventions in school-age children from systematic reviews of randomised trials in LMICs is scarce compared with children younger than 5 years, several interventions do exist (eg, universal and targeted interventions supporting vaccine uptake, injury prevention, mental health, sexual and reproductive health, and care for chronic non-communicable diseases)
- Robust health systems and key delivery platforms and strategies (eg, community, school, digital, and financial platforms) are essential to reach vulnerable mothers, children, and adolescents in greatest need

Search strategy and selection criteria

A scoping review was done initially with a compilation of all existing systematic reviews of intervention effectiveness cited in comprehensive overviews (appendix p 2). Additional focused searches of PubMed, Cochrane Library, 3ie DEP, EPPI DoPHER, and Google Scholar were done for systematic reviews, which must have synthesised the evidence for the effectiveness of an intervention targeting women of reproductive age, pregnancy, childhood, or adolescence from trials or quasi-experimental designs. The focused searches identified intervention reviews in children younger than 5, older children (aged 5–9 years), and adolescents (aged 10–19). We updated existing systematic reviews for interventions in children younger than 5 years (including preconception, pregnancy, and childbirth) and adolescents only if the most recent review on a specific intervention was done before January, 2018. For interventions targeting older children, in whom no comprehensive syntheses have been done, a series of de novo systematic reviews was done. A more detailed description of data sources and the methodology for evidence review and synthesis is outlined in the appendix (p 2).

Series. This Series paper will principally focus on what can be done within the health and nutrition sectors.

Figure 1 summarises the conceptual framework of key intervention domains and opportunities to address risk factors for child and adolescent mortality and morbidity (adapted from Disease Control Priorities 3[15,16]), with a focus on targeting the most vulnerable. Additional details on the effectiveness of the interventions described in the following sections can be found in the appendix (pp 5–54).

See Online for appendix

Preconception and antenatal care

Interventions before conception

Opportunities for optimising the health and development of children exist well before conception (table 1),[17–50] although a clear definition of what that period constitutes is unclear. Ensuring adequate access to family planning services for all women can contribute to optimising inter-pregnancy intervals and improving maternal nutritional status during pregnancy and fetal growth. Interventions to delay age at first pregnancy to prevent adolescent pregnancies can also help to improve fetal health and development and reduce the risk of complications for this vulnerable group at high risk of adverse pregnancy outcomes. Despite evidence highlighting the importance of risk factors in this period, such as obesity, mental health, and exposure to violence,[51–53] evidence from actual interventions is scarce. Optimising maternal nutrition during the early stages of fetal development is crucial, with avoidance of either obesity or undernutrition. Periconceptional folic acid supplementation can reduce the risk of neural tube defects by 47% (95% CI 33–59).[19] Care for type I and II diabetes given to women before pregnancy can reduce the risk of congenital malformations and perinatal mortality,[18] and tetanus toxoid immunisation—either before or after conception—can substantially reduce the risk of neonatal mortality.[17,22] Interventions to address mental health needs and reduce intimate partner violence are clearly important at every stage and should be considered when these risks exist.[54]

Antenatal care interventions to support maternal and fetal health

Ensuring adequate access to high-quality antenatal care in appropriate facility settings throughout pregnancy is essential to support maternal health, ensure optimal fetal growth and development, and improve birth outcomes (table 1). Integrating educational components into maternal and newborn community-based intervention packages—which include antenatal registration and care, nutrition supplementation and advice, infection prevention and management, tetanus toxoid administration, recognition of high-risk pregnancies, and treatment of underlying medical conditions—can reduce the risk of neonatal

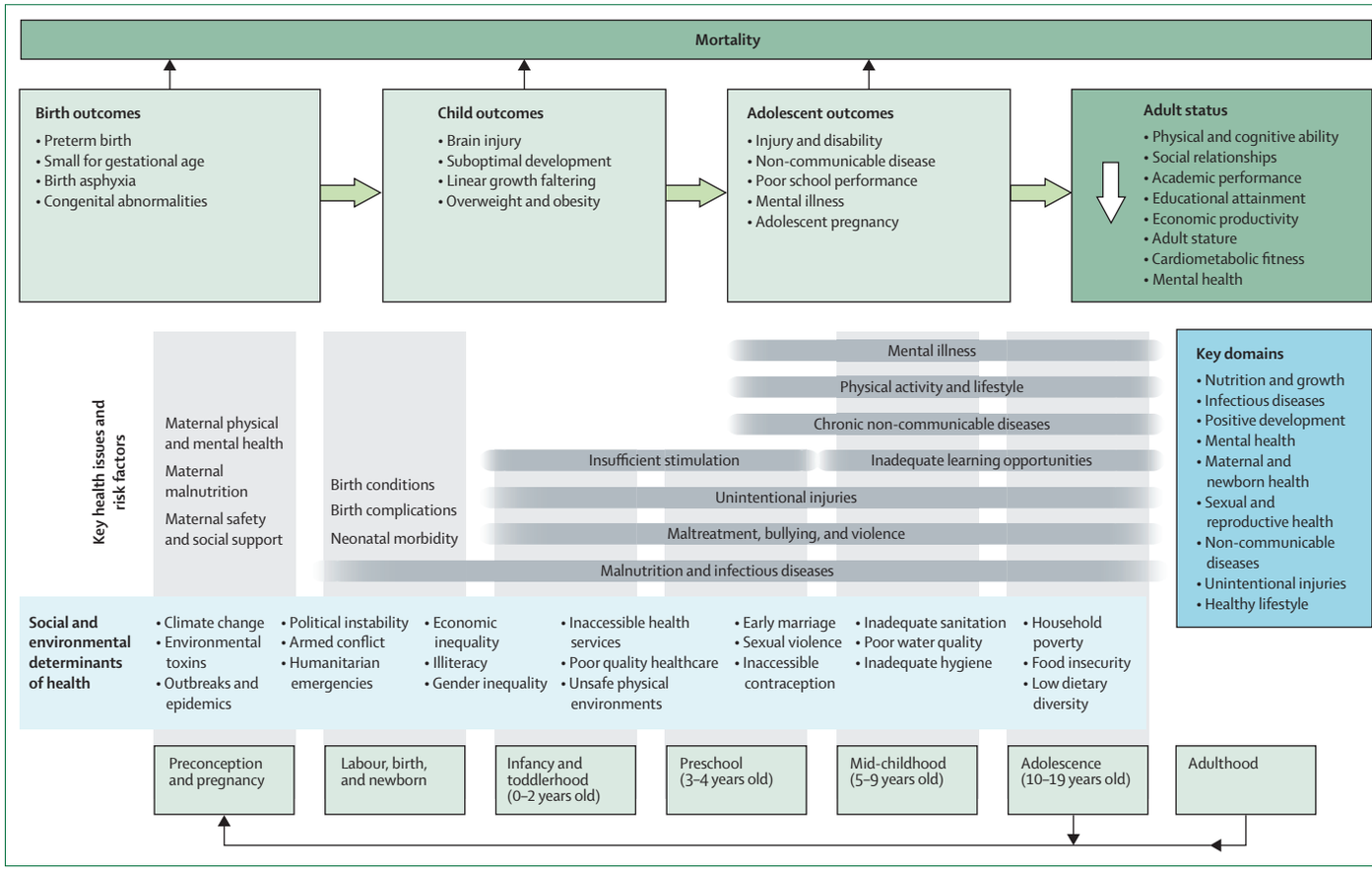

Figure 1: **Conceptual framework of risk factors and opportunities for intervention across the life course**

mortality by 13% (95% CI 4–20) and perinatal mortality by 17% (9–25).[34] Contact with the health system during pregnancy also presents opportunities to provide nutrition counselling and supplements. Antenatal iron-folic acid supplementation prevents maternal anaemia.[20] Multiple micronutrient supplementation containing iron might reduce the risk of stillbirth by 9% (95% CI 2–14) and small for gestational age birth by 7% (2–12) compared with iron-folic acid.[20] Small-quantity lipid nutrient supplements provided to healthy pregnant women in LMICs can reduce the risk of small for gestational age birth by 6% (1–11) compared with iron-folic acid alone, and balanced protein energy supplements can reduce the risk of stillbirth by 61% (20–81), perinatal mortality by 50% (16–70), and small for gestational age births by 29% (6–46; appendix p 51).[21]

Prevention and treatment of infectious diseases in pregnant women can reduce the risk of poor birth outcomes. Detecting and treating asymptomatic bacteriuria can reduce preterm birth risk by 66% (95% CI 12–87).[35] Insecticide-treated nets prevent malaria transmission; additional protection through intermittent antimalarial drug prophylaxis can reduce maternal anaemia by 17% (7–26) and placental parasitaemia by 46% (31–57), and increase birthweight (mean difference 92·7 g [62·1–123·4]).[55] Highlighting the importance of vaccination, evidence exists for an increased risk for adverse pregnancy and birth outcomes with severe maternal COVID-19 infection, which is more likely in mothers who smoke, have obesity or diabetes, or have pre-eclampsia.[56]

Complications in pregnancy can be effectively diagnosed and addressed to improve maternal and neonatal outcomes. Lifestyle interventions to manage gestational diabetes mellitus can reduce preterm birth risk by 35% (95% CI 14–51%).[57] In functioning health systems with requisite quality services, for pregnant women at high risk of complications, doppler velocimetry can help identify at-risk pregnancies requiring mitigation strategies, and reduce perinatal mortality by 29% (2–48).[58] Antithrombotic therapy for placental dysfunction can also reduce preterm birth by 26% (8–40) and perinatal mortality by 60% (22–80).[23] Although cervical cerclage might reduce the risk of preterm birth in women at high-risk,[59] given technical skills needed for execution, it should be used with caution in LMICs in comparison with other effective approaches.[60]

	Effects		Key outcomes
	Mortality	Morbidity or development	
Community-based interventions			
Preconception and periconception			
Preconception tetanus toxoid immunisation (2–3 doses)[17]	Yes	Uncertain	Neonatal mortality OR 0·28 (0·15–0·52)
Maternal prepregnancy diabetic care[18]	Yes	Yes	Perinatal mortality RR 0·57 (0·41–0·79); and congenital anomalies RR 0·30 (0·22–0·40)
Periconceptional folic acid supplementation[19]	Uncertain	Yes	Congenital anomalies RR 0·53 (0·41–0·67)
Pregnancy			
MMN supplementation *vs* iron with or without folic acid[20]	Yes	Yes	Stillbirth RR 0·91 (0·86–0·98); and small for gestational age RR 0·93 (0·88–0·98)
Balanced protein-energy supplementation[21]	Yes	Yes	Stillbirth RR 0·39 (0·19–0·80); perinatal mortality RR 0·50 (0·30–0·84); and small for gestational age RR 0·71 (0·54–0·94)
Maternal tetanus toxoid immunisation (2–3 doses)[22]	Yes	Uncertain	Neonatal mortality RR 0·32 (0·17–0·55)
Antithrombotic therapy for placental dysfunction[23]	Yes	Yes	Preterm birth RR 0·74 (0·60–0·92); and perinatal mortality RR 0·40 (0·20–0·78)
SQ-LNS *vs* iron-folic acid[20]	Uncertain	Yes	Small for gestational age RR 0·94 (0·89–0·99)
Labour and childbirth			
Clean birth kits[24]	Yes	Uncertain	Perinatal mortality OR 0·70 (0·59–0·82)
Neonatal			
Neonatal resuscitation training[25]	Yes	Uncertain	Early neonatal mortality RR 0·88 (0·78–1·00); and 28-day neonatal mortality RR 0·55 (0·33–0·91)
Kangaroo mother care *vs* standard of care for LBW newborns[26]	Yes	Uncertain	Mortality RR 0·74 (0·61–0·89); severe infection and sepsis RR 0·85 (0·79–0·92); and EBF (1–3 months) RR 1·20 (1·01–1·43)
Umbilical cord antiseptics[27]	Yes	Uncertain	Neonatal mortality RR 0·79 (0·69–0·90); and omphalitis RR 0·65 (0·56–0·75)
Effect of preventive zinc supplementation in LBW neonates for neonatal sepsis[28,29]	Yes	Uncertain	Neonatal mortality RR 0·28 (0·12–0·67)
Community-based antibiotic delivery for possible serious bacterial infections[30]	Yes	Uncertain	Neonatal mortality RR 0·82 (0·68–0·99)
Breastfeeding promotion *vs* standard of care[31]	Yes	Uncertain	Diarrhoea prevalence RR 0·76 (0·67–0·85); early EBF initiation RR 1·20 (1·12–1·28); EBF at 3 months RR 2·02 (1·88–2·17); and EBF at 6 months RR 1·53 (1·47–1·58)
Kangaroo mother care *vs* standard of care for healthy term or late preterm newborns[32]	Uncertain	Yes	Neonatal infection RR 0·68 (0·50–0·91); EBF at 1 month RR 1·26 (1·07–1·50); and EBF at 6 weeks to 6 months RR 1·41 (1·18–1·69)
Community-based intervention package for maternal and newborn health[33]	Yes	Yes	Neonatal mortality RR 0·75 (0·67–0·83); stillbirths RR 0·81 (0·73–0·91); perinatal mortality RR 0·78 (0·70–0·86); and early breastfeeding rate RR 1·93 (1·55–2·39)
Community-based maternal and newborn educational care packages for neonatal health and survival[34]	Yes	Yes	Neonatal mortality RR 0·87 (0·78–0·96); perinatal mortality RR 0·83 (0·75–0·91); Timely initiation of breastfeeding RR 1·56 (1·37–1·77)

(Table 1 continues on next page)

Interventions during labour, childbirth, and the neonatal period

Community-based interventions for labour and childbirth

Labour and birth represent a high-risk period, requiring a set of interventions to prevent maternal and perinatal mortality (table 1). Community-based intervention packages targeting women of reproductive age, pregnant women, and newborns in LMICs can improve health-care seeking behaviour for neonatal morbidities by 42% (95% CI 14–77) and improve early breastfeeding rates by 93% (55–139).[33] Subgroup analyses of community mobilisation and home visitation found that these interventions reduced stillbirth by 24% (15–32) and neonatal mortality by 40% (28–51); community support and women's groups have been shown to reduce neonatal mortality by 16% (4–27).[33] The distribution and use of clean birth kits in LMIC community settings can reduce umbilical cord infections by 58% (3–82) and the odds of perinatal mortality by 30% (18–41).[24]

Facility-based interventions for labour and childbirth

Attendance of a skilled health-care professional at birth is required to provide a safe and hygienic environment for the mother and newborn and for recognising and addressing potential complications—for which adequate access to high-quality emergency obstetric care is essential. Labour induction after 41 weeks' gestation can reduce perinatal mortality by 69% (95% CI 36–85).[39] Provision of antibiotics to mothers with preterm premature rupture of membranes can reduce neonatal infections by 34% (16–48).[42] For mothers at risk for imminent preterm birth, antenatal corticosteroids for fetal lung maturation can reduce neonatal respiratory distress syndrome by 29% (22–35), intraventricular haemorrhage by 42% (25–55), necrotising enterocolitis by 50% (22–68), neonatal mortality by 22% (13–30), and the risk of developmental delay in childhood by 49% (3–73).[38] Although a large population-based trial[61] reported the potential for antenatal corticosteroids to cause harm to mothers and newborns in LMICs, evidence from WHO ACTION-I, a multicountry randomised trial,[62] done in five LMICs, showed a significant reduction in neonatal mortality by 16% (3–28), with no evidence of harm. WHO recommends that certain conditions be met to reduce risks associated with this intervention, including imminent preterm birth, absence of maternal infection, accurate gestational age assessment, and availability of adequate childbirth and newborn care.[63] Magnesium sulfate can also provide neuroprotection to the fetus in mothers at risk of giving birth before term and has been shown to reduce risk of cerebral palsy by 32% (13–46).[40,41]

Routine interventions for all neonates

Simple, low-cost, and highly effective neonatal interventions have the potential to prevent a large proportion of child mortality during the highly vulnerable first

month after birth.[64] Prompt neonatal resuscitation is necessary when birth asphyxia occurs, and appropriate birth attendant training might reduce neonatal mortality in LMICs.[25,65] Proper cord cleansing, adequate thermal care, and promotion of early and exclusive breastfeeding should be delivered to all newborns (table 1). Delayed cord clamping (1–3 min after birth) is recommended for all neonates because it can reduce the risk of intraventricular haemorrhage by 17% (95% CI 1–30), neonatal mortality by 27% (2–46) in preterm neonates, and it might improve infant neurodevelopmental outcomes.[43] Hygienic cord care through topical application of 4% chlorhexidine reduced occurrence of omphalitis by 35% (25–44) and neonatal mortality by 21% (10–31) when used in community settings with high-risk of neonatal mortality and unclean births.[66] Incentives to promote breastfeeding, including education and support for optimal breastfeeding practices, delivered by health-care workers and telephone platforms can improve early initiation of breastfeeding by 20% (12–28).[31] Observational evidence also suggests substantial benefits of early breastfeeding initiation on neonatal survival.[67] A review of community-based delivery platforms suggests that home visits from community health workers might improve the rates of early initiation of and exclusive breastfeeding, and that peer and mother groups are effective in increasing children's dietary diversity and meal frequency.[68] The combination of home visits and group platforms are effective in improving early initiation and exclusive breastfeeding rates and children's growth outcomes.[69] More research is required to determine the mechanisms by which community groups have their effect and which enabling factors and barriers must be addressed.[70]

Home and community-based interventions for preterm, low birthweight, and ill newborns

Infants born too small or too early are an especially vulnerable group that requires special attention and care—including screening and management of serious infections—to reduce the risk of mortality and morbidity (table 1). Community-based thermal care using a plastic wrap can significantly increase neonatal core body temperatures.[69] A large trial in India found substantial reductions in infant mortality when kangaroo mother care—in which the infant is carried with skin-to-skin contact—is initiated in community settings for babies with low birthweight.[70] Evidence from both HICs and LMICs suggests topical emollient therapy with oil for preterm neonates can reduce invasive infections by 29% (95% CI 4–48) and improve weight gain (mean difference 2·93 g/kg per day [95% CI 2·11–3·76]).[49] Findings from a large community-based trial in India on the effect of sunflower seed oil to prevent invasive infections and neonatal mortality have shown a significant 52% (12–74) reduction in mortality in infants with a very low birthweight (≤1500 g).[71] In settings in which hospitalisation is not feasible, community-based provision of antibiotics for possible serious bacterial infection in newborns compared with standard hospital referral can reduce neonatal mortality.[30]

	Effects		Key outcomes
	Mortality	Morbidity or development	
(Continued from previous page)			
Facility-based interventions			
Pregnancy			
Asymptomatic bacteriuria detection and treatment[35]	Uncertain	Yes	Preterm birth RR 0·34 (0·13–0·88)
Periodontal disease management[36]	Uncertain	Yes	Low birthweight RR 0·67 (0·48–0·95)
Antenatal lower genital tract infection screening and treatment[37]	Uncertain	Yes	Preterm low birthweight RR 0·48 (0·34–0·66)
Labour and childbirth			
Corticosteroid for fetal lung maturation[38]	Yes	Yes	Neonatal mortality RR 0·78 (0·70–0·87); and developmental delay in childhood (2–12 years) RR 0·51 (0·27–0·97)
Induction of labour at or after 37 weeks[39]	Yes	Uncertain	Perinatal mortality RR 0·31 (0·15–0·64)
Magnesium sulfate for neuroprotection[40,41]	Uncertain	Yes	Cerebral palsy RR 0·68 (0·54–0·87)
Antibiotics for preterm premature rupture of membrane[42]	Uncertain	Yes	Neonatal infection RR 0·66 (0·52–0·84)
Neonatal			
Delayed cord clamping for preterm and LBW neonates[43]	Yes	Yes	Neonatal mortality RR 0·73 (0·54–0·98); and intraventricular haemorrhage RR 0·83 (0·70–0·99)
Probiotic supplementation for LBW or preterm neonates[44,45]	Yes	Yes	All-cause mortality RR 0·80 (0·66–0·96); necrotising enterocolitis RR 0·46 (0·35–0·61); neonatal sepsis RR 0·78 (0·70–0·86); all-cause mortality (very preterm or low birthweight) RR 0·76 (0·65–0·89); and necrotising enterocolitis (very preterm or low birthweight) RR 0·54 (0·45–0·65)
Therapeutic hypothermia for newborns with hypoxic ischaemic encephalopathy or asphyxia (≥35 weeks)[46]	Yes	Yes	Mortality RR 0·68 (0·59–0·79); and neurodevelopmental disability RR 0·72 (0·59–0·88)
Continuous distending pressure, prongs, and tubes for RDS in preterm infants[47]	Yes	Uncertain	Overall mortality RR 0·53 (0·34–0·83); and mortality in babies with birthweight >1500 g RR 0·24 (0·07–0·84)
Surfactant therapy for RDS in at-risk preterm neonates (<37 weeks)[48]	Yes	Yes	Mortality RR 0·89 (0·79–0·99)
Topical emollient therapy for preterm neonates (<37 weeks)[49]	Uncertain	Yes	Invasive infection (topical oil) RR 0·71 (0·52–0·96)
Prophylactic phototherapy for preterm (<37 weeks) and low birthweight neonates with jaundice[50]	Uncertain	Yes	Neurodevelopmental impairment RR 0·85 (0·74–0·99)

Data are effect estimates (95% CI). EBF=exclusive breastfeeding. LBW=low birthweight. OR=odds ratio. RDS=respiratory distress syndrome. RR=relative risk. SQ-LNS=small-quantity lipid-nutrient supplements.

Table 1: **Effects of selected interventions before and during pregnancy, labour, childbirth, and the neonatal period on key outcomes.**

	Effects		Key outcomes
	Mortality	Morbidity or Development	
Facility-based interventions			
Effect of therapeutic zinc supplementation on young infant sepsis[29]	Yes	Yes	Mortality in infants <3 months who received 3 mg/kg twice daily RR 0·61 (0·41 to 0·93)
Community-based interventions			
Preventive vitamin A supplementation for 1–6 months[83] and 1–59 months[94]	Yes	Yes	All-cause mortality (1–59 months) RR 0·88 (0·83 to 0·93); and diarrhoeal mortality (1–6 months) RR 0·88 (0·79 to 0·98)
Effect of breastfeeding on diarrhoea and pneumonia (not breastfed *vs* breastfed)[85,86]	Yes	Yes	All-cause mortality (0–5 months) RR 14·40 (6·13 to 33·86); all-cause mortality (6–23 months) RR 3·69 (1·49 to 9·17); pneumonia prevalence (0–5 months) RR 5·61 (1·23 to 25·53); pneumonia prevalence (6–23 months) RR 1·93 (1·39 to 2·69); and diarrhoea incidence (6–23 months; not EBF *vs* EBF) RR 2·65 (1·72 to 4·07)
Effect of complementary feeding education and supplementary foods[31]	Uncertain	Yes	Stunting (food provision – food secure) RR 0·47 (0·37–0·59); WAZ (education – food secure) MD 0·41 (0·07 to 0·75); and WHZ (supplementary feeding) MD 0·15 (0·08 to 0·22)
Prevention and management of malaria in children with insecticide-treated nets[87]	Yes	Uncertain	All-cause child mortality RR 0·83 (0·77 to 0·89)
Oral rehydration salts for diarrhoea in children <5 years old[88]	Yes	Uncertain	Diarrhoea mortality OR 0·31 (0·20 to 0·49)
Preventive zinc supplementation[89]	Uncertain	Yes	Diarrhoea RR 0·89 (0·82 to 0·97); and height (undernourished subgroup) MD 0·09 (0·02 to 0·16)
Therapeutic zinc supplementation for diarrhoea in children aged 1–59 months[90]	Uncertain	Yes	Diarrhoea duration MD –11·46 hours (–19·72 to –3·19); and persistent diarrhoea (≥7 days) RR 0·73 (0·61 to 0·88)
Preventive SQ-LNS compared with control for children aged 6–24 months[84,91]	Yes	Yes	Severe stunting RR 0·83 (0·70 to 0·99); moderate wasting RR 0·83 (0·73 to 0·95); moderate underweight RR 0·88 (0·80 to 0·96); and all-cause child mortality RR 0·73 (0·59 to 0·89)
Iron supplementation for children aged 1–59 months[84]	Uncertain	Yes	Anaemia RR 0·55 (0·44 to 0·70); haemoglobin MD 6·02 g/L (4·28 to 7·76); iron deficiency RR 0·21 (0·12 to 0·39); iron deficiency anaemia RR 0·14 (0·04 to 0·54); mental development SMD 0·14 (0·01 to 0·28); and motor development SMD 0·28 (0·15 to 0·40)
Multiple micronutrient supplementation including iron for children aged 1–59 months[84]	Uncertain	Yes	Anaemia RR 0·69 (0·56 to 0·85); haemoglobin MD 4·40g/L (2·91 to 5·90); iron deficiency RR 0·41 (0·25 to 0·66); and height MD 0·36cm (0·01 to 0·71)
MMH interventions[89,92]	Uncertain	Yes	EBF (primary MMH focus) SMD 0·155 (0·065 to 0·246); cognitive development (secondary MMH focus) SMD 0·568 (0·238 to 0·899); expressive language development SMD 0·372 (0·045 to 0·699); EBF (focused MMH and integrated interventions) RR 1·39 (1·13 to 1·71); and height SMD 0·13 (0·02 to 0·24)
Integrated caregiving and early learning interventions[89]	Uncertain	Yes	Cognitive development SMD 0·57 (0·32 to 0·82); language development SMD 0·40 (0·17 to 0·63); and motor development SMD 0·40 (0·26 to 0·53)

Data are pooled effect estimates RR (95% CI), MD (95% CI), or SMD (95% CI). EBF=exclusive breastfeeding. MD=mean difference. MMH=maternal mental health. RR=relative risk. SMD=standardised mean difference. SQ-LNS=small-quantity lipid-nutrient supplements. WAZ=weight-for-age Z score. WHZ=weight-for-height Z score.

Table 2: **Effects of selected interventions on key outcomes in children younger than 5 years**

Facility-based interventions for preterm, low birthweight, and ill newborns

Neonates requiring special attention must receive care in a specialised facility with skilled health professionals (table 1). Therapeutic hypothermia for prevention of hypoxic ischaemic encephalopathy has been shown to reduce both mortality by 32% (95% CI 21–41) and neurodevelopmental disability by 28% (12–41) in HICs.[46] However, emerging evidence suggests that this might not be the case in LMICs with higher risk of adverse outcomes.[72] Prevention of respiratory distress syndrome with surfactant therapy in at-risk preterm neonates can reduce mortality by 11% (1–21),[48] and management with continuous distending pressure can reduce mortality by 47% (17–66);[47] however, this evidence is mainly derived from studies in HICs. The introduction of low-cost nasal continuous positive airway pressure systems in LMICs has improved survival and outcomes.[73–76]

The benefits of early initiation and exclusive breastfeeding for newborns and young infants are well established,[77] and a range of packages are available to implement exclusive breastfeeding in early infancy.[78] There are also emerging interventions with evidence of benefit in diverse settings. Probiotic supplementation in preterm and low birthweight neonates in neonatal intensive care units in LMICs can reduce necrotising enterocolitis by 54% (95% CI 39–65), sepsis by 22% (14–30), and mortality by 20% (4–34),[44] but caution has been advised because supplementation has not been standardised and there is a scarcity of pharmaceutical grade products.[79] Emerging evidence also suggests that therapeutic zinc supplementation (3 mg/kg twice daily) for neonates and young infants with sepsis in LMICs can reduce mortality by 51% (13–73); preventive zinc supplementation in neonates with low birthweight can reduce mortality by 72% (33–88).[28,29] Prophylactic postnatal anti-D immunoglobulin administration is highly effective in preventing Rhesus alloimmunisation in Rhesus-negative mothers with a Rhesus-positive child,[80] although more research is needed to establish the benefits of antenatal anti-D administration.[81] Phototherapy for treatment of neonatal jaundice can reduce risk of severe hyperbilirubinaemia and neurodevelopmental impairment by 15% (1–26) in low birthweight infants.[50]

Promotion of kangaroo mother care for preterm and low birthweight infants born in health facilities reduces the risk of infant mortality by 26% (95% CI 11–39) and severe neonatal infection or sepsis by 15% (8–21).[18] In healthy term (≥37 weeks gestation) or late preterm (34–36 weeks gestation) newborns, kangaroo mother care can also reduce neonatal infection risk by 32% (9–50) and increase coverage of early and exclusive breastfeeding until 6 months by 41% (18–69).[26] Emerging evidence also supports the benefits of immediate kangaroo mother care in low birthweight newborns (1000–1799 g) at birth in LMICs.[82]

Interventions for infants and young children (<5 years)

Interventions supporting the health, growth, and development of infants and young children (<5 years; table 2)[29,31,83–92] involve addressing several different domains of risk factors, the most effective of which are improving nutrition, reducing the burden of infectious disease, and supporting optimal development.[92] Although they represent a smaller proportion of the global burden of disease, addressing non-communicable diseases (NCDs), supporting children with disabilities, and preventing unintentional injuries are increasingly important and merit greater attention as countries continue to reduce their burdens of disease attributable to infectious disease and malnutrition.

Infant and young child feeding

Supporting mothers in practicing optimal breastfeeding is the cornerstone of early infant nutrition. Early and exclusive breastfeeding until 6 months reduces infant exposure to harmful pathogens present in foods and untreated drinking water. Infants in LMICs who are not breastfed are at substantially higher risk of morbidity and mortality from diarrhoea[83] and pneumonia.[86] Evidence from LMICs shows that promotion of breastfeeding can substantially increase the likelihood of early and exclusive breastfeeding at both 3 months (102% [95% CI 88–117]) and 6 months (53% [47–57]), in addition to reducing the prevalence of diarrhoea by 24% (95% CI 15–33).[31]

Complementary feeding education and food provision has substantial growth benefits in 6–24-month-old children in LMICs. In food secure populations, complementary feeding education alone can improve weight-for-age Z score (mean difference 0·41 [95% CI 0·07–0·75]) and height-for-age Z score (0·25 [0·04–0·45]), and food provision can reduce the risk of stunting by 53% (95% CI 41–63%).[31] In food insecure populations, complementary feeding education alone also increases weight-for-age Z score (mean difference 0·47 [95% CI 0·35–0·59]) and height-for-age Z score (0·26 [0·10–0·42]); additionally, food provision also increases height-for-age Z score and reduces the risk of stunting by 36% (95% CI 8–56).[32] Supplementary food provision might reduce infant mortality risk by 39% (3–62).[31]

Micronutrient supplementation in children is particularly important in populations at risk of deficiency. Vitamin A supplementation for 6–59-month-old children living in LMICs can reduce the risk of diarrhoea by 15% (95% CI 13–18) and all-cause mortality by 12% (7–17).[93] In the neonatal period, vitamin A supplementation has shown benefits only in subgroup meta-analyses of trials from south Asia,[94] which can be explained by inclusion of trials in populations with high prevalence of vitamin A deficiency.[95]

Preventive zinc supplementation reduces zinc deficiency, reduces the incidence of diarrhoea by 11% (95% CI 3–18), pneumonia by 13% (6–19), and might improve linear growth in undernourished 6–59-month-old children.[87] Zinc supplementation can modestly increase weight-for-age (SMD 0·16 [0·03–0·29]) and weight-for-length (SMD 0·15 [0·02–0·28]) Z scores in 1–6-month-old infants.[96]

In 1–59-month-olds, iron supplements can reduce the risk of anaemia by 45% (95% CI 30–56) and multiple micronutrient supplements containing iron can reduce the risk of anaemia by 31% (15–44).[87] Multiple micronutrients could have an effect on linear growth (height mean difference 0·36cm [95% CI 0·01–0·71]), and iron supplementation might affect mental and motor development.[87] Micronutrient powders for home food fortification have been reported to reduce the risk of anaemia by 24% (16–31), but have been associated with an increase in the risk of diarrhoea by 30% (11–53).[87] Newer developments with small-quantity lipid-nutrient supplements given to infants (aged 6–23 months) in LMICs can reduce the risk of severe stunting by 17% (95% CI 1–30), moderate wasting by 17% (5–27), and moderate underweight by 12% (4–20%); they are generally more effective in supplementation durations of more than 12 months.[87] Small-quantity lipid-nutrient supplements might also reduce child mortality by 27% (11–41), but more research is needed to clarify the mechanisms for this effect.[89]

The community-based management of acute malnutrition with ready-to-use supplementary foods can effectively reduce wasting,[97] although inpatient care is necessary if complications are evident in the case of severe acute malnutrition.

Dietary modification interventions delivered alongside physical activity promotion can reduce the risk of obesity in 0–5-year-old children, whereas physical activity promotion alone appears to only be effective in reducing obesity in 6–18-year-olds.[98]

Prevention, treatment, and case management of infectious diseases

Administration of the full schedule of recommended routine vaccinations during infancy and childhood is the first line of defence against common infections and remains one of the most cost-effective public health interventions. Use of insecticide-treated nets in highly malaria-endemic regions can reduce all-cause child mortality by 17% (95% CI 11–23).[88] *Haemophilus influenzae* B vaccine and pneumococcal conjugate vaccine can also reduce the incidence and severity of pneumonia in children.[99] Typhoid fever conjugate vaccines effectively reduce disease incidence when given to children older than 2 years.[100] Targeted oral cholera vaccination[101,102] in high-risk areas can reduce risk in outbreak situations. Meningococcal conjugate vaccines effectively reduce the risk of invasive meningococcal disease.[103] Although children were not prioritised for COVID-19 vaccine research and development, trials have progressively included

adolescents, school-age children, and children younger than 5 years. Currently COVID-19 vaccines (mainly mRNA based) are being used for school-age children and adolescents, mainly in HICs. Research is underway to assess efficacy and optimal dosage and frequency in children younger than 5 years.

Intermittent malaria chemoprophylaxis for seasonal transmission reduces clinical malaria risk in infants[104] and children.[105] Artemisinin-based combination therapy is effective for treatment of uncomplicated *P falciparum* malaria.[106,107] Effective case management for pneumonia requires the provision of appropriate antibiotics and oxygen therapy.[99]

Deaths caused by diarrhoea are preventable with timely rehydration. The provision of oral rehydration salts for the treatment of diarrhoea in children younger than 5 years reduces the risk of diarrhoeal mortality by 69% (95% 51–80).[90] Therapeutic zinc supplementation can significantly shorten diarrhoea duration, including reducing the risk of diarrhoea persisting for more than 7 days by 27% (12–39).[85] Continued feeding during diarrhoea is also essential to maintain nutritional status in children; locally sourced home-made foods have been shown to be as effective as commercially prepared foods for dietary management of diarrhoea.[108] In cases of diarrhoea or dysentery caused by cholera, shigella, or cryptosporidiosis, antibiotics are effective treatments.[99]

Mass drug administration delivering azithromycin every 6 months was shown to reduce child mortality by 13·5% (95% CI 6·7–19·8%) in three African countries: Malawi, Tanzania, and Niger.[109] However, WHO recommends this intervention only for 1–11-month-old children in very high mortality settings, alongside continuous antibiotic resistance monitoring.[110] The potential emergence of macrolide resistance in these populations might restrict the public health use of this strategy.[111]

Improving water, sanitation, and hygiene

Increasing access to safe drinking water and sanitation infrastructure and improving handwashing practices are key preventive measures that benefit entire households, but particularly affect young children. These interventions have the potential to improve child growth by mitigating environmental enteric dysfunction; however, trials with the commonly used, low cost technologies to improve water supply and disposal of human waste have not shown benefits for growth of children.[112,113]

Point-of-use water filtration can reduce the risk of diarrhoea in children younger than 5 years by 53% (95% CI 38–64); water disinfection can reduce the risk of diarrhoea, in the same age group, by 29% (19–37).[114] Promotion of handwashing with soap reduces the risk of diarrhoea by 25% (6–40),[114] and fly control with insecticide spraying can reduce the risk by 23% (11–33).[115]

Nurturing care to optimise cognitive, motor, language, and socioemotional development

Ensuring children reach their full developmental potential requires nurturing care interventions that address a set of risk factors during the crucial periods of preconception, pregnancy, infancy, and early childhood.[92] In addition to supporting early child health and nutrition, the Nurturing Care Framework[1,116,117] describes three additional domains that are required to support optimal child development: responsive caregiving, safety and security, and early learning. Key effective interventions in this area encompass parenting support, prevention of child maltreatment, out-of-home early learning programmes, and social safety nets.[92]

WHO has released guidelines[84] on recommended responsive caregiving and maternal psychotherapeutic interventions; both sets of guidelines describe interventions that might improve multiple domains of child development, particularly when responsive caregiving and nutrition interventions are integrated with early learning. Evidence for the effect of maternal mental health interventions on direct measures of early child development is mixed,[84,91] with integrated interventions seeming to have larger effects. Maternal mental health interventions can also improve exclusive breastfeeding practices,[84,89] and they might also have small benefits on child height.[91] Promoting safety and security and preventing child maltreatment through home visiting and positive parenting programmes have the potential to improve parent–child interaction and reduce abusive parenting in LMICs.[118]

Support for infants and children with intellectual, sensory, and physical disabilities

The early detection and management of rare congenital diseases through prenatal and postnatal screening and ongoing medical care is necessary to ensure that children affected by these conditions are given the opportunity to grow and develop optimally and survive into adulthood. An association between developmental delay and premature mortality in school-age children in LMICs has been reported.[119] Special attention must be given to children living with a disability, who might require specialised care or accommodation to support their learning and development. This includes children with impaired sight and those with hearing loss—which is common in LMICs due to high rates of chronic ear infections.

Interventions in school-age children (5–9 years)

As children continue to grow, develop, and enter the school system, they experience the transitionary period between early childhood and adolescence. Autonomy and independence increase as children begin to form closer peer relationships and spend more time away from their families. Children continue to develop lifestyle habits (eg, physical activity, eating behaviours,

and use of electronic devices), and are influenced by the social and physical environments they reside in. Although rates of mortality are lower compared with children younger than 5 years, infectious diseases and nutritional deficiencies associated with poverty continue to be important causes of death and disability in school-age children in LMICs.[1] NCDs and injuries also become important causes of death and disability in this age group, particularly in middle-income and high-income countries.[11] Although the evidence base from appropriate randomised trials is scarce, school-based and digital platforms (including use of

	Key outcomes
School-age children (5–9 years old)	
Vaccinations	
Vaccination education[120]	Vaccination coverage RR 2·10 (1·03 to 4·31)
Vaccination reminders[120]	Vaccination coverage RR 1·57 (1·20 to 2·06)
Provider-based intervention[120]	Vaccination coverage RR 1·22 (1·10 to 1·35)
School-based intervention[120]	Vaccination coverage RR 1·22 (1·13 to 1·33)
Multilevel intervention[120]	Vaccination coverage RR 1·08 (1·06 to 1·09)
Neglected tropical diseases	
Mass drug administration for STH infection[121]	Prevalence of ascaris RR 0·42 (0·35 to 0·52); prevalence of trichuris RR 0·64 (0·53 to 0·77); prevalence of hookworm RR 0·43 (0·29 to 0·64); and height MD 0·35 (0·01 to 0·68)
Micronutrient (iron) for STH[121]	Anaemia prevalence RR 0·34 (0·14 to 0·81); and end of treatment haemoglobin MD 2·29 (0·48 to 4·09)
Mass drug administration for trachoma[121]	Ocular chlamydial infection prevalence RR 0·19 (0·04 to 0·94)
Health education for trachoma[121]	Mean prevalence of active trachoma MD –4·00 (–7·80 to –0·20)
Health education for *Schistosoma*[121]	Prevalence of *S mansoni* RR 0·10 (0·05 to 0·19)
Prevention and case management of high-burden infectious diseases	
Point of use water treatment for diarrhoea prevention[122]	Diarrhoea RR 0·61 (0·49 to 0·75)
Nutrition and physical activity	
Micronutrient supplements and fortification (general population and mostly school-age children)[123]	Anaemia RR 0·68 (0·56 to 0·84); iron deficiency anaemia RR 0·28 (0·19 to 0·39); WAZ MD 0·10 (0·02 to 0·17); WHZ MD 0·10 (0·02 to 0·18); HAZ MD 0·09 (0·01 to 0·18); vitamin A deficiency RR 0·42 (0·28 to 0·62); vitamin B2 deficiency RR 0·36 (0·19 to 0·68); vitamin B6 deficiency RR 0·09 (0·02 to 0·38); and vitamin B12 deficiency RR 0·42 (0·25 to 0·71)
Lifestyle modification: obesity prevention (school-age children and adolescents)[124]	Combination of diet and exercise BMI Z score MD –0·12 (–0·18 to –0·06); behavioural interventions BMI Z score MD –0·07 (–0·14 to 0·00); and behavioural interventions and exercise BMI Z score –0·08 (–0·16 to 0·00)
Lifestyle modification: obesity management (school-age children and adolescents)[124]	Exercise only BMI Z score MD –0·13 (–0·20 to –0·06); exercise and behavioural therapy BMI Z score MD –0·08 (–0·16 to 0·00); diet and behavioural therapy BMI Z score MD –0·16 (–0·26 to –0·07); and diet and exercise and behavioural therapy BMI Z score MD –0·09 (–0·14 to –0·05)
School food environment policies[125]	Direct provision of healthful foods: consumption of fruits and vegetables 0·28 servings per day (0·17 to 0·40); competitive food and beverage standards: sugar-sweetened beverage intake –0·18 servings per day (–0·31 to –0·05) and unhealthy snack intake –0·17 servings per day (–0·22 to –0·13); and school meal standards: fruit intake 0·76 servings per day (0·37 to 1·16) and total fat intake –1·49% energy (–2·42 to –0·57)
Digital-based interventions to improve health and healthy lifestyle choices[126]	Body fat percentage MD –0·35 (–0·63 to –0·06); vegetable and fruit intake MD 0·63 (0·21–1·04) servings per day
Non-digital interventions for screen time and sedentary behaviour reduction[127]	General screen time (mins per day) MD –11·45 (–19·18 to –3·73); TV screen time (mins per day) MD –12·46 (–20·82 to –4·10); and sedentary behaviour (mins per day, by accelerometery) MD –3·86 (–6·30 to –1·41)
Non-communicable diseases	
Red cell transfusions for sickle cell disease[128]	Clinical stroke risk reduction 0·12 (0·03 to 0·49)
Treatment of streptococcal pharyngitis for rheumatic heart disease prevention[129]	Rheumatic fever risk reduction 0·41 (0·23 to 0·70)
Mental health and positive development	
Vision screening and provision of free corrective lenses[130]	Wearing corrective lenses RR 1·60 (1·34 to 1·90)
School-based social and emotional learning interventions[131]	Positive social behaviour ES (Hedges' g) 0·13 (0·05 to 0·21); academic performance ES 0·33 (0·17 to 0·49); behaviour problems ES 0·14 (0·07 to 0·21); emotional distress ES 0·16 (0·08 to 0·23); and drug use ES 0·16 (0·09 to 0·24)
School-based psychosocial interventions[129]	Internalising disorders ES (Hedges' g) 0·13 (0·002 to 0·26)
Cognitive-behavioural interventions for prevention and treatment of anxiety[132]	Anxiety score SMD –0·81 (–1·00 to –0·63)

(Table 3 continues on next page)

	Key outcomes
(Continued from previous page)	
Adolescents (10–19 years old)	
Mental health	
School-based targeted group-based interventions and cognitive behavioural therapy[133]	Depressive symptoms SMD –0·16 (–0·26 to –0·05); and anxiety SMD –0·33 (–0·59 to –0·06)
School-based suicide prevention programmes[133]	Short-term knowledge of suicide SMD 1·51 (0·57 to 2·45); and knowledge of suicide prevention SMD 0·72 (0·36 to 1·07)
Exercise interventions[133]	Self-esteem SMD 0·49 (0·16 to 0·81); depression SMD –0·62 (–0·81 to –0·42); and depression score (vigorous exercise compared with no intervention) SMD –0·66 (–1·25 to –0·08)
Cognitive behavioural therapy compared with waitlist for anxiety[133]	Anxiety remission OR 7·85 (5·31 to 11·6)
Substance use	
School-based interventions for smoking, drug, or alcohol use[134]	Smoking uptake RR 0·80 (0·82 to 0·96); new smokers RR 0·76 (0·68 to 0·84); marijuana use (>12 months) RR 0·83 (0·69 to 0·99); any drug use (<12 months) RR 0·76 (0·64 to 0·89); alcohol consumption frequency SMD –0·91 (–1·21 to -0·61); alcohol consumption RR 0·34 (0·11 to 0·56); alcohol consumption (quantity per week per month) SMD 0·13 (0·07 to 0·19); and frequency of drinking days SMD 0·07 (0·02 to 0·13)
Family and community-based interventions for smoking[134]	Smoking prevention RR 0·81 (0·70 to 0·93)
Digital platform interventions for alcohol use[134]	Alcohol-related problems ES 0·16 (0·03 to 0·30); and total alcohol consumption MD –0·65 (–1·23 to –0·07)
Unintentional injuries	
Motor-vehicle injury prevention interventions[135]	Mean road accidents SMD –2·15 (–2·62 to –1·67)
Helmet use[135]	Road accidents RR 0·27 (0·09 to 0·77)
Sport-related injury prevention interventions[135]	Incidence of sport-related injuries RR 0·59 (0·49 to 0·72)
Vaccinations	
Vaccination education[136]	Vaccination coverage RR 1·13 (1·06 to 1·21)
Provider-based intervention[136]	Vaccination coverage RR 1·09 (1·03 to 1·16)
School-based intervention[136]	Vaccination coverage RR 1·46 (1·22 to 1·57)
Multilevel intervention[136]	Vaccination coverage RR 1·16 (1·05 to 1·28)
Vaccine reminders[136]	Vaccination coverage RR 1·19 (1·14 to 1·23)
Policy and legislative interventions[136]	Vaccination coverage RR 1·85 (1·58 to 2·17)
SRH	
School-based SRH education[137]	Use of any contraception RR 1·36 (1·05 to 1·75)
Parent-based intervention	Condom use RR 1·19 (1·05 to 1·34)
Multi-component SRH education and counselling intervention[137]	Use of any contraception RR 1·76 (1·01–3·07); and condom use RR 1·28 (1·16–1·41)
Prevention of FGM[137]	FGM prevalence RR 0·86 (0·75 to 0·99); and knowledge of harmful consequences of FGM RR 1·53 (1·08 to 2·16)
Adolescent nutrition	
Obesity prevention and management[138]	BMI (management) SMD –0·24 (–0·36 to –0·13); and BMI (prevention) SMD –0·05 (–0·11 to 0·01)
Folic acid supplementation[138]	Serum folate SMD 1·89 (1·00 to 2·79)
Iron and folic acid supplementation[138]	Anaemia RR 0·48 (0·24–0·96); and haemoglobin concentration SMD 2·95 (1·96–3·95)
Vitamin A supplementation[138]	Anaemia RR 0·73 (0·56 to 0·93)
Multiple micronutrient supplementation[138,139]	Haemoglobin concentration (non-pregnant) SMD 0·55 (0·30 to 0·81); and haemoglobin concentration (pregnant) SMD 1·0 (0·31 to 2·28)
Nutrition education and counselling in pregnancy[138]	Preterm delivery RR 0·74 (0·57 to 0·97); birthweight SMD 0·09 (0·02 to 0·17); low birthweight RR 0·70 (0·54 to 0·90); and birth length MD 0·30 (0·05 to 0·55)
Protein-energy supplementation for pregnant adolescents[138]	Anaemia RR 0·32 (0·26 to 0·69)
Any MMN Supplementation in pregnancy[138]	Iron deficiency anaemia RR 0·34 (0·13 to 0·89)

Data are estimates (95% CI). BMI=body-mass index. ES=effect size. FGM=female genital mutilation. HAZ=height-for-age Z score. MD=mean difference. MMN=multiple micronutrients. OR=odds ratio. RR=relative risk. SMD=standardised mean difference. SRH=sexual and reproductive health. STH=soil transmitted helminth. WAZ=weight-for-age Z score. WHZ=weight-for-height Z score.

***Table 3*: Effects of selected interventions key outcomes in 5–9-year-olds and 10–19-year-olds**

hand-held devices and internet-based learning) present opportunities for the delivery of interventions to school-age children (table 3).[120–139]

Prevention, treatment, and case management of infectious diseases

Additional routine vaccinations are required during the school-age period, either as new vaccines targeting infections more common in this age group or as catch-up or boosters to previous immunisations. Effective interventions to increase vaccine coverage (eg, human papillomavirus [HPV] vaccine and diphtheria, pertussis, and tetanus vaccine boosters) include reminders, which increased coverage by 57% (95% CI 20–106); education, which increased coverage by 110% (3–331); school-based programmes, which increased coverage by 22% (13–33); and provider-based interventions, which increased coverage by 22% (10–35).[120] Effective vaccines for preventing typhoid fever in school-age children and adolescents, such as the Vi polysaccharide and Ty21A vaccines, are available.[140] Provider-based interventions, financial incentives, and multicomponent or multilevel interventions that combine several delivery strategies are also effective in improving HPV vaccine coverage.[141] Alternative dosing schedules can also improve operational flexibility in reaching adolescents with HPV vaccines,[142] and preliminary evidence suggests that interventions can address inequities in coverage in marginalised populations.[143] Policy change and legislative action at the national level can help improve the coverage of a variety of routine vaccinations and address vaccine hesitancy.

Point of use water treatment can reduce diarrhoea risk by 39% (95% CI 25–51) in school-age children and adolescents.[122] Addressing high burdens of neglected tropical diseases with targeted strategies is necessary to reduce avoidable morbidity in vulnerable child populations—particularly people living in extreme poverty. In addition to improving water, sanitation, and hygiene conditions through continued implementation of strategies discussed previously, a combination of health education, behaviour change, vector control, and drug administration can help to prevent and treat neglected tropical diseases.[121]

Mass drug administration is effective in reducing the prevalence of infection by multiple species of soil-transmitted helminths, although evidence for the effect of mass drug administration on other outcomes is mixed. Meta-analyses using a variety of methods found little to no benefit of mass drug administration for deworming on height, weight, haemoglobin concentration, or cognition.[121,144–146] Mass drug administration of azithromycin and health education is also effective in reducing the prevalence of trachoma caused by ocular chlamydial infection.

Nutrition and physical activity for school-age children

Combined diet and exercise interventions for obesity prevention in children and adolescents might reduce body-mass index (BMI; mean difference –0·41 [95% CI –0·60 to –0·21]);[124] however, high-quality evidence from LMICs, in which obesity is a growing problem, is scarce. For management of obesity, exercise alone; combination of diet and behavioural therapy; and combination of diet, exercise, and behavioural therapy might reduce BMI. Physical activity promotion alone appears to be effective in reducing obesity in 6–18-year-olds.[98] Evidence from HICs suggests school food environment policies can increase healthy eating behaviour.[125] School feeding programmes containing meals fortified with key micronutrients might provide small benefits to disadvantaged children, including improved school attendance.[147]

Prevention of unintentional injuries

The proportion of child mortality and disability resulting from unintentional injuries is higher in 5–9-year-olds due to increased exposure to situations in which drowning, road traffic injuries, falls, burns, and poisonings can occur. Key interventions identified by a targeted systematic review[148] of experimental evidence in this age group included laws and legislation, infrastructure development, education (eg, cycling courses, helmet use, and swimming instruction), and multiple modes of general safety training that include digital and school-based platforms. However, the evidence for the effects of these interventions on outcomes was mainly restricted to knowledge and practice of safe or unsafe behaviours, with injury-related and mortality outcomes sparsely reported. Formal swimming lessons provided to children and adolescents younger than 19 years might substantially reduce drowning risk,[149] and some evidence suggests that the use of crèches or nursery schools in younger children (aged 12–47 months) might effectively prevent drowning in rural Bangladesh.[150]

Sexual and reproductive health and rights

A targeted systematic review[151] examining interventions promoting sexual and reproductive health and rights for school-age children identified effective educational interventions designed to prevent childhood sexual abuse and HIV in children, and reported strong evidence for improved knowledge of childhood sexual abuse prevention concepts, and low and very low certainty evidence of improved protective attitudes, behaviours, and skills to protect against childhood sexual abuse, gender-based violence, and HIV infection.

Promoting positive child development and mental health

In addition to the continued provision of the elements of nurturing care (ie, responsive relationships, safety and security, and learning opportunities) supporting positive development and mental health in school-

age children involves nurturing resilience, self-esteem, socioemotional skills, and wellbeing. A meta-analysis of the effects of school-based social and emotional learning interventions[131] found significant benefits on social-emotion skills, attitudes, and wellbeing indicators across racial, socioeconomic, and geographical contexts. For children who have difficulty learning due to visual acuity issues, vision screening and the provision of free corrective lenses can increase the proportion of children in need who are wearing glasses.[130]

A meta-analysis of the effectiveness of school-based, teacher-delivered psychosocial interventions found significant reductions in internalising outcomes such as anxiety or depression.[152] Evidence from HICs suggests that cognitive behavioural intervention to prevent and treat anxiety in younger children can effectively and sustainably reduce measures of anxiety (standardised mean difference –0·81 [95% CI –1·00 to –0·63]).[132] Parenting programmes to prevent or treat problems with behaviour in 3–10-year-old children have been found to be effective and translatable to a variety of settings with diverse cultural and socioeconomic contexts.[153] The findings of a global overview of systematic reviews[154] suggest that violence prevention through parent education programmes can prevent and reduce child maltreatment, although high-quality evidence of effectiveness from LMICs is scarce.

Specialised interventions for neglected NCDs and disabilities

The *Lancet* Commission on NCDs and injuries in the world's poorest billion people,[155] published in 2020, identified some key NCD care priorities relevant to school-age children. At a hospital level, these include treatment of early-stage childhood cancers and universal newborn screening for sickle cell disease. At a primary-care facility level, these include treatment of acute pharyngitis for rheumatic fever prevention, which can be reduced by 59% (95% CI 30–77) through treatment of streptococcal pharyngitis with penicillin in school-based and community-based programmes,[129] and secondary penicillin prophylaxis for rheumatic fever treatment and rheumatic heart disease prevention. Additional priorities include low-dose inhaled corticosteroids for asthma, and acute stabilisation and long-term management of epilepsy.

Although hydroxyurea has been shown to be effective in reducing the frequency of pain crises and increasing fetal haemoglobin concentration in those with sickle cell disease, the long-term benefits, potential risks, and optimal dose are not yet known.[156] In a trial in sub-Saharan Africa, which evaluated the feasibility, safety, and benefits of hydroxyurea treatment in young children (1–10 years), the overall rate of sickle cell-related events was significantly reduced (incidence rate ratio 0·47 [95% CI 0·38–0·57]), which was mainly due to reduced incidence of vaco-occlusive pain or dactylitis (IRR 0·45 [0·37–0·56]).[157] Additionally, prompt detection and treatment of children with thalassemia or other haemoglobinopathies is crucial to support healthy growth and development, with a focus on ensuring adequate serum haemoglobin concentrations through transfusions and managing iron overload with chelation therapy.[158]

Interventions for adolescents

Adolescence (10–19 years of age) represents a period of rapid change in the lives of children, involving rapid growth, pubertal development, sexual maturation, and increased autonomy in decision making and relationships. This new stage presents emergent risks and conditions, including the development of non-communicable diseases, mental health conditions, injuries, adolescent pregnancy, and sexually transmitted infections. School-based interventions that work for younger school-age children might not have the same effect when delivered to adolescents, and so should be tailored to this more mature age group to maximise effectiveness.[159]

Mortality outcomes are sparsely reported in studies evaluating interventions directed at adolescents, especially younger adolescents (10–14 years of age; table 3). Outcomes such as self-reported knowledge and behaviour are common, but links to clinical and functional outcomes are not always clear. Notwithstanding the variable quantum and quality of evidence from LMICs, studies reporting prevalence of morbidities, such as clinically diagnosed mental illness or injury, provide much insight into the ultimate effectiveness of these interventions on adolescent health, agency, and wellbeing.

Infection prevention and treatment

Catch-up vaccinations and recommended boosters should be provided during adolescence to maximise coverage of key immunisations (eg, HPV vaccine), for which school requirements, vaccine reminders, and national permissive recommendations are effective.[133] The provision of sexual health education can increase the rate of condom use for the prevention of sexually transmitted infections.[137]

Adolescent nutrition

Evidence on the effects of micronutrient supplementation or fortification on the health and nutritional status of adolescents in LMICs is scarce.[139] Multiple micronutrient supplementation in non-pregnant adolescents can effectively improve haemoglobin concentrations,[138] potentially reduce micronutrient deficiencies, and support adequate folate status for subsequent pregnancy.[138] Adolescent obesity management interventions might have a small effect on BMI reduction.[138]

Supporting adolescent mental health

Supportive strategies for adolescent mental health can include universal interventions, delivered in schools, which promote positive development and social

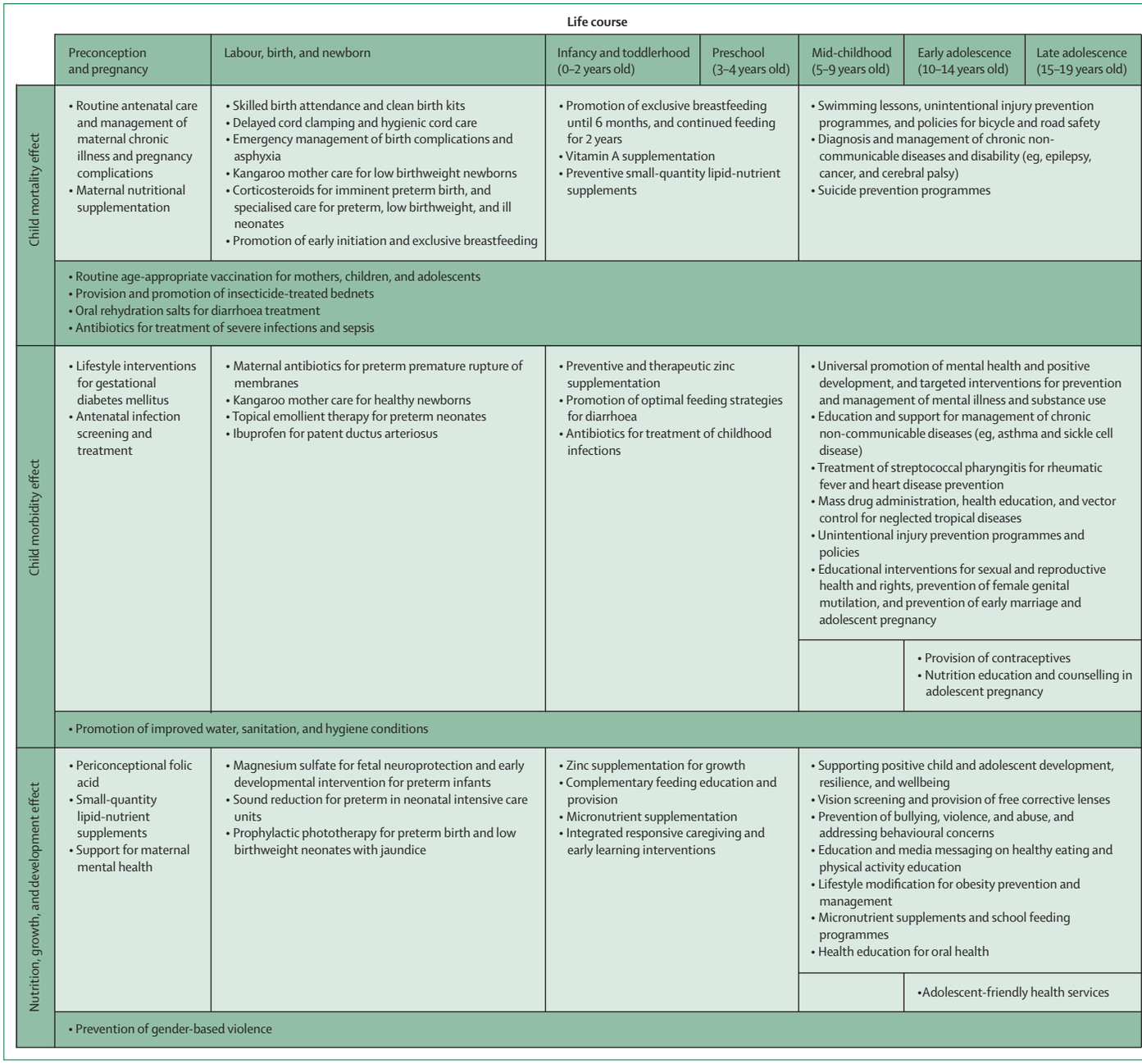

Figure 2: **Intervention packages by age group and effect on mortality, morbidity, nutrition, growth, and development**
More detail is provide in the appendix (p 5).

relationships, resilience, and healthy coping strategies. School-based, targeted, and group-based interventions; exercise; and cognitive behavioural therapy can reduce symptoms of depression and anxiety and improve self-esteem.[133] Interventions for the prevention of substance abuse can be effectively delivered through schools, families, communities, and digital platforms.[3,134] A large meta-analysis[160] of universal and selective interventions for mental health promotion (eg, psychoeducation and psychotherapy) in young people found improved outcomes across a range of domains, with greatest effects seen on improved mental health literacy, emotional states, and self-perceptions and values.

Restriction of access to lethal means (eg, firearms), analgesics, and suicide hotspots, are key population-based actions to help prevent suicide.[161] Prevention of self-harm through school-based suicide prevention programmes can effectively improve short-term knowledge of suicide and prevention strategies in adolescents,[133] and some evidence exists that

Panel: Cross-cutting interventions and delivery strategies

Delivery strategies to improve vaccination coverage

In hard to reach areas outreach programmes, such as home visits or community immunisation days, can improve community ownership and vaccination coverage. Health education for caregivers and community members aims to aid in informed decision making. A systematic review found that face-to-face interventions to inform or educate parents might improve vaccination status by 20% (risk ratio [RR] 1·20 [95% CI 1·04–1·37]).[167] Another review found that postal and telephone reminders to parents for vaccinations were quite effective.[168] SMS messages to caregivers alongside compliance-linked incentives have been shown to improve immunisation coverage.[169,170] Similarly, automated calls paired with SMS message reminders improved coverage of all routine immunisations by 12 months of age by 22% (RR 1·22 [95% CI 1·04–1·43]).[171] In summary, multiple delivery platforms might be required to maximise vaccine coverage, and the relative importance of the different interventions changes across the life course.

Financial platforms and social safety nets

Financial incentive programmes have been hypothesised to improve child health through increased coverage of interventions and access to healthcare; however, evidence is scarce and of low quality.[172] The effects of financial services on poverty indicators, women's empowerment, meaningful behavioural change outcomes, health status, and other social outcomes appears to be small and inconsistent.[173]

Conditional cash transfers can affect determinants of health[174] and, depending upon the conditionality,[175] are effective in improving access to health-care services, maternal and child nutrition, immunisation coverage, health service use, reducing morbidity risk, addressing household poverty, and encouraging healthy behaviours.[176–178]

A Cochrane review[179] examined the effect of conditional cash transfers in community settings in low-income and middle-income countries on food security. The study reported that they did not affect child stunting or wasting rates, but they could improve cognitive functioning.

Unconditional cash transfers can also improve household food security, reduce childhood stunting,[179] and have also been shown to reduce likelihood of illness (odds ratio 0·73 [95% CI 0·57–0·93]), increase dietary diversity (mean difference 0·59 [95% CI 0·18–1·01]), and school attendance (RR 1·06 [95% CI 1·03–1·09]).[180] Vouchers for maternity care services can increase antenatal care visits by more than five percentage points, the proportion of births in health-care facilities by five percentage points, births with skilled attendants by 12–13 percentage points,[181] and general delivery of health services.[182] Although microcredit and microsavings can positively affect health, food security, and housing, some counterintuitive effects have been noted on child education and women's empowerment,[183] underscoring the importance of functional and well connected health and education systems.[184]

suggests that they can also prevent suicidal ideation and attempts.[162]

Prevention of unintentional injuries

Road traffic injuries represent a significant cause of morbidity and mortality in this age group because adolescents generally become more independently mobile in cars and public transport than their younger counterparts. Interventions to prevent motor vehicle injury can reduce road traffic injury frequency.[135] Additionally, school-based prevention interventions can reduce the risk of sport-related injuries by 41% (28–51).[135]

Sexual and reproductive health and rights for adolescents

Single and multicomponent education and empowerment interventions leveraging multiple delivery platforms, including peer-led, parent-based, school-based, clinic-based, and technology-based interventions, can improve adolescents' knowledge of sexual and reproductive health and rights, the use of modern contraceptive methods, and reduce the risk of adolescent pregnancy.[137] A variety of effective interventions exist to help prevent unintended pregnancies during adolescence, and the combination of education and promotion of contraceptives can reduce rates of unintended adolescent pregnancy.[163] A review of school-based condom availability programmes found that they can increase condom obtainment and use, and do not increase sexual activity.[164]

A meta-analysis of three randomised trials examined the effect of interventions modifying the school environment (including social inclusion and support, changing norms and school climate, and educational engagement), and found these reduced the odds of sexual debut at longest follow-up (odds ratio 0·5 [95% CI 0·4–0·7]).[165] Key characteristics of effective sexual health promotion interventions identified in an overview of reviews included longer programme duration, increased session frequency, multisetting implementation, parental involvement, and tailoring to the age, gender, and culture of the participants.[166] Interventions to prevent female genital mutilation can also help increase knowledge of the harmful consequences of female genital mutilation, and might help to reduce its prevalence.[137]

Combining interventions as packages of care for child survival, health, and development

We highlight key interventions to include in a set of recommended packages of care to support child and adolescent survival, health, and human capital

development over the life course (figure 2). These interventions were selected based on several criteria, including evidence of benefit in the context of total disease burden; fit with existing services and training needs; ease of integration and costs of scale-up; feasibility and contextual flexibility (eg, extreme poverty, conflict, and displacement); and cross-sectoral planning and integration. We modified the recommendations for these expanded packages from the essential interventions within Disease Control Priorities 3 compilation.[15,16]

Effective cross-cutting strategies that can be delivered across the life course—including vaccination promotion, financial platforms, and social safety nets—are summarised in the panel.[167–184] We also specifically reviewed additional interventions involving the promotion of healthy lifestyle choices and digital delivery strategies, which are described in the appendix (p 3).[126,127]

Conclusions and implications for action

Our review of a broad landscape of interventions to address fetal health and the spectrum of newborns, children younger than 5 years, school-age children (5–9 years), and adolescents (10–19 years), suggests that, despite limitations and a focus of the published literature on children younger than 5 years, we know enough to integrate interventions to promote child health and development across the entire period encompassing pregnancy, early childhood, school-age, and adolescence. As underscored in an in-depth review of interventions to address maternal and child undernutrition,[77] many evidence-based nutrition interventions in the preconception and pregnancy period can influence fetal growth as well as linear growth and developmental outcomes in childhood. The key challenge relates to selecting appropriate delivery platforms and ensuring continuation of services across age bands.

We also identify several new and promising opportunities for promoting and delivering interventions beyond traditional community outreach and health systems. For school-age children and adolescents, in addition to the need for strengthening quality care within health systems, schools provide additional exciting opportunities for delivering preventive, promotive, and supportive care, especially when linked with their catchment communities. In addition to addressing common ailments and immunisations, school health programmes can help screen children for nutritional problems, anaemia, vision and dental problems, mental health (including anxiety and depression), and learning disabilities. Some school-based programmes, especially health days and campaigns, can also serve as a mechanism for attracting children not enrolled in schools and their families and provide important epidemiological information on health and nutrition in the catchment population. Adolescent groups and youth groups provide important opportunities for learning and reaching out at a sensitive age to identify individuals at risk, and could be linked to digital platforms.

As the COVID-19 pandemic and its related restrictions and school closures have shown, the mental health needs of school-age children and adolescents are considerable and both schools and health systems need to gear up to these emerging needs as we rebuild equitable and resilient services after the COVID-19 pandemic.

A core principle of these opportunities is the ability to reach those in greatest need at scale. Universal health coverage is the dominant mechanism proposed for health equity and for reaching health and health-related SDGs.[185] An important component of universal health coverage in the context of addressing all health and development needs of children and adolescents is the inclusion of interventions for NCDs, especially those that affect the poorest populations.[155] Given the dominance of mental health disorders[186] and accidents and injuries[149] as children transition to adolescence, health systems will need to deal with these challenges by engaging competent and well trained multidisciplinary teams, and by providing the requisite financial protection to families to enable quality care. Addressing relatively neglected areas in child health, such as the care of children with sickle cell disease[187] or potentially curable haematological malignancies (eg, acute lymphoblastic leukaemia),[188] and addressing childhood rheumatological disorders will also prevent amenable child deaths. Global success in reducing infectious disease-related morbidity and mortality in early childhood also encourages us to increase the repertoire of interventions across the life course to age 20 years, such as those related to NCD prevention. With less than a decade left to achieve the SDG 3 targets, adding additional evidence-informed interventions that can be implemented across the entire age continuum of childhood to optimise health and developmental outcomes and build human capital are essential.

Contributors

ZAB conceptualised the work and secured project funding. TV, ZSL, RAS, JKD, OI, ECK, NS, RPJ, DA, CO, and BC curated and analysed the data. OI and ZSL contributed the data and tables for the under-5 age group. ZSL, RAS, JKD, RPJ, DA, CO, and BC contributed the data and tables for the school-age child and adolescent age groups. NS, RPJ, and TV wrote the delivery strategies panel. CO and BC wrote the digital health and platforms panel. ECK, ZSL, RAS, JKD, and OI contributed the data and tables related to nutrition interventions. MEK, GCP, REB, and ZAB critically reviewed the manuscript. TV coordinated the writing across all sections and incorporated revisions from authors. All authors contributed to the original manuscript draft and appendices. All authors contributed to manuscript revisions and have approved the final version for submission.

Declaration of interests

We declare no conflicts of interest.

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Optimising Child and Adolescent Health and Development 4

Improving health and social systems for all children in LMICs: structural innovations to deliver high-quality services

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Despite health gains over the past 30 years, children and adolescents are not reaching their health potential in many low-income and middle-income countries (LMICs). In addition to health systems, social systems, such as schools, communities, families, and digital platforms, can be used to promote health. We did a targeted literature review of how well health and social systems are meeting the needs of children in LMICs using the framework of *The Lancet Global Health* Commission on high-quality health systems and we reviewed evidence for structural reforms in health and social sectors. We found that quality of services for children is substandard across both health and social systems. Health systems have deficits in care competence (eg, diagnosis and management), system competence (eg, timeliness, continuity, and referral), user experience (eg, respect and usability), service provision for common and serious conditions (eg, cancer, trauma, and mental health), and service offerings for adolescents. Education and social services for child health are limited by low funding and poor coordination with other sectors. Structural reforms are more likely to improve service quality substantially and at scale than are micro-level efforts. Promising approaches include governing for quality (eg, leadership, expert management, and learning systems), redesigning service delivery to maximise outcomes, and empowering families to better care for children and to demand quality care from health and social systems. Additional research is needed on health needs across the life course, health system performance for children and families, and large-scale evaluation of promising health and social programmes.

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Introduction

A 2018 analysis estimated that 8·6 million deaths from treatable conditions occur annually, including more than 1 million deaths in neonates.[1] Two-thirds of these infants were born in health facilities, showing that low-quality health systems, and not solely scarce access to care, undermine progress.[1] The cumulative health and developmental losses in infants, children, and adolescents increasingly result from a failure of governance, implementation, and integration of policies and interventions across health systems and other social institutions.[2]

Health systems are crucial for child and adolescent health and wellbeing, but need to be augmented by social systems to reach this age group with promotive, preventive, and curative services relevant to their life stage. In this Series paper, the social systems that we examine include programmes and policies delivered by families, communities, schools, and digital platforms (appendix p 2). We use the definition of a quality health system from *The Lancet Global Health* Commission on high-quality health systems[3] as one that is for people, that consistently delivers services that improve or maintain health, that builds trust in the population, and that adapts to changing population and health needs, including changing needs along a child's life course.

High-quality systems and health-promoting elements of social systems should be primarily judged by processes and health outcomes, confidence, and economic benefits. Furthermore, health and social systems need to empower families, as well as children and adolescents, to take an active role in their health that is consistent with their developmental course.

As Black and colleagues[4] note in the first paper of this Series, human capital (ie, health, wellbeing, knowledge, and interpersonal and socioemotional skills) needed to achieve individual and societal potential is built though interactive biological, environmental, and behavioural processes that begin before conception and continue into childhood, adolescence, and adulthood. In the second Series paper, Victora and colleagues[5] review data on key conditions related to human capital in children, adolescents, and adults, and analyse how early-life poverty contributes to their enduring prevalence throughout the life course. In the third paper of the Series, Vaivada and colleagues[6] point to a large array of effective and affordable interventions to promote child health and development; however, large gaps in survival, health, and function remain between countries. These gaps reflect the difference between families' aspirations for their children and the reality of inadequate health and social systems.

In this fourth Series paper, we explore the quality of health systems and social systems (ie, service delivery platforms outside of health care) in promoting child health, with a focus on low-income and middle-income countries (LMICs). We assess the performance of these systems in real-world settings, identify knowledge gaps, and propose structural and societal innovations that could help to overcome current challenges. We point to the crucial role of research into health systems to gauge large-scale effectiveness of new ideas.

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See **Online** for appendix

Key messages

- Despite growing evidence of effective interventions, health and social systems (including family, community, and school programmes) are failing to implement these interventions to address the health needs of individuals from birth to adolescence
- Preventive and curative care is often substandard, with low diagnostic accuracy, treatment delays, and non-adherence to evidence-based standards, and quality is often worst for low-income communities
- Poor user experience for parents, children, and adolescents leads to non-adherence and low trust in health systems
- These deficits in health system quality lead to excess morbidity and mortality in children and adolescents
- Families, communities, schools, and digital platforms are well positioned to augment health systems, although research and investment are needed to identify the best means of designing and integrating services in coherent ways
- Structural reforms are needed for high-quality health and social systems, including committed leadership, skilled management teams that are committed to learning, reorganisation of service delivery, and empowerment of children, adolescents, and families to recognise and demand quality care
- A strong multisectoral approach can help to meet the aspirations of universal health coverage, limit the negative effects of COVID-19, and realise better health across childhood and adolescence

Methods

We used several literature scoping strategies to identify relevant evidence that describes the performance of health and social systems for children and adolescents in LMICs, as well as innovative structural strategies to improve child and adolescent health. We focused on the conditions that most contribute to mortality, morbidity, and disability in infants, children, and adolescents, including those that have been less explored in the context of LMICs (eg, preterm birth, infections, injuries, and depression).

To guide our search, we used the framework of care processes as reported in *The Lancet Global Health* Commission,[3] comprising care competence (ie, provider provision of effective care), system competence (ie, safe, continuous, and integrated services over the course of care), and user experience (ie, respectful, convenient, and low-hassle care that is appropriate for each developmental stage). Outcomes included positive health outcomes for conditions treatable by health care, user confidence, and economic benefits and harms for users. Because the first[4] and second[5] papers in this Series examine mortality and morbidity, in this fourth Series paper, we report on the Commission's non-health outcomes (ie, financial protection and confidence). For non-health system platforms, we assessed the performance of the most common health-promoting activities for infants, children, and adolescents. Further details on the search strategy, including example search terms, are provided in the appendix (p 4).

To highlight innovations, we identified promising programmes for children in health and social sectors that were consistent with the key structural reforms proposed by the Commission.[3] Within their sector of expertise, the authors drew on their disciplinary literatures, reviews, meta-analyses, previous *Lancet* Series,[7,8,9,10] and WHO–UNICEF evidence maps to identify novel approaches that adapted the Commission's recommendations to these new platforms. Methods used for primary visualisations, data synthesis, and data analysis based on publicly available data are described in the appendix (pp 4–12).

Health system quality for infants, children, and adolescents: care and system competence

Health needs in pregnancy and the neonatal period

Despite progress, the number of neonatal deaths and stillbirths remains high in LMICs, with preterm births, intrapartum-associated complications, and infections as the leading causes of mortality.[4,11] Although three-quarters of all births in LMICs take place in health facilities (figure 1A), this high mortality rate is largely attributable to inadequate provision of rapid and effective treatments for obstetric and neonatal emergencies, which require a highly skilled, organised, and coordinated system response to save lives.[14–16]

Opportunities to prevent these deaths are missed even before birth. Despite how high-quality antenatal care can reduce risk of preterm birth, low birthweight, and stillbirth, only 73% of women who attended antenatal visits in 91 LMICs from 2007 to 2016 had their blood pressure measured and their urine and blood tested.[7,17–19] Across the 91 LMICs, the wealthiest women are four times more likely to report good quality antenatal care than are the poorest women.[19]

High-quality labour and delivery care, including rapid recognition of problems and provision of interventions (eg, caesarean section, blood transfusion, and resuscitation), could prevent 1·3 million intrapartum stillbirths.[7] Care for babies with low birthweight and for sick newborn babies, who are at greatest risk of mortality, often does not reflect best practice guidelines.[20] In Kenya, 45% of small and sick newborn babies who accessed a health facility received good quality care.[21] In five sub-Saharan African countries, only 39% of health-care providers were able to correctly diagnose neonatal asphyxia.[3] Medication errors for neonates were common, even in clinical training centres across Kenya.[22] Although early postnatal care can detect problems and promote good health practices, across 82 LMICs, 58% of newborn babies received postnatal care within 48 h of birth (figure 1A; appendix pp 4–10).

Good quality neonatal care is hampered by shortages of key items, such as blood transfusion sets, positive airway pressure devices, kangaroo mother care, formulas, vitamin K, or intravenous penicillin.[21] Additionally, provider performance is problematic for neonates who are commonly admitted to the wrong level of care and are inadequately monitored.[23,24] Many facilities serving neonates are severely understaffed and overcrowded, which inhibits infant monitoring.[25]

Early childhood: cognitive and socioemotional development

An estimated 249 million children younger than 5 years in LMICs experience poverty and growth stunting that threaten their development and 50 million children globally have a developmental disability that impairs physical, learning, or behavioural functioning.[8,26–29] These risks can be mitigated by delaying pregnancy in adolescents, reducing birth asphyxia, improving nutrition, and supporting parental nurturing care, learning, secure attachment, and safety.[9,30–32] Especially when delivered during the first 1000 days after birth, health system and social interventions can improve physical and mental health across the life course.[10,33] Many of these programmes were disrupted during the COVID-19 pandemic with potentially long-lasting adverse consequences, particularly for low-income communities.[34]

Childhood: infections and acute conditions

Immunisation is a highly cost-effective health system activity; however, in 2019, almost 20 million infants were unvaccinated or undervaccinated.[35] Beyond immunisation, health-care providers in 17 LMICs performed only 41% of the clinical actions recommended by WHO.[3] Performance was minimally better for severely ill children, indicating failure of differential diagnosis and detection.[36] Studies from Kenya show inadequate assessment of children with fever; variable adherence to guidelines for treatment of pneumonia, meningitis, and malaria; and inadequate admission assessment and patient monitoring.[37]

Even simple interventions are inconsistently provided. In 94 LMICs, only 28% of children who sought care for diarrhoea received oral rehydration solution (figure 1B).

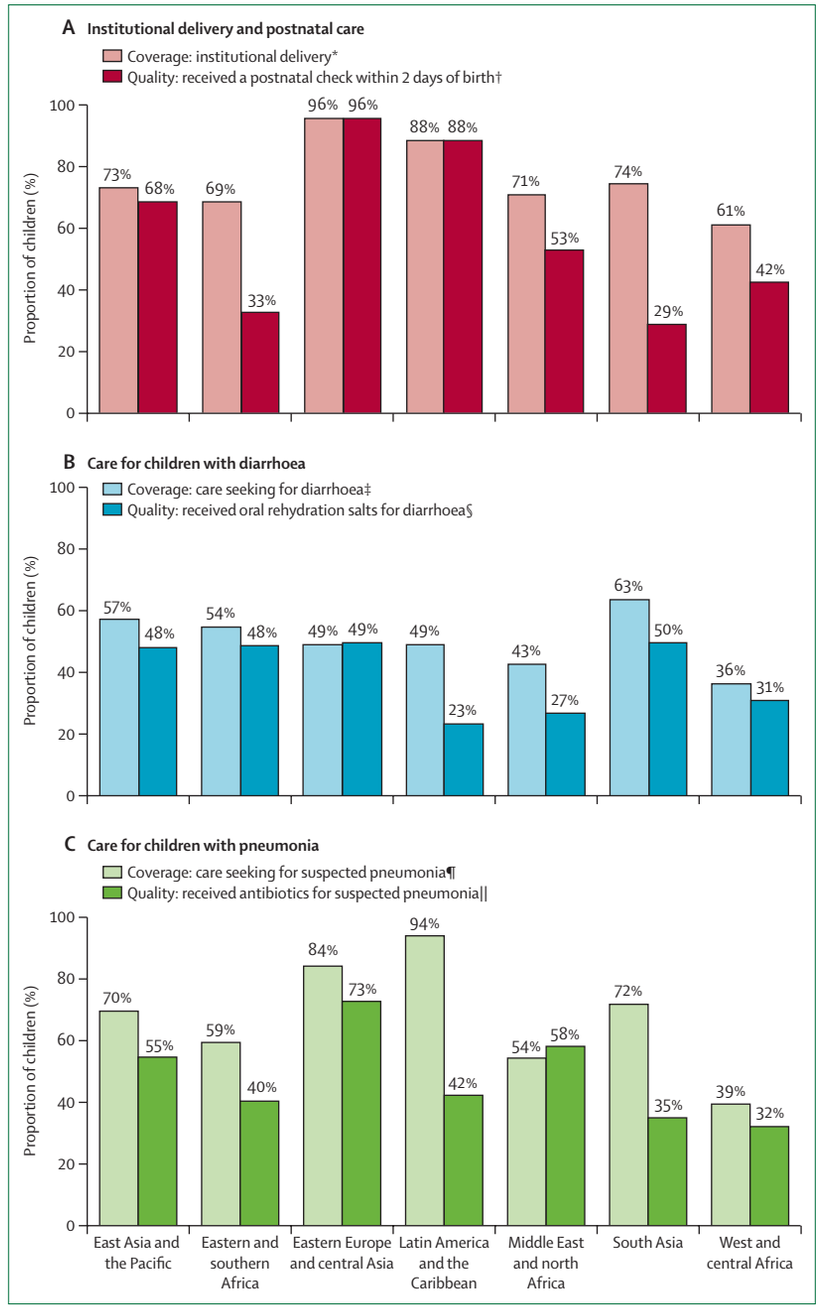

Figure 1: **Coverage versus quality of care in the neonatal and early childhood periods by region**

Data on coverage and quality of care provided for institutional delivery and postnatal care (A), care for children with diarrhoea (B), and care for children with suspected pneumonia. Data taken from the latest Demographic and Health Survey and Multiple Indicator Cluster Survey conducted in 95 countries between 2010 and 2018.[12,13] Country-level estimates are weighted using individual survey weights and regional averages are weighted according to each country's weighted sample size. Countries, survey years, and regional classification are available in the appendix (pp 4–10). *Proportion of all live births in the past 3 or 5 years (Demographic and Health Survey) or last live birth in the past 2 years (Multiple Indicator Cluster Survey) born in a health facility (n=97 countries). †Proportion of last live birth in the past 2 years who received postnatal care within 2 days of birth (n=82 countries). ‡Proportion of all children aged 0–59 months with diarrhoea in the past 2 weeks who sought care from an appropriate facility or provider (excluding traditional attendant, pharmacy, or shop; n=77 countries). §Proportion of all children aged 0–59 months with diarrhoea in the past 2 weeks who received oral rehydration solution (n=94 countries). ¶Proportion of all children aged 0–59 months with suspected pneumonia (ie, cough, short and rapid breaths, and problem in the chest) in the past 2 weeks for whom advice or treatment was sought from an appropriate facility or provider (excluding traditional attendant, pharmacy, or shop; n=90 countries). ||Proportion of all children aged 0–59 months with suspected pneumonia (ie, cough, short and rapid breaths, and problem in the chest) in the past 2 weeks who took antibiotics (n=84 countries).

A study of child deaths in Mali and Uganda found that most parents sought care but encountered multiple system failures, including provider failure to act on signs of serious illness, to prescribe essential medicines, and to refer to a higher level of care, as well as an inadequate response to observed parental neglect.[38]

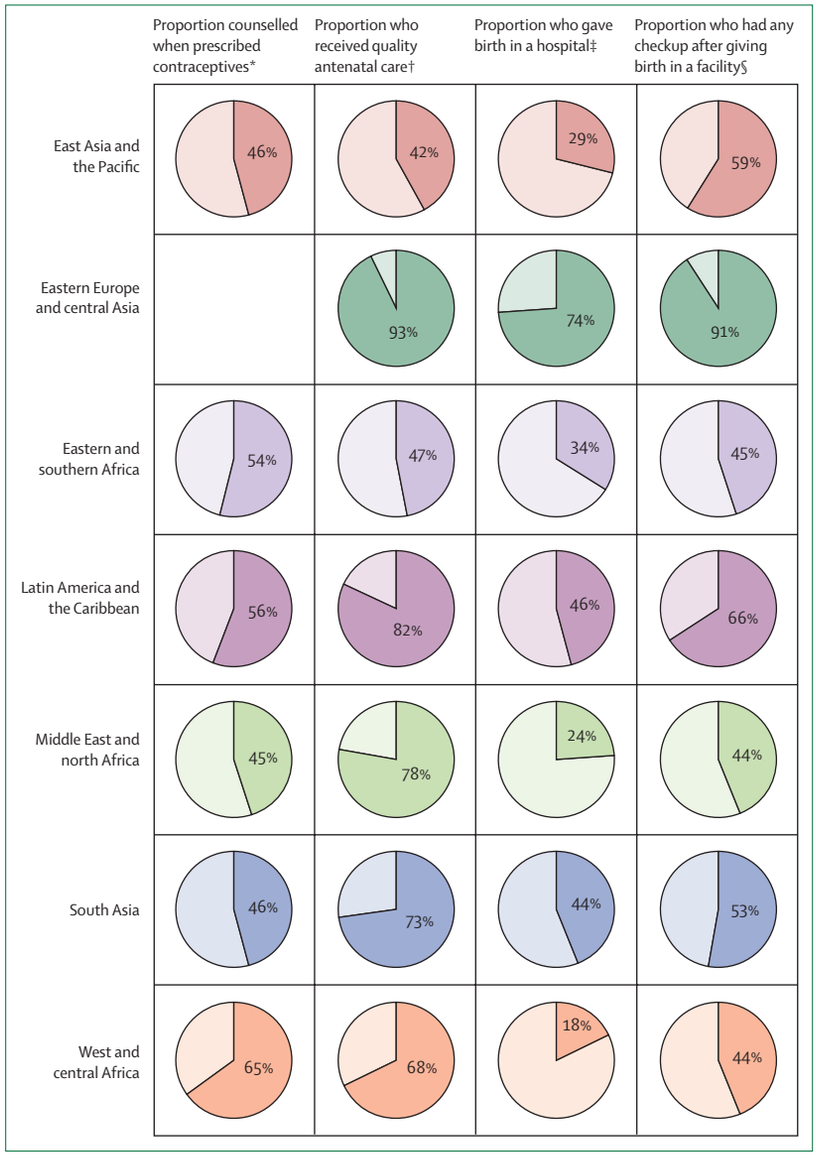

Figure 2: **Quality of reproductive health services for adolescent girls (aged 13–19 years) by region**
Data taken from the latest Demographic and Health Survey conducted in 58 countries between 2010 and 2018.[12] Country-level estimates are weighted using individual survey weights and regional averages are weighted according to each country's weighted sample size. Countries, survey years, and regional classification are available in the appendix (pp 4–10). *Proportion of adolescent girls who were informed about potential side-effects when first prescribed the modern contraceptive method they were using. In each country in eastern Europe and central Asia, the surveys included fewer than 25 adolescent girls who obtained a modern contraceptive method; therefore, that region was not included. †Proportion of adolescent girls who had their blood pressure checked, and urine and blood taken at any point during pregnancy. ‡Proportion of adolescent girls who gave birth in a hospital according to the facility categories used in the Demographic and Health Survey. §Proportion of adolescent girls who had any health checkup by a health provider (ie, by asking questions or examining them) after giving birth in any facility before discharge.

Childhood and adolescence: injuries, trauma, and disability

More than 5% of children from birth to age 14 years live with a moderate or severe disability.[39] In Africa, war and unintentional injuries are the second leading cause of disability in children.[40] Prevalence of traumatic brain injuries is disproportionally concentrated in LMICs; the odds of dying from this type of injury in Uganda are more than four times higher than are those in high-income countries (HICs).[41] Comprehensive injury care requires high-quality care across the health system, including prehospital care at the scene of the injury, transport to a trauma centre, an effective emergency department, operating room, intensive care unit, and rehabilitation services, which comprise a set of services not often available in LMICs.[42] A survey of surgical hospitals in Zambia showed that only 14% of hospitals met the minimum criteria for paediatric surgical safety.[43] Weak triage and delayed surgical interventions were blamed for the excess mortality from traumatic brain injury in Uganda.[41]

Childhood and adolescence: mental health

Mental health disorders, such as anxiety and depression, conduct disorders, and substance use, are an important contributor to poor health in children and adolescents.[4] Gender-based violence is distressingly common and often leads to severe mental health sequelae.[44] In adolescents globally, suicide is the second most common cause of death.[33,45] Preventive interventions can build mental health literacy, promote timely help seeking, reduce stigma, and decrease disparities when targeted to groups at high risk.[33] Interventions need to be age-sensitive, given that risk factors and incidence shift across the life course.[46] Despite the frequently early age of onset of incident mental disorders, children and adolescents access mental health services less frequently than do any other age group.[33,47] To compound this situation, mental health services for children and adolescents worldwide are frequently unavailable, underfunded, or of poor quality.[33,48]

Childhood and adolescence: cancer

80% of children and adolescents with cancer globally live in LMICs, where access to high-quality care is scarce.[49] For example, for treatable cancers that predominantly affect young children (eg, neuroblastoma), mean 5-year survival rates range from 6·7% in Africa and 24·5% in Asia to more than 80% in North America.[50] Overall, 5-year survival rates for children in HICs are much higher than for those in LMICs (80% *vs* 30%).[51,52] Poor cancer outcomes for children in LMICs are due to delayed presentation and diagnosis, misdiagnosis or underdiagnosis, scarcity of specialised facilities and providers, treatment toxicity, treatment abandonment, excess relapse, drug shortages, and high prevalence of comorbidities (eg, malnutrition).[52–55] Family poverty has a negative effect on adherence to treatment for paediatric cancer.[56–58] Furthermore, children in LMICs have poor access to palliative care.[49,52]

Adolescence: sexual and reproductive health

Delaying early pregnancy (ie, before age 18 years) is crucial for improving maternal and child health and social wellbeing, yet 66 million women aged 20–24 years were married before age 18 years between 2003 and 2016.[59,60] In LMICs, adolescent girls are less likely to use modern contraceptives than are older women (appendix p 3).[59]

Beyond access to family planning services, the quality of these resources remains poor in many LMICs for both adolescents and older women. When prescribed contraceptives, only 45–65% of adolescent girls reported being appropriately counselled on potential side-effects (figure 2). In addition, only a small proportion of adolescent girls in LMICs give birth in a hospital, ranging from 18% in west and central Africa to 74% in eastern Europe and central Asia (figure 2). These findings are concerning because adolescent girls are at higher risk of complications than are older women. As well as adolescent girls, adolescent boys have been neglected in the areas of sexual and reproductive health and parenthood.[61,62]

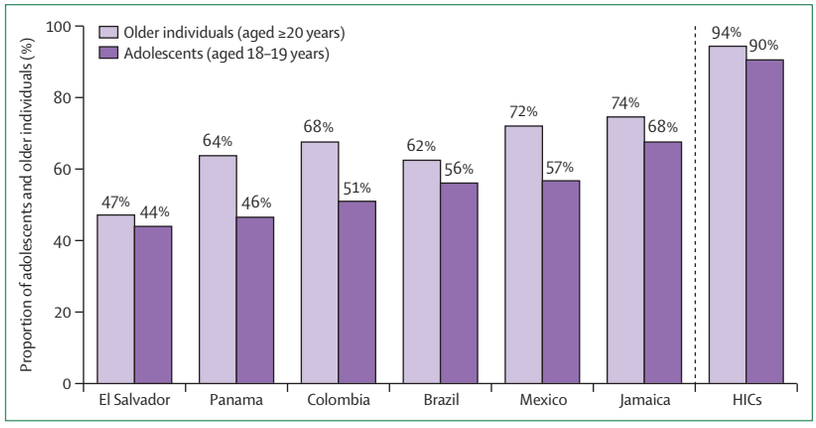

Figure 3: **Proportion of adolescents and older individuals across middle-income countries in Latin America and the Caribbean, and HICs who report having a regular doctor or usual place for medical care**
Data in six middle-income Latin American and Caribbean countries taken from the Inter-American Development Bank survey conducted in 2013 on primary care access, use, and quality.[69] Data for HICs taken from the International Health Policy Survey conducted by the Commonwealth Fund across 11 HICs in 2013.[70] Country-level estimates are weighted using individual survey weights. Countries, survey years, income groups, and regional classification are available in the appendix (p 11). HICs=high-income countries.

Health system quality for children and adolescents: user experience, confidence, and financial burden

User experience

Positive user experience in the health system requires both respectful care and care that is person-centred, family-friendly, and easy to navigate.[3] However, children and their caregivers often struggle to navigate health systems.[38,63] In eight countries (DR Congo, Ethiopia, Haiti, Kenya, Malawi, Nepal, Senegal, and Tanzania), a quarter of caregivers bringing sick children to facilities reported problems with wait times and availability of medicines. More than 10% of caregivers had problems with the amount of explanation received from providers, their ability to discuss problems, the cleanliness and hours of operation of the facility, or the cost of the services (appendix p 12). Of note, caregivers often under-report problems due to courtesy bias and low expectations.[64]

Adolescents particularly value accessible services, friendly and respectful providers, clear communication, medical competency, confidentiality, age-appropriate environment, involvement in decisions, and positive health outcomes.[65] Their experience is often far from optimal, especially for adolescents who are sexually active, pregnant, unmarried, or from low-income families, and who commonly face disrespect and mistreatment.[66] This situation is similar during labour and delivery, with adolescent girls at higher risk of mistreatment than older women.[66,67] In four countries (Ghana, Guinea, Myanmar, and Nigeria), more than a third of women faced verbal and physical abuse, stigma, or discrimination during labour.[66,67] In turn, mistreatment deters future care seeking.[68] Furthermore, although high-quality, person-centred care requires having a regular doctor or place of care, adolescents are less likely to report having a usual source of care than are older individuals (figure 3).

Confidence in health systems

Negative experiences with health care can result in mistrust of the health system and can reduce care seeking, retention, and adherence to treatment.[3] Across 17 LMICs, between 7% and 47% of adolescent respondents agreed that their health system worked well and that only minor changes were needed to improve it, compared with 59% of adolescents across 11 HICs (figure 4A).[63] Compared with adolescents in HICs, far fewer adolescents in LMICs reported being somewhat or very confident in their ability to receive the care they needed from their health system (figure 4B).

Preventing financial hardship

An important function of high-quality health systems is to reduce financial hardship from care seeking, including impoverishment, catastrophic spending, borrowing money with high interest rates, and household asset sales.[71,72] Removal of fee exemptions for health system users in Africa resulted in immediate increases in care use; however, in many cases, informal, drug, and transport payments still caused substantial financial hardship.[73–75] Several studies have identified substantial financial harms from undergoing a caesarean section and its cost is a barrier to health care use.[76–79] Although insurance can reduce financial hardship, little evidence is available about its effects on children. A 2019 systematic review found that no studies had addressed the effects of health insurance on children or adolescents with chronic conditions in LMICs.[80] Issues that need to be addressed

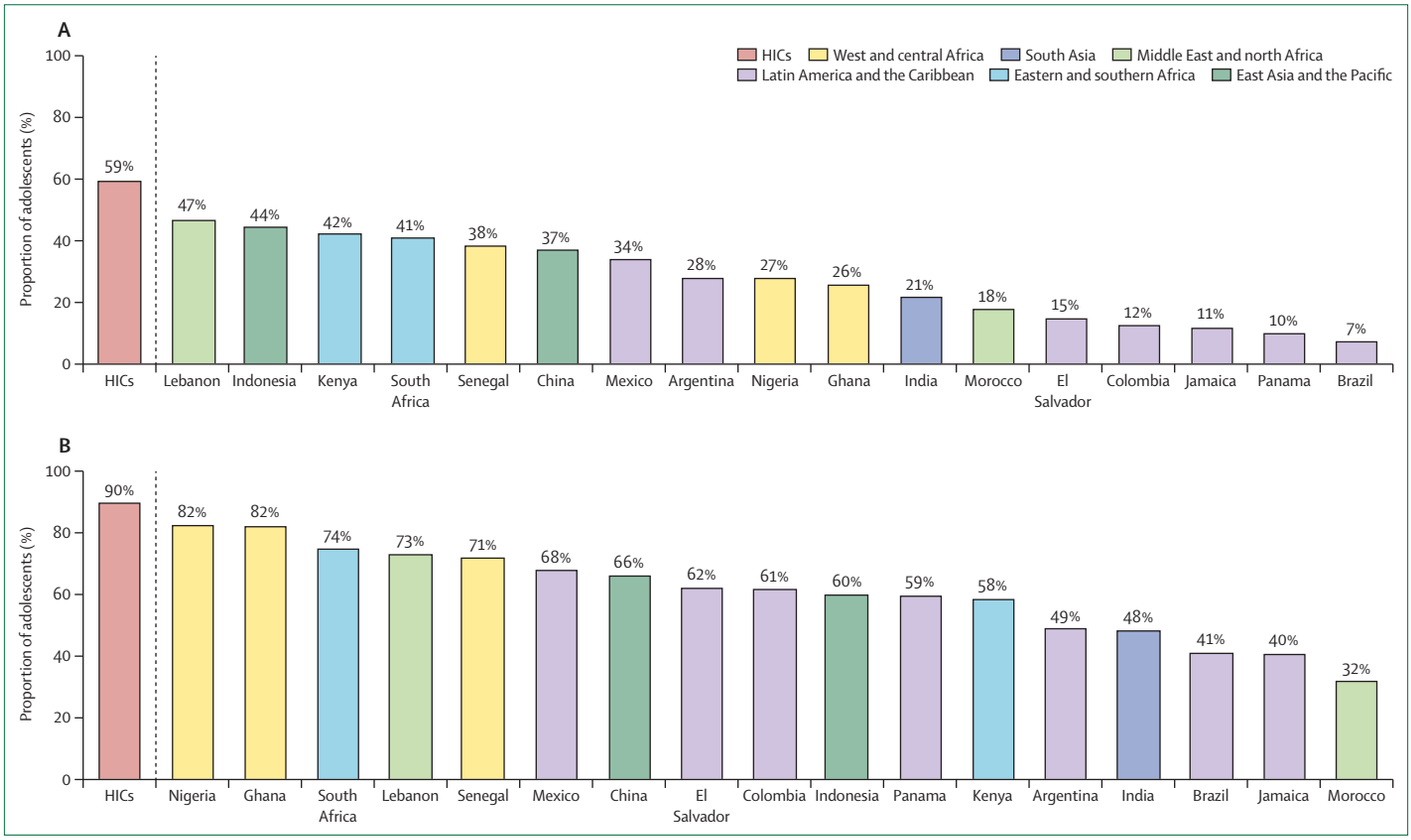

Figure 4: **Endorsement and confidence in health systems among adolescents (aged 18–19 years) in 17 LMICs and 11 HICs**
Proportion of adolescents who agreed that their health system worked pretty well and that only minor changes were needed (A) and who were confident that they could get the care they needed if they got sick the following day (B). Data for LMICs taken from a nationally representative survey conducted by the Inter-American Development Bank on primary care access, use, and quality across five middle-income Latin American and Caribbean countries in 2013[69,70] and an internet survey conducted by *The Lancet Global Health* Commission on high-quality health systems in the Sustainable Development Goals era across 12 LMICs in 2017.[3] Data for HICs taken from the International Health Policy Survey conducted by the Commonwealth Fund across 11 HICs in 2013. Country-level estimates are weighted using individual survey weights. Countries, survey years, income groups, and regional classification are available in the appendix (p 11). HICs=high-income countries. LMICs=low-income and middle-income countries.

in insurance design include the scope of child and adolescent services and the maximum age that adolescents can remain on parental insurance for countries with social insurance systems.

Social system performance for children and adolescents: family, community, and school

Family support programmes

Health systems alone cannot address all child and adolescent health needs. At different ages, children and adolescents might be more readily and effectively reached through other social touchpoints to improve health.

Conditional cash transfer programmes aim to improve health and wellbeing by incentivising use of essential health care, promoting nutrition, and encouraging children from low-income families to attend school. These programmes have reduced the mortality rate of children younger than 5 years and improved other health outcomes in Brazil, India, Mexico, and other countries, generally with the greatest effects in children from families with the lowest income.[81,82]

Parenting support programmes aim to target risks to child health and development, while improving relationships between parents and children.[83,84] Research shows that, when delivered in the first 5 years of life, these programmes have consistent small-to-medium sized effects on cognitive, language, motor, and socioemotional development.[9,85,86] Additionally, these programmes can enhance caregiver knowledge, improve interactions between parents and children, and reduce parental violence against children.[87,88]

Community health workers (CHWs) and community groups

CHWs are community members who have received training in basic health services and who provide health education, screening and treatment of some conditions, and community mobilisation.[89–92] A review of care delivered by CHWs showed reductions in perinatal and neonatal mortality, as well as benefits to mental health and early childhood development.[93] Studies from Africa show that CHWs might be able to treat uncomplicated cases of

pneumonia, malaria, and diarrhoea.[94,95] However, the quality of care provided by CHWs, especially for more complex curative services, is variable and often low.[96–100] For example, an evaluation in Ethiopia found that health extension workers correctly managed only 34% of children with severe illness, and that there was no effect on mortality.[99] Most CHWs are women, are generally unpaid, and are often poorly supported by health systems.[101]

Community groups, in which community members analyse their situation and translate solutions into action, can improve maternal and neonatal health.[102] A Cochrane review found that community support or women's groups reduced perinatal mortality by 12%, neonatal mortality by 16%, and early neonatal mortality by 24%, identifying improved care seeking in facilities as an important driver.[93] The positive effects of women's groups depend on the existence of strong local social networks.[102] Little is known about family and community approaches to foster health in middle childhood (age 5–14 years) and adolescence, despite evidence from neuroscientific and psychological research suggesting that intervening in this period can help to support healthy development.[103]

Schools

Education is one of the strongest determinants of health and human capital, and has intergenerational benefits.[104] The longer a child spends in school, the greater their potential for health improvement. Early childhood education has large benefits on cognitive development and small benefits on socioemotional development of children.[9] A study exploring the association between educational attainment and health outcomes in young people (aged 15–24 years) found major reductions in national adolescent fertility, all-cause mortality, and HIV prevalence with an increase in the number of years in school.[105] These benefits were greatest in south Asia and sub-Saharan Africa.

Additionally, schools are a platform to deliver specific health programmes. School health services are provided in over 100 countries globally and include vaccination, nutrition, disease screening, treatment (eg, vision screening and mental health counselling), and referral.[106,107] There is much interest in whether school health services can overcome the challenges faced by children, and especially by adolescents, in accessing quality health services, and requires further evaluation.[108]

Structural improvements and innovations in health and social systems

Improving the quality of health systems can be pursued at three levels: macro (ie, system-wide), meso (ie, region, area, or community), and micro (ie, clinic, provider, or individual user). Most attempts to improve system quality in LMICs have been at the micro level; however, many of these strategies have yielded disappointing results. A large review found that job aids or new technologies for providers were ineffective, whereas training and supervision had, at best, moderate effects.[109] Additionally, these programmes are difficult to scale and sustain over time. Of note, no HICs have relied on quality improvement as the primary mechanism for building high-quality health systems.

Because health systems are complex adaptive systems that require clear aims, adequate resources, and enforced prohibitions against substandard care, structural approaches (ie, macro-level and meso-level) are more promising for building high-quality systems. Macro-level approaches intervene on the social, political, economic, and organisational structures that shape the health system, whereas meso-level approaches intervene on the subnational level across regions, districts, and networks of facilities or communities. *The Lancet Global Health* Commission on high-quality health systems[3] proposed four such approaches: governing for quality, reforms to clinical education, redesign of service delivery to maximise quality, and increased involvement of people. We present high-potential macro-level strategies in three of these areas (ie, governance, service redesign, and empowering people) to improve neonatal, child, and adolescent health across health and social sectors.

Governing for quality

Good governance is a prerequisite for high-quality health systems. Well performing health systems manifest at least two interlinked functions: learning and strong leadership and management. These functions aim to promote a culture of performance and accountability to the population and to payers, including governments and insurers.[110]

Leadership, management, and coordination

Effective leadership and management require clear goals for each level of the health system; health managers who are professional and competent, and health providers that are incentivised with intrinsic and extrinsic motivators. One crucial leadership decision is the degree of specialisation and competence expected of providers for infants, children, and adolescents. Increased numbers of highly competent providers—generalists and specialists alike—will be needed in the coming decades.[111,112]

In particular, subnational health systems have a scarcity of managers with data, analytical, and planning capacity, which inhibits priority setting and quality management. This situation is especially acute as more countries devolve health sector governance. Health system management is a specialised area that requires dedicated training.[113,114] In Ghana, management capacity in district health managers was significantly higher in high-performing districts than in low-performing districts; managers in high-performing districts had better communication, teamwork, and organisational commitment.[115] In South Africa, monitoring and response units involved managers and clinicians from a

cross-section of the health system to implement joint actions to improve maternal, neonatal, and child health.[116] In Pakistan, optimising the nutrition and development of children across sectors required policy makers and managers to recognise and use policy windows, to have a clear and specific agenda of actions and coalitions, to seek cofinancing and shared platforms, and to integrate human resources and tracking systems.[117]

Health systems are often hampered by vertical projects led by multiple actors, such as governments, non-governmental organisations, donors, and researchers,[118] which complicate effective management. These projects often do not have domestic budgets and supervision. Institutionalising and scaling new projects to realise health gains will require strong central leadership that demands programmatic coherence in the health system, greater decision space for district leaders, accountability mechanisms, increased stewardship by local leadership instead of external partners, and the ongoing involvement of community and district actors.

Learning health systems

High-quality health systems are learning health systems because they analyse their performance and use data to improve and innovate.[119] Health systems in HICs use standardised data sources, such as national clinical registries (eg, perinatal, neonatal, paediatric, or cancer registries), audits, and mortality or morbidity reviews, to compare and improve outcomes across facilities and regions.[120] Most HICs use a combination of routine and periodic data collection from multiple sources to monitor and enhance health system performance. Learning systems need individual patient data, yet most health management information systems operating in LMICs nowadays provide aggregate data only. Platforms established to track patient-level care and outcomes for HIV and immunisation programmes in many LMICs could be a useful model.[121] The foundation of health system learning and accountability is a civil registration and vital statistics system, still far from complete in many countries globally.

Redesigning service delivery

Redesigning service delivery is a structural reform that rationalises the health system so that services are provided at the right level, by the right provider, and at the right time to optimise process quality and outcomes.[3] This redesign can mean shifting services from one level of the health system to another or out of the health system to social platforms. Universal health coverage reforms might offer an opening for designating the correct platform for service delivery.

Service delivery redesign for neonatal health and COVID-19 service shifts

Despite increased use of facilities for childbirth, reductions in neonatal mortality and morbidity have stagnated in many LMICs.[122–124] This situation might be because 30–45% of facility deliveries occur below the level of a hospital, in primary-care facilities that cannot effectively handle complications.[125–127] Redesign to reduce neonatal and maternal mortality is a model in which all deliveries occur in either health-care facilities that can provide advanced obstetric and neonatal care in the case of complications (eg, caesarean section, blood transfusion, and care for sick mothers and newborn babies) or in nearby affiliated birthing facilities, while primary-care facilities provide quality antenatal, postnatal, and neonatal care. This model is the predominant approach in HICs and most middle-income countries.[128–130] It is essential to develop locally appropriate models and to avoid overcrowding hospitals and unnecessary interventions, which can be done by placing birthing units that are led by midwives onsite or nearby, as in South Africa.[131]

Important innovations in service delivery are occurring in real time as a result of the COVID-19 pandemic, including a shift from clinic visits to telehealth, the use of primary care to detect infection, and the upgrading of hospitals and health centres with intensive care capability.[132–135] These natural experiments need to be studied to yield insights for future health system responses to public health emergencies.[136,137]

Whole-school approaches to promoting health

In addition to specific school-based health programmes, the health-promoting school framework provides a whole-school approach to strengthening the capacity of schools as a healthy setting for living.[138] Whole-school approaches concurrently address health within the school curriculum, promote health through changes to social and physical environments at school, and engage with families and communities.[138] Consistent with this approach, a study of 75 secondary schools in Bihar, India, found that a whole-school approach had large effects on school climate, depressive symptoms, bullying, violence perpetration and victimisation, attitudes towards gender, and knowledge of reproductive and sexual health.[139]

Community outreach to tackle mental health and to support nurturing care

Increasing evidence suggests that CHWs can provide mental health and social services to parents, children, and adolescents.[140–143] These services are frequently unavailable from nearby health facilities.[143] CHWs in rural areas of HICs can provide various mental health services, including visits for pregnant women, support for parents of young children and adolescents with mental health disorders or stress management, and counselling or referral for substance misuse, domestic violence, depression, and anxiety.[144] A systematic review in LMICs found that the provision of psychosocial interventions by CHWs was effective in reducing perinatal mental disorders and improving interactions between mother and infant; child cognition, development, and growth; and immunisation

rates.[142] Successful provision will require additional training and compensation of CHWs and the development of clear links to formal care for serious cases.[145] COVID-19 and attendant school closures resulted in a surge of cases of psychological distress in children and adolescents in LMICs, leading to calls to substantially expand mental health services in and outside of the health system, including through community and digital approaches.[146]

Turning phones into health assistants

Health interventions can be delivered to mothers, children, and adolescents through various digital and mass communication platforms, including radio, television, mobile phones, and the internet. A systematic review of eight meta-analyses (mostly from HICs) supported the effectiveness of digital platforms to augment quality of care for depression and anxiety in children and adolescents, with child age, illness severity, and clinician outcome identified as key moderators of effect size.[147]

There is more evidence from LMICs on mobile health interventions. Automated telephone communication systems can improve health-related behaviours, clinical outcomes, health service use, immunisation, screening, appointment attendance, and adherence to medications and testing.[148] A review of mobile health interventions in LMICs found improved rates of early and exclusive breastfeeding.[149,150]

Use of digital and mobile technologies has increased over the COVID-19 pandemic.[151,152] For example, in South Africa, nearly 30 000 trained CHWs are using a mobile health platform for community screening, referral for testing, and communication of results. In Kenya, the incentive to make cashless health-care payments via mobile phone has been expanded to help prevent the transmission of SARS-CoV-2. In Uganda, SMS-based virtual care has been used to monitor COVID-19 cases and contacts.[134]

Services delivered through digital technology and mobile phones need careful assessment before they are expanded, or before current care models are replaced, to identify effects on outcomes, care processes, cost, and equity, as well as both beneficial and detrimental system-wide effects (eg, reductions in needed in-person care).

Empowering families: raising the capacities and expectations of parents, children, and adolescents

A potentially large opportunity for improving child health is through encouraging families and adolescents to take a greater role in their health and to apply pressure on the health and social systems around them to improve service quality. Activated patients, defined as having "the skills and confidence that equip patients to become actively engaged in their health care",[153] report improved health outcomes and care experiences. Activation can be hindered by a paucity of power and knowledge, and by low expectations shaped by chronic exposure to low-quality health systems.[154]

Panel: Engaging fathers to empower families and optimise child health and wellbeing

In the past 5 years, several innovative interventions have shown the effectiveness and promise of engaging fathers for improving caregiving practices and early child outcomes within health and social systems.

First, Doyle and colleagues[161] investigated the effects of a community group-based intervention in Rwanda, which engaged fathers and their respective partners with a child younger than 5 years. The intervention addressed fatherhood, communication and decision making between the couple, male engagement in maternal and child health, and violence prevention. Results from the randomised controlled trial found improvements in women's attendance of and men's accompaniment at antenatal care visits, paternal engagement in household responsibilities, relationships between couples, and reductions in paternal violence against women and children.

Second, Rempel and colleagues[162] studied a community health intervention in Vietnam, which engaged couples expecting a child through prenatal group sessions at health clinics and postnatal home visits. These sessions were delivered by community health workers until infants reached age 9 months. The intervention also broadcasted weekly radio messages over community loudspeakers and included fathers' clubs to enhance peer support. Results from the quasi-experimental study found improvements in paternal support and responsiveness to maternal needs, exclusive breastfeeding duration, quality of couple relationships, and infant motor, language, and social development.

Building parental capacities to care for children from the earliest years of life

The nurturing care framework promotes multi-input interventions, comprising health, nutrition, responsive caregiving, safety and security, and early learning, delivered by or in coordination with health services.[155] Parenting interventions can improve the nurturing environment, which in turn boosts children's cognitive and socioemotional development. These interventions have been effectively delivered via community health services through home visits and parenting groups, and in primary health services.[86,156–159] However, to date, family-based programmes for children have exclusively focused on mothers and overlooked fathers as parents and partners.[160] Engaging with and supporting fathers can empower families to optimally care for and promote child health, nutrition, and development (panel). Similarly, more attention is warranted in LMICs to build parental skills in promoting adolescent wellbeing.

For young children facing multiple adversities, a multisector approach is needed. One of the few programmes currently delivered at scale is the *Chile Crece Contigo*, which targets interventions from

pregnancy through the first 4 years of life in partnership with health departments, social development, and education sectors.[163] Key reasons for the success of this initiative are a shared vision, high-level political leadership, and a permanent line in the national budget. An evaluation of this cost-effective programme reported a decrease in the prevalence of developmental delay in children over 10 years. Furthermore, multisectoral and community-engaged programmes can reduce gender-based violence and help to prevent victimisation of adolescent girls.[44]

Engaging parents, children, and adolescents in prevention and self-management

Schools can help to build self-management skills for children and adolescents with chronic physical or mental health conditions. School-based programmes for the self-management of children with asthma reduced emergency department visits and hospital admission rates.[164] Interventions promoting self-management might improve children's lung function, glycaemic control, and symptoms of anxiety and depression.[165–168] Self-management of HIV in adolescents might increase adherence to care; however, outcomes vary across settings.[44] To date, most studies have originated in HICs, limiting generalisability to LMICs. To yield health gains, self-management interventions require coordination with existing services, a supportive local sociopolitical context, and an enabling environment.[169]

Empowering families to raise their expectations of health systems

A well informed population, which is engaged in the design of health systems and in providing feedback, is a vital asset in building high-quality systems.[3] Families (and adolescents) with low expectations of care have reduced agency in their interactions with providers.[3] Informing communities of what they should expect ahead of a visit can empower people to demand quality care. One way to empower communities is through participatory women's and youth groups.[170,171] Mobile messaging can also be effective. MomConnect, a programme established in South Africa to promote safe motherhood and a healthy pregnancy, used a two-way messaging platform in which mothers received information on patient rights, and could ask questions and provide feedback on quality of care. The programme is widely used and has improved the health system's response to the needs and expectations of expectant mothers.[172–174]

Conclusions

Over the past three decades, health systems in LMICs have achieved important health gains; however, as mortality rates fall and expectations rise, reforms are needed to meet the greater scope and complexity of health needs for newborn babies, children, and adolescents. Beyond health systems, a multisectoral approach is essential for and consistent with achieving the Sustainable Development Goals. Accountability is central to success: both health and social systems for children should be subject to high performance standards and be responsive to their communities.

As countries look beyond 2022, the landscape of neonatal, child, and adolescent health is rapidly shifting. The clinical effects of COVID-19 on the health and wellbeing of this population, particularly in the long term, are not fully known.[175] However, disruption to health services, including interruptions to preventive activities (eg, vaccination and nutritional programmes) and decreased attendance at clinical appointments, is likely to result in excess mortality and morbidity for infants, children, and adolescents, undermining hard fought gains in recent years.[137,176,177] This situation is compounded by an economic crisis, which has led to more families falling into poverty and facing food insecurity, and by an estimated 1·5 billion children and adolescents being out of school, which can have adverse economic consequences and an increased risk of child marriage, among other concerns.

In this fourth paper of the Series, we have proposed a shift from individual-level or clinical-level approaches to macro-level reforms that span not only the health system but also other social systems. We call for stronger leadership and governance in health, education, and social systems that are jointly focused on the health needs of children and engaged in ongoing learning; a redesign of health systems to optimise quality, right-place services by competent providers rather than contacts or proximity; and multisector actions to empower families and communities to take greater charge of their health and to demand better quality from their health systems.

Supporting structural change and monitoring progress requires agile, accurate measurements and robust research into health systems. We found substantial gaps in data on the health needs of children and adolescents. Available data are not collected in a timely fashion and do not capture all critical threats to health across the life course, nor of morbidity and physical function. Without a comprehensive measurement framework for child and adolescent health and wellbeing, as well as major investments in locally collected, reliable, and disaggregated data, substantial progress will be elusive. Rigorous and generalisable research into health systems across LMICs is scarce, despite decades of investments into improving child health. More implementation science research of higher quality to study care models and the conditions required for their implementation will be essential to inform reforms and to reduce expensive mistakes.

Although the agenda outlined in this Series paper will benefit from global support, success will be foremost determined by high-level domestic political

commitment and investment. The focus on universal health coverage and the reassessment of care models accelerated by COVID-19 provides an opportunity to think anew about what it will take to change the futures of children today.

Contributors

MEK, TPL, and CA designed the study and planned the data analyses. MEK, TPL, and CA verified the underlying data and CA 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.

Declaration of interests

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