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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This is the third in a **Series** of four papers about optimising child and adolescent health and development

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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.

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

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).

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

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See **Online** for appendix

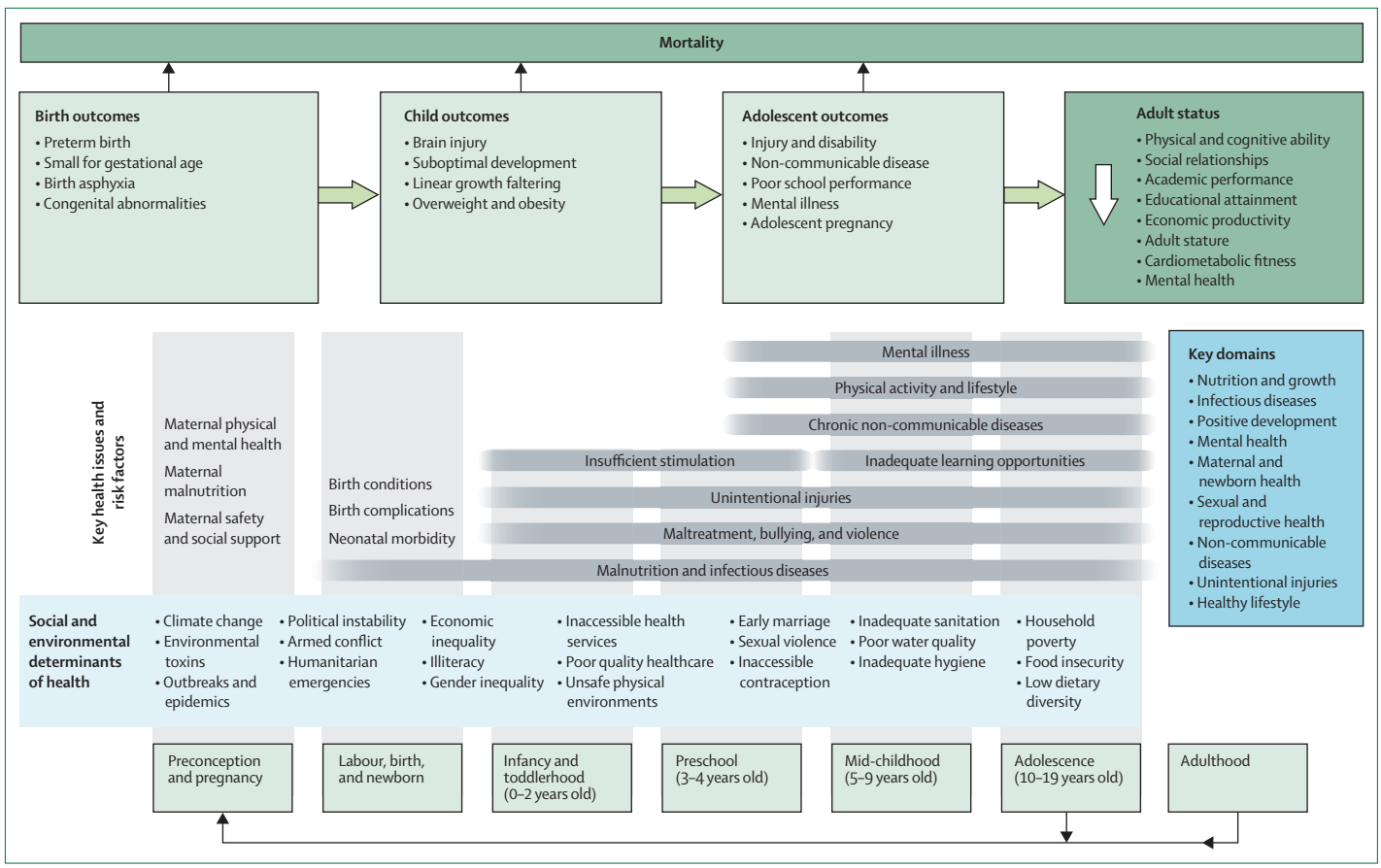

Figure 1: **Conceptual framework of risk factors and opportunities for intervention across the life course**

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]

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

	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)

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]

	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.**

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]

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]

	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 0·49 (0·27 to 0·87)
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 0·36 cm (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**

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 hand-held devices and internet-based learning) present

	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 on key outcomes in 5–9-year-olds and 10–19-year-olds**

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 relationships, resilience, and healthy coping strategies.

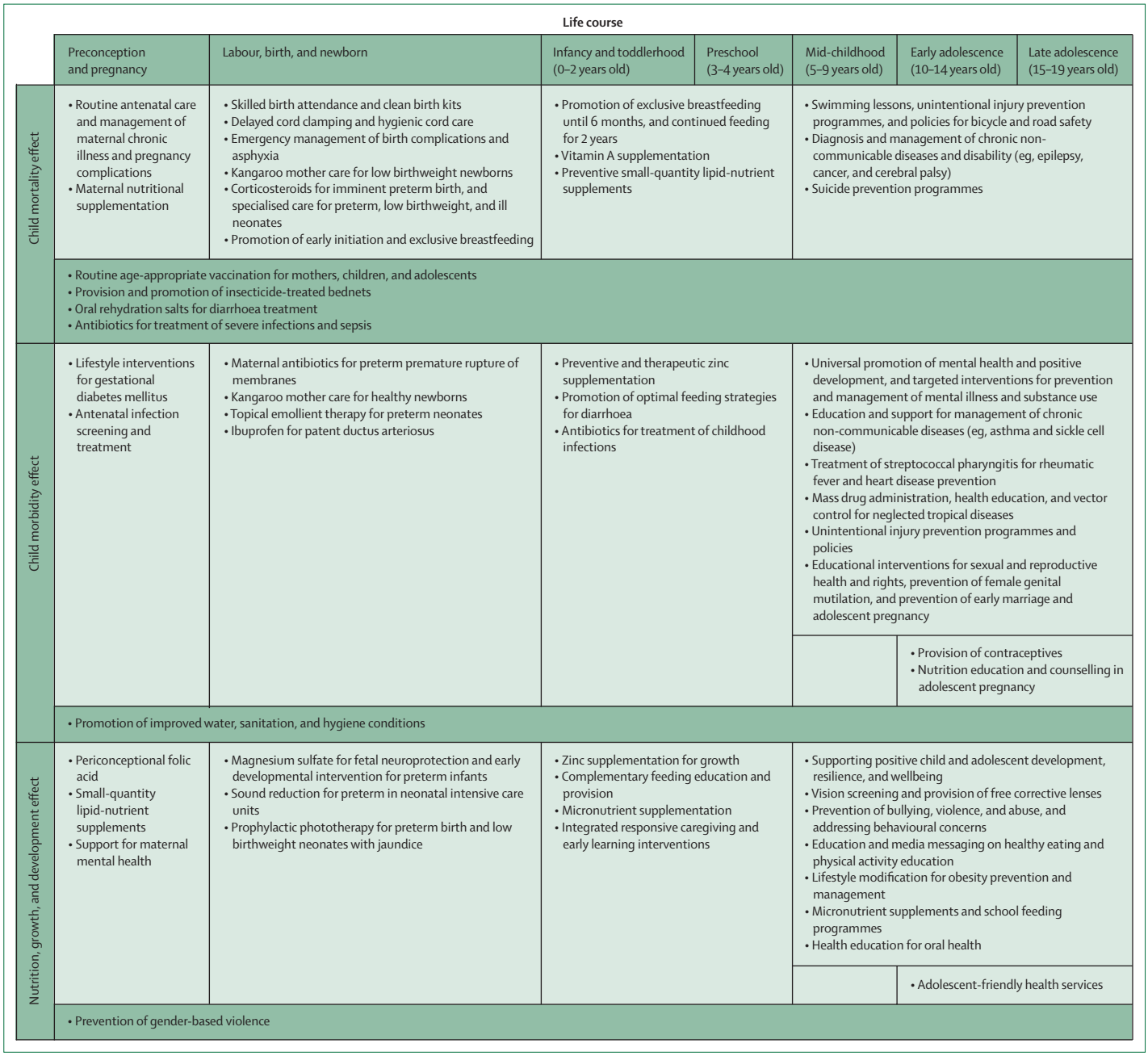

***Figure 2*: Intervention packages by age group and effect on mortality, morbidity, nutrition, growth, and development**
More detail is provided in the appendix (p 4).

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

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]

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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References

1 Black RE, Liu L, Hartwig FP, et al. Health and development from preconception to 20 years of age and human capital. *Lancet* 2022; published online April 27. https://doi.org/10.1016/S0140-6736(21)02533-2.

2 Victora CG, Hartwig FP, Vidaletti LP, et al. Effects of early-life poverty on health and human capital in children and adolescents: analyses of national surveys and birth cohort studies in LMICs. *Lancet* 2022; published online April 27. https://doi.org/10.1016/S0140-6736(21)02716-1.

3 Kruk ME, Lewis TP, Arsenault C, et al. Improving health and social systems for all children in LMICs: structural innovations to deliver high-quality services. *Lancet* 2022; published online April 27. https://doi.org/10.1016/S0140-6736(21)02532-0.

4 United Nations. The Millennium Development Goals Report 2015. 2015. http://mdgs.un.org/unsd/mdg/Resources/Static/Products/Progress2015/English2015.pdf (accessed Jan 29, 2021).

5 Heidkamp R, Piwoz E, Gillespie S, et al. Mobilising evidence, data, and resources to achieve global maternal and child undernutrition targets and the Sustainable Development Goals: an agenda for action. *Lancet* 2021; **397:** 1400-18.

6 The WHO–UNICEF–Lancet Commissioners. After COVID-19, a future for the world's children? *Lancet* 2020; **396:** 298–300.

7 Akseer N, Kandru G, Keats EC, Bhutta ZA. COVID-19 pandemic and mitigation strategies: implications for maternal and child health and nutrition. *Am J Clin Nutr* 2020; **112:** 251–56.

8 Roberton T, Carter ED, Chou VB, et al. Early estimates of the indirect effects of the COVID-19 pandemic on maternal and child mortality in low-income and middle-income countries: a modelling study. *Lancet Glob Health* 2020; **8:** e901–08.

9 Jones G, Steketee RW, Black RE, Bhutta ZA, Morris SS, Group BCSS. How many child deaths can we prevent this year? *Lancet* 2003; **362:** 65–71.

10 Patton GC, Azzopardi P. Missing in the middle: measuring a million deaths annually in children aged 5–14 years. *Lancet Glob Health* 2018; **6:** e1048–49.

11 Fadel SA, Boschi-Pinto C, Yu S, et al. Trends in cause-specific mortality among children aged 5-14 years from 2005 to 2016 in India, China, Brazil, and Mexico: an analysis of nationally representative mortality studies. *Lancet* 2019; **393:** 1119–27.

12 Ahmed SM, Rawal LB, Chowdhury SA, et al. Cross-country analysis of strategies for achieving progress towards global goals for women's and children's health. *Bull World Health Organ* 2016; **94:** 351–61.

13 Bishai DM, Cohen R, Alfonso YN, Adam T, Kuruvilla S, Schweitzer J. Factors contributing to maternal and child mortality reductions in 146 low-and middle-income countries between 1990 and 2010. *PLoS One* 2016; **11:** e0144908.

14 Kuruvilla S, Schweitzer J, Bishai D, et al. Success factors for reducing maternal and child mortality. *Bull World Health Organ* 2014; **92:** 533–44B.

15 Black R, Laxminarayan R, Temmerman M, Walker N. Disease control priorities, 3rd edn (vol 2): reproductive, maternal, newborn, and child health. Washington, DC: World Bank; 2016.

16 Bundy D, de Silva N, Horton S, Jamison D, Patton G. Disease control priorities, 3rd edn (vol 8): child and adolescent health and development. Washington, DC: World Bank; 2017.

17 Lassi ZS, Imam AM, Dean SV, Bhutta ZA. Preconception care: preventing and treating infections. *Reprod Health* 2014; **11** (Suppl 3)**:** S4.

18 Lassi ZS, Imam AM, Dean SV, Bhutta ZA. Preconception care: screening and management of chronic disease and promoting psychological health. *Reprod Health* 2014; **11** (suppl 3)**:** S4.

19 Lassi ZS, Kedzior SGE, Tariq W, Jadoon Y, Das JK, Bhutta ZA. Effects of preconception care and periconception interventions on maternal nutritional status and birth outcomes in low- and middle-income countries: a systematic review. *Nutrients* 2020; **12:** 606.

20 Oh C, Keats EC, Bhutta ZA. Vitamin and mineral supplementation during pregnancy on maternal, birth, child health and development outcomes in low- and middle-income countries: a systematic review and meta-analysis. *Nutrients* 2020; **12:** 491.

21 Lassi ZS, Padhani ZA, Rabbani A, et al. Impact of dietary interventions during pregnancy on maternal, neonatal, and child outcomes in low- and middle-income countries. *Nutrients* 2020; **12:** 531.

22 Demicheli V, Barale A, Rivetti A. Vaccines for women for preventing neonatal tetanus. *Cochrane Database Syst Rev* 2015; **7:** CD002959.

23 Dodd JM, McLeod A, Windrim RC. Antithrombotic therapy for improving maternal or infant health outcomes in women considered at risk of placental dysfunction. *Cochrane Database Syst Rev* 2013; **7:** CD006780.

24 Lassi ZS, Fisher Z, Andraweera P, Cummins A, Roberts CT. Effectiveness of birthing kits for clean childbirth: a systematic review. *Int Health* 2020; **12:** 3–10.

25 Dempsey E, Pammi M, Ryan AC, Barrington KJ. Standardised formal resuscitation training programmes for reducing mortality and morbidity in newborn infants. *Cochrane Database Syst Rev* 2015; **9:** CD009106.

26 Conde-Agudelo A, Díaz-Rossello JL. Kangaroo mother care to reduce morbidity and mortality in low birthweight infants. *Cochrane Database Syst Rev* 2016; **8:** CD002771.

27 Mekonnen AG, Yehualashet SS, Bayleyegn AD. The effects of kangaroo mother care on the time to breastfeeding initiation among preterm and LBW infants: a meta-analysis of published studies. *Int Breastfeed J* 2019; **14:** 12.

28 Tang Z, Wei Z, Wen F, Wu Y. Efficacy of zinc supplementation for neonatal sepsis: a systematic review and meta-analysis. *J Matern Fetal Neonatal Med* 2019; **32:** 1213–18.

29 Irfan O, Black RE, Lassi ZS, Bhutta ZA. Zinc supplementation and the prevention and treatment of sepsis in newborns and young infants: a systematic review and meta-analysis. *Neonatology* 2022; **1:** 1–12.

30 Duby J, Lassi ZS, Bhutta ZA. Community-based antibiotic delivery for possible serious bacterial infections in neonates in low- and middle-income countries. *Cochrane Database Syst Rev* 2019; **4:** CD007646.

31 Lassi ZS, Rind F, Irfan O, Hadi R, Das JK, Bhutta ZA. Impact of infant and young child feeding (IYCF) nutrition interventions on breastfeeding practices, growth and mortality in low- and middle-income countries: systematic review. *Nutrients* 2020; **12:** 722.

32 Moore ER, Bergman N, Anderson GC, Medley N. Early skin-to-skin contact for mothers and their healthy newborn infants. *Cochrane Database Syst Rev* 2016; **11:** CD003519.

33 Lassi ZS, Bhutta ZA. Community-based intervention packages for reducing maternal and neonatal morbidity and mortality and improving neonatal outcomes. *Cochrane Database Syst Rev* 2015; **3:** CD007754.

34 Lassi ZS, Kedzior SG, Bhutta ZA. Community-based maternal and newborn educational care packages for improving neonatal health and survival in low-and middle-income countries. *Cochrane Database Syst Rev* 2019; **11:** CD007647.

35 Smaill FM, Vazquez JC. Antibiotics for asymptomatic bacteriuria in pregnancy. *Cochrane Database Syst Rev* 2019; **11:** CD000490.

36 Iheozor-Ejiofor Z, Middleton P, Esposito M, Glenny AM. Treating periodontal disease for preventing adverse birth outcomes in pregnant women. *Cochrane Database Syst Rev* 2017; **6:** CD005297.

37 Sangkomkamhang US, Lumbiganon P, Prasertcharoensuk W, Laopaiboon M. Antenatal lower genital tract infection screening and treatment programs for preventing preterm delivery. *Cochrane Database Syst Rev* 2015; **2:** CD006178.

38 McGoldrick E, Stewart F, Parker R, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. *Cochrane Database Syst Rev* 2020; **12:** CD004454.

39 Middleton P, Shepherd E, Morris J, Crowther CA, Gomersall JC. Induction of labour at or beyond 37 weeks' gestation. *Cochrane Database Syst Rev* 2020; **7:** CD004945.

40 Crowther CA, Middleton PF, Voysey M, et al. Assessing the neuroprotective benefits for babies of antenatal magnesium sulphate: an individual participant data meta-analysis. *PLoS Med* 2017; **14:** e1002398.

41 Shepherd E, Salam RA, Middleton P, et al. Antenatal and intrapartum interventions for preventing cerebral palsy: an overview of Cochrane systematic reviews. *Cochrane Database Syst Rev* 2017; **8:** CD012077.

42 Kenyon S, Boulvain M, Neilson JP. Antibiotics for preterm rupture of membranes. *Cochrane Database Syst Rev* 2013; **12:** CD001058.

43 Rabe H, Gyte GM, Díaz-Rossello JL, Duley L. Effect of timing of umbilical cord clamping and other strategies to influence placental transfusion at preterm birth on maternal and infant outcomes. *Cochrane Database Syst Rev* 2019; **9:** CD003248.

44 Imdad A, Rehman F, Davis E, et al. Effect of synthetic vitamin A and probiotics supplementation for prevention of morbidity and mortality during the neonatal period. A systematic review and meta-analysis of studies from low- and middle-income countries. *Nutrients* 2020; **12:** 791.

45 Sharif S, Meader N, Oddie SJ, Rojas-Reyes MX, McGuire W. Probiotics to prevent necrotising enterocolitis in very preterm or very low birth weight infants. *Cochrane Database Syst Rev* 2020; **10:** CD005496.

46 Jacobs SE, Berg M, Hunt R, Tarnow-Mordi WO, Inder TE, Davis PG. Cooling for newborns with hypoxic ischaemic encephalopathy. *Cochrane Database Syst Rev* 2013; **1:** CD003311.

47 Ho JJ, Subramaniam P, Davis PG. Continuous positive airway pressure (CPAP) for respiratory distress in preterm infants. *Cochrane Database Syst Rev* 2020; **10:** CD002271.

48 Ardell S, Pfister RH, Soll R. Animal derived surfactant extract versus protein free synthetic surfactant for the prevention and treatment of respiratory distress syndrome. *Cochrane Database Syst Rev* 2015; **8:** CD000144.

49 Cleminson J, McGuire W. Topical emollient for preventing infection in preterm infants. *Cochrane Database Syst Rev* 2021; **5:** CD001150.

50 Okwundu CI, Okoromah CA, Shah PS. Prophylactic phototherapy for preventing jaundice in preterm or low birth weight infants. *Cochrane Database Syst Rev* 2012; **1:** CD007966.

51 Barker M, Dombrowski SU, Colbourn T, et al. Intervention strategies to improve nutrition and health behaviours before conception. *Lancet* 2018; **391:** 1853–64.

52 Fleming TP, Watkins AJ, Velazquez MA, et al. Origins of lifetime health around the time of conception: causes and consequences. *Lancet* 2018; **391:** 1842–52.

53 Keenan K, Hipwell AE, Class QA, Mbayiwa K. Extending the developmental origins of disease model: impact of preconception stress exposure on offspring neurodevelopment. *Dev Psychobiol* 2018; **60:** 753–64.

54 Stephenson J, Heslehurst N, Hall J, et al. Before the beginning: nutrition and lifestyle in the preconception period and its importance for future health. *Lancet* 2018; **391:** 1830–41.

55 Radeva-Petrova D, Kayentao K, ter Kuile FO, Sinclair D, Garner P. Drugs for preventing malaria in pregnant women in endemic areas: any drug regimen versus placebo or no treatment. *Cochrane Database Syst Rev* 2014; **10:** CD000169.

56 Lassi ZS, Ana A, Das JK, et al. A systematic review and meta-analysis of data on pregnant women with confirmed COVID-19: clinical presentation, and pregnancy and perinatal outcomes based on COVID-19 severity. *J Glob Health* 2021; **11:** 05018.

57 Brown J, Alwan NA, West J, et al. Lifestyle interventions for the treatment of women with gestational diabetes. *Cochrane Database Syst Rev* 2017; **5:** CD011970.

58 Alfirevic Z, Stampalija T, Dowswell T. Fetal and umbilical Doppler ultrasound in high-risk pregnancies. *Cochrane Database Syst Rev* 2017; **6:** CD007529

59 Alfirevic Z, Stampalija T, Medley N. Cervical stitch (cerclage) for preventing preterm birth in singleton pregnancy. *Cochrane Database Syst Rev* 2017; **6:** CD008991.

60 Eleje GU, Eke AC, Ikechebelu JI, Ezebialu IU, Okam PC, Ilika CP. Cervical stitch (cerclage) in combination with other treatments for preventing spontaneous preterm birth in singleton pregnancies. *Cochrane Database Syst Rev* 2020; **9:** CD012871.

61 Althabe F, Belizán JM, McClure EM, et al. A population-based, multifaceted strategy to implement antenatal corticosteroid treatment versus standard care for the reduction of neonatal mortality due to preterm birth in low-income and middle-income countries: the ACT cluster-randomised trial. *Lancet* 2015; **385:** 629–39.

62 Oladapo OT, Vogel JP, Piaggio G, et al. Antenatal dexamethasone for early preterm birth in low-resource countries. *N Engl J Med* 2020; **383:** 2514–25.

63 WHO. WHO recommendations on interventions to improve preterm birth outcomes. 2015.

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

65 Patel A, Khatib MN, Kurhe K, Bhargava S, Bang A. Impact of neonatal resuscitation trainings on neonatal and perinatal mortality: a systematic review and meta-analysis. *BMJ Paediatr Open* 2017; **1:** e000183–e.

66 Roba AA, Tefera M, Worku T, Dasa TT, Estifanos AS, Assefa N. Application of 4% chlorhexidine to the umbilical cord stump of newborn infants in lower income countries: a systematic review and meta-analysis. *Matern Health Neonatol Perinatol* 2019; **5:** 16.

67 Khan J, Vesel L, Bahl R, Martines JC. Timing of breastfeeding initiation and exclusivity of breastfeeding during the first month of life: effects on neonatal mortality and morbidity—a systematic review and meta-analysis. *Matern Child Health J* 2015; **19:** 468–79.

68 Janmohamed A, Sohani N, Lassi ZS, Bhutta ZA. The effects of community home visit and peer group nutrition intervention delivery platforms on nutrition outcomes in low and middle-income countries: a systematic review and meta-analysis. *Nutrients* 2020; **12:** 440.

69 McCall EM, Alderdice F, Halliday HL, Vohra S, Johnston L. Interventions to prevent hypothermia at birth in preterm and/or low birth weight infants. *Cochrane Database Syst Rev* 2018; **2:** CD004210.

70 Mazumder S, Taneja S, Dube B, et al. Effect of community-initiated kangaroo mother care on survival of infants with low birthweight: a randomised controlled trial. *Lancet* 2019; **394:** 1724–36.

71 Kumar A, Mishra S, Singh S, et al. Effect of sunflower seed oil emollient therapy on newborn infant survival in Uttar Pradesh, India: a community-based, cluster randomized, open-label controlled trial. ISRCTN38965585. *PLoS Med* 2021; **18:** e1003680.

72 Thayyil S, Pant S, Montaldo P, et al. Hypothermia for moderate or severe neonatal encephalopathy in low-income and middle-income countries (HELIX): a randomised controlled trial in India, Sri Lanka, and Bangladesh. *Lancet Glob Health* 2021; **9:** e1273–85.

73 Aneji C, Hartman T, Olutunde O, et al. Implementing bubble continuous positive airway pressure in a lower middle-income country: a Nigerian experience. *Pan Afr Med J* 2020; **37:** 10.

74 Jensen EA, Chaudhary A, Bhutta ZA, Kirpalani H. Non-invasive respiratory support for infants in low- and middle-income countries. *Semin Fetal Neonatal Med* 2016; **21:** 181–88.

75 Mwatha AB, Mahande M, Olomi R, John B, Philemon R. Treatment outcomes of Pumani bubble-CPAP versus oxygen therapy among preterm babies presenting with respiratory distress at a tertiary hospital in Tanzania-randomised trial. *PLoS One* 2020; **15:** e0235031.

76 Okello F, Egiru E, Ikiror J, et al. Reducing preterm mortality in eastern Uganda: the impact of introducing low-cost bubble CPAP on neonates. *BMC Pediatr* 2019; **19:** 311.

77 Keats EC, Das JK, Salam RA, Lassi ZS, Imdad A, Black RE, Bhutta ZA. Effective interventions to address maternal and child malnutrition: an update of the evidence. *Lancet Child Adolesc Health* 2021; **5:** 367–84.

78 Rana R, McGrath M, Sharma E, Gupta P, Kerac M. Effectiveness of breastfeeding support packages in low- and middle-income countries for infants under six months: a systematic review. *Nutrients* 2021; **13:** 681.

79 Poindexter B. Use of probiotics in preterm infants. *Pediatrics* 2021; **147:** e2021051485.

80 Crowther CA, Middleton P. Anti-D administration after childbirth for preventing Rhesus alloimmunisation. *Cochrane Database Syst Rev* 1997; **2:** CD000021.

81 McBain RD, Crowther CA, Middleton P. Anti-D administration in pregnancy for preventing Rhesus alloimmunisation. *Cochrane Database Syst Rev* 2015; **9:** CD000020.

82 Arya S, Naburi H, Kawaza K, et al. Immediate "kangaroo mother care" and survival of infants with low birth weight. *N Engl J Med* 2021; **384:** 2028–38.

83 Lamberti LM, Fischer Walker CL, Noiman A, Victora C, Black RE. Breastfeeding and the risk for diarrhea morbidity and mortality. *BMC Public Health* 2011; **11** (suppl 3): S15.

84 WHO. Improving early childhood development: WHO guideline. Geneva: World Health Organization, 2020.

85 Lazzerini M, Wanzira H. Oral zinc for treating diarrhoea in children. *Cochrane Database Syst Rev* 2016; **12:** CD005436.

86 Lamberti LM, Zakarija-Grković I, Fischer Walker CL, et al. Breastfeeding for reducing the risk of pneumonia morbidity and mortality in children under two: a systematic literature review and meta-analysis. *BMC Public Health* 2013; **13** (suppl 3)**:** S18.

87 Tam E, Keats EC, Rind F, Das JK, Bhutta AZA. Micronutrient supplementation and fortification interventions on health and development outcomes among children under-five in low- and middle-income countries: a systematic review and meta-analysis. *Nutrients* 2020; **12:** 289.

88 Pryce J, Richardson M, Lengeler C. Insecticide-treated nets for preventing malaria. *Cochrane Database Syst Rev* 2018; **11:** 30398672.

89 Stewart CP, Wessells KR, Arnold CD, et al. Lipid-based nutrient supplements and all-cause mortality in children 6-24 months of age: a meta-analysis of randomized controlled trials. *Am J Clin Nutr* 2020; **111:** 207–18.

90 Munos MK, Walker CLF, Black RE. The effect of oral rehydration solution and recommended home fluids on diarrhoea mortality. *Int J Epidemiol* 2010; **39**(suppl 1)**:** i75–87.

91 Tol WA, Greene MC, Lasater ME, et al. Impact of maternal mental health interventions on child-related outcomes in low- and middle-income countries: a systematic review and meta-analysis. *Epidemiol Psychiatr Sci* 2020; **29:** e174.

92 Britto PR, Lye SJ, Proulx K, et al. Nurturing care: promoting early childhood development. *Lancet* 2017; **389:** 91–102.

93 Imdad A, Mayo-Wilson E, Herzer K, Bhutta ZA. Vitamin A supplementation for preventing morbidity and mortality in children from six months to five years of age. *Cochrane Database Syst Rev* 2017; **3:** CD008524.

94 Haider BA, Sharma R, Bhutta ZA. Neonatal vitamin A supplementation for the prevention of mortality and morbidity in term neonates in low and middle income countries. *Cochrane Database Syst Rev* 2017; **2:** CD006980.

95 Neonatal Vitamin A Supplementation Evidence group. Early neonatal vitamin A supplementation and infant mortality: an individual participant data meta-analysis of randomised controlled trials. *Arch Dis Child* 2019; **104:** 217–26.

96 Lassi ZS, Kurji J, Oliveira CSD, Moin A, Bhutta ZA. Zinc supplementation for the promotion of growth and prevention of infections in infants less than six months of age. *Cochrane Database Syst Rev* 2020; **4:** 32266964.

97 Das JK, Salam RA, Saeed M, Kazmi FA, Bhutta ZA. Effectiveness of interventions for managing acute malnutrition in children under five years of age in low-income and middle-income countries: a systematic review and meta-analysis. *Nutrients* 2020; **12:** 116.

98 Brown T, Moore THM, Hooper L, et al. Interventions for preventing obesity in children. *Cochrane Database Syst Rev* 2019; **7:** CD001871.

99 Bhutta ZA, Das JK, Walker N, et al. Interventions to address deaths from childhood pneumonia and diarrhoea equitably: what works and at what cost? *Lancet* 2013; **381:** 1417–29.

100 Milligan R, Paul M, Richardson M, Neuberger A. Vaccines for preventing typhoid fever. *Cochrane Database Syst Rev* 2018; **5:** CD001261.

101 Bi Q, Ferreras E, Pezzoli L, et al. Protection against cholera from killed whole-cell oral cholera vaccines: a systematic review and meta-analysis. *Lancet Infect Dis* 2017; **17:** 1080–88.

102 Lopez AL, Deen J, Azman AS, et al. Immunogenicity and protection from a single dose of internationally available killed oral cholera vaccine: a systematic review and metaanalysis. *Clin Infect Dis* 2018; **66:** 1960–71.

103 McMillan M, Chandrakumar A, Wang HLR, et al. Effectiveness of meningococcal vaccines at reducing invasive meningococcal disease and pharyngeal Neisseria meningitidis carriage: A systematic review and meta-analysis. *Clin Infect Dis* 2020.

104 Esu EB, Oringanje C, Meremikwu MM. Intermittent preventive treatment for malaria in infants. *Cochrane Database Syst Rev* 2019; **12:** CD011525.

105 Meremikwu MM, Donegan S, Sinclair D, Esu E, Oringanje C. Intermittent preventive treatment for malaria in children living in areas with seasonal transmission. *Cochrane Database Syst Rev* 2012; **2:** CD003756.

106 Esu EB, Effa EE, Opie ON, Meremikwu MM. Artemether for severe malaria. *Cochrane Database Syst Rev* 2019; **6:** CD010678.

107 Pryce J, Hine P. Pyronaridine-artesunate for treating uncomplicated *Plasmodium falciparum* malaria. *Cochrane Database Syst Rev* 2019; **1:** CD006404.

108 Gaffey MF, Wazny K, Bassani DG, Bhutta ZA. Dietary management of childhood diarrhea in low- and middle-income countries: a systematic review. *BMC Public Health* 2013; **13** (suppl 3)**:** S17.

109 Keenan JD, Bailey RL, West SK, et al. Azithromycin to reduce childhood mortality in sub-Saharan Africa. *N Engl J Med* 2018; **378:** 1583–92.

110 WHO. WHO guideline on mass drug administration of azithromycin to children under five years of age to promote child survival. Geneva: World Health Organization, 2020.

111 Doan T, Worden L, Hinterwirth A, et al. Macrolide and nonmacrolide resistance with mass azithromycin distribution. *N Engl J Med* 2020; **383:** 1941–50.

112 Pickering AJ, Null C, Winch PJ, et al. The WASH Benefits and SHINE trials: interpretation of WASH intervention effects on linear growth and diarrhoea. *Lancet Glob Health* 2019; **7:** e1139–46.

113 Tofail F, Fernald LCH, Das KK, et al. Effect of water quality, sanitation, hand washing, and nutritional interventions on child development in rural Bangladesh (WASH Benefits Bangladesh): a cluster-randomised controlled trial. *Lancet Child Adolesc Health* 2018; **2:** 255–68.

114 Darvesh N, Das JK, Vaivada T, Gaffey MF, Rasanathan K, Bhutta ZA. Water, sanitation and hygiene interventions for acute childhood diarrhea: a systematic review to provide estimates for the Lives Saved Tool. *BMC Public Health* 2017; **17** (suppl 4)**:** 776.

115 Das JK, Hadi YB, Salam RA, Hoda M, Lassi ZS, Bhutta ZA. Fly control to prevent diarrhoea in children. *Cochrane Database Syst Rev* 2018; **12:** CD011654.

116 Richter LM, Daelmans B, Lombardi J, et al. Investing in the foundation of sustainable development: pathways to scale up for early childhood development. *Lancet* 2017; **389:** 103–18.

117 Trude ACB, Richter LM, Behrman JR, Stein AD, Menezes AMB, Black MM. Effects of responsive caregiving and learning opportunities during pre-school ages on the association of early adversities and adolescent human capital: an analysis of birth cohorts in two middle-income countries. *Lancet Child Adolesc Health* 2021; **5:** 37–46.

118 Knerr W, Gardner F, Cluver L. Improving positive parenting skills and reducing harsh and abusive parenting in low- and middle-income countries: a systematic review. *Prev Sci* 2013; **14:** 352–63.

119 Abuga JA, Kariuki SM, Kinyanjui SM, Boele Van Hensbroek M, Newton CR. Premature mortality in children aged 6–9 years with neurological impairments in rural Kenya: a cohort study. *Lancet Glob Health* 2019; **7:** e1728–35.

120 Siddiqui FA, Padhani ZA, Salam RA, et al. Interventions to improve immunization coverage among children and adolescents: a meta-analysis. *Pediatrics* (in press).

121 Naqvi FA, Das JK, Salam RA, Raza SF, Lassi ZS, Bhutta ZA. Interventions for neglected tropical diseases among children and adolescents: a meta-analysis. *Pediatrics*.

122 Khan DSA, Naseem R, Salam RA, Lassi ZS, Das JK, Bhutta ZA. Interventions for high-burden infectious diseases in children and adolescents: a meta-analysis. *Pediatrics* (in press).

123 Das JK, Salam RA, Mahmood SB, et al. Food fortification with multiple micronutrients: impact on health outcomes in general population. *Cochrane Database Syst Rev* 2019; **12:** CD011400.

124 Salam RA, Padhani ZA, Das JK, et al. Effects of lifestyle modification interventions to prevent and manage child and adolescent obesity: a systematic review and meta-analysis. *Nutrients* 2020; **12:** 2208.

125 Micha R, Karageorgou D, Bakogianni I, et al. Effectiveness of school food environment policies on children's dietary behaviors: a systematic review and meta-analysis. *PLoS One* 2018; **13:** e0194555.

126 Oh C, Carducci B, Vaivada T, Bhutta ZA. Digital interventions for universal health promotion in children and adolescents: a systematic review. *Pediatrics* (in press).

127 Oh C, Carducci B, Vaivada T, Bhutta ZA. Interventions to promote physical activity and healthy digital media use in children and adolescents: a systematic review. *Pediatrics* (in press).

128 Estcourt LJ, Kohli R, Hopewell S, Trivella M, Wang WC. Blood transfusion for preventing primary and secondary stroke in people with sickle cell disease. *Cochrane Database Syst Rev* 2020; **7:** CD003146.

129 Lennon D, Kerdemelidis M, Arroll B. Meta-analysis of trials of streptococcal throat treatment programs to prevent rheumatic fever. *Pediatr Infect Dis J* 2009; **28:** e259–64.

130 Evans JR, Morjaria P, Powell C. Vision screening for correctable visual acuity deficits in school-age children and adolescents. *Cochrane Database Syst Rev* 2018; **2:** CD005023.

131 Taylor RD, Oberle E, Durlak JA, Weissberg RP. Promoting positive youth development through school-based social and emotional learning interventions: a meta-analysis of follow-up effects. *Child Dev* 2017; **88:** 1156–71.

132 Howes Vallis E, Zwicker A, Uher R, Pavlova B. Cognitive-behavioural interventions for prevention and treatment of anxiety in young children: a systematic review and meta-analysis. *Clin Psychol Rev* 2020; **81:** 101904.

133 Das JK, Salam RA, Lassi ZS, et al. Interventions for adolescent mental health: an overview of systematic reviews. *J Adolesc Health* 2016; **59:** S49–60.

134 Das JK, Salam RA, Arshad A, Finkelstein Y, Bhutta ZA. Interventions for adolescent substance abuse: an overview of systematic reviews. *J Adolesc Health* 2016; **59:** S61–75.

135 Salam RA, Arshad A, Das JK, et al. Interventions to prevent unintentional injuries among adolescents: a systematic review and meta-analysis. *J Adolesc Health* 2016; **59:** S76–87.

136 Das JK, Salam RA, Arshad A, Lassi ZS, Bhutta ZA. Systematic review and meta-analysis of interventions to improve access and coverage of adolescent immunizations. *J Adolesc Health* 2016; **59:** S40–48.

137 Salam RA, Faqqah A, Sajjad N, et al. Improving adolescent sexual and reproductive health: a systematic review of potential interventions. *J Adolesc Health* 2016; **59:** S11–28.

138 Lassi ZS, Moin A, Das JK, Salam RA, Bhutta ZA. Systematic review on evidence-based adolescent nutrition interventions. *Ann N Y Acad Sci* 2017; **1393:** 34–50.

139 Salam RA, Das JK, Ahmed W, Irfan O, Sheikh SS, Bhutta ZA. Effects of preventive nutrition interventions among adolescents on health and nutritional status in low- and middle-income countries: a systematic review and meta-analysis. *Nutrients* 2019; **12:** 49.

140 Milligan R, Paul M, Richardson M, Neuberger A. Vaccines for preventing typhoid fever. *Cochrane Database Syst Rev* 2018; **5:** CD001261.

141 Abdullahi LH, Kagina BM, Ndze VN, Hussey GD, Wiysonge CS. Improving vaccination uptake among adolescents. *Cochrane Database Syst Rev* 2020; **1:** CD011895.

142 Secor AM, Driver M, Kharono B, et al. Immunogenicity of alternative dosing schedules for HPV vaccines among adolescent girls and young women: a systematic review and meta-analysis. *Vaccines* 2020; **8:** e618.

143 Lott BE, Okusanya BO, Anderson EJ, et al. Interventions to increase uptake of Human Papillomavirus (HPV) vaccination in minority populations: a systematic review. *Prev Med Rep* 2020; **19:** 101163.

144 Taylor-Robinson DC, Maayan N, Donegan S, Chaplin M, Garner P. Public health deworming programmes for soil-transmitted helminths in children living in endemic areas. *Cochrane Database Syst Rev* 2019; **9:** CD000371.

145 Welch VA, Ghogomu E, Hossain A, et al. Mass deworming to improve developmental health and wellbeing of children in low-income and middle-income countries: a systematic review and network meta-analysis. *Lancet Glob Health* 2017; **5:** e40–50.

146 Welch VA, Ghogomu E, Hossain A, et al. Mass deworming for improving health and cognition of children in endemic helminth areas: a systematic review and individual participant data network meta-analysis. *Campbell Syst Rev* 2019; **15:** e1058.

147 Kristjansson B, Petticrew M, MacDonald B, et al. School feeding for improving the physical and psychosocial health of disadvantaged students. *Cochrane Database Syst Rev* 2007; **1:** CD004676.

148 Bou-Karroum L, El-Jardali F, Jabbour M, et al. Preventing unintentional injuries in school-age children: a systematic review. *Pediatrics* (in press)

149 Vecino-Ortiz AI, Jafri A, Hyder AA. Effective interventions for unintentional injuries: a systematic review and mortality impact assessment among the poorest billion. *Lancet Glob Health* 2018; **6:** e523–34.

150 Alonge O, Bishai D, Wadhwaniya S, et al. Large-scale evaluation of interventions designed to reduce childhood drownings in rural Bangladesh: a before and after cohort study. *Inj Epidemiol* 2020; **7:** 17.

151 Fantaye AW, Buh AW, Idriss-Wheeler D, Fournier K, Yaya S. Interventions promoting child sexual & reproductive health & rights in LMICs: a systematic review. *Pediatrics* (in press).

152 Franklin C, Kim JS, Beretvas TS, et al. The effectiveness of psychosocial interventions delivered by teachers in schools: a systematic review and meta-analysis. *Clin Child Fam Psychol Rev* 2017; **20:** 333–50.

153 Gardner F, Montgomery P, Knerr W. Transporting evidence-based parenting programs for child problem behavior (age 3–10) between countries: systematic review and meta-analysis. *J Clin Child Adolesc Psychol* 2016; **45:** 749–62.

154 Coore Desai C, Reece JA, Shakespeare-Pellington S. The prevention of violence in childhood through parenting programmes: a global review. *Psychol Health Med* 2017; **22** (suppl 1)**:** 166–86.

155 Bukhman G, Mocumbi AO, Atun R, et al. The *Lancet* NCDI Poverty Commission: bridging a gap in universal health coverage for the poorest billion. *Lancet* 2020; **396:** 991–1044.

156 Nevitt SJ, Jones AP, Howard J. Hydroxyurea (hydroxycarbamide) for sickle cell disease. *Cochrane Database Syst Rev* 2017; **4:** CD002202.

157 Tshilolo L, Tomlinson G, Williams TN, et al. Hydroxyurea for children with sickle cell anemia in sub-Saharan Africa. *N Engl J Med* 2019; **380:** 121–31.

158 Bollig C, Schell L, Rücker G, et al. Deferasirox for managing iron overload in people with thalassaemia. *Cochrane Database Syst Rev* 2017; **8:** CD007476.

159 Yeager DS, Dahl RE, Dweck CS. Why interventions to influence adolescent behavior often fail but could succeed. *Perspect Psychol Sci* 2018; **13:** 101–22.

160 Salazar de Pablo G, De Micheli A, Nieman DH, et al. Universal and selective interventions to promote good mental health in young people: Systematic review and meta-analysis. *Eur Neuropsychopharmacol* 2020; **41:** 28–39.

161 Zalsman G, Hawton K, Wasserman D, et al. Suicide prevention strategies revisited: 10-year systematic review. *Lancet Psychiatry* 2016; **3:** 646–59.

162 Morken IS, Dahlgren A, Lunde I, Toven S. The effects of interventions preventing self-harm and suicide in children and adolescents: an overview of systematic reviews. *F1000 Res* 2019; **8:** 890.

163 Oringanje C, Meremikwu MM, Eko H, Esu E, Meremikwu A, Ehiri JE. Interventions for preventing unintended pregnancies among adolescents. *Cochrane Database Syst Rev* 2016; **2:** CD005215.

164 Wang T, Lurie M, Govindasamy D, Mathews C. The effects of school-based condom availability programs (CAPs) on condom acquisition, use and sexual behavior: a systematic review. *AIDS Behav* 2018; **22:** 308–20.

165 Peterson AJ, Donze M, Allen E, Bonell C. Effects of interventions addressing school environments or educational assets on adolescent sexual health: systematic review and meta-analysis. *Int Perspect Sex Reprod Health* 2018; **44:** 111–31.

166 Bowring AL, Wright CJC, Douglass C, Gold J, Lim MSC. Features of successful sexual health promotion programs for young people: findings from a review of systematic reviews. *Health Promot J Austr* 2018; **29:** 46–57.

167 Kaufman J, Ryan R, Walsh L, et al. Face-to-face interventions for informing or educating parents about early childhood vaccination. *Cochrane Database Syst Rev* 2018; **5:** CD010038.

168 Harvey H, Reissland N, Mason J. Parental reminder, recall and educational interventions to improve early childhood immunisation uptake: a systematic review and meta-analysis. *Vaccine* 2015; **33:** 2862–80.

169 Gibson DG, Ochieng B, Kagucia EW, et al. Mobile phone-delivered reminders and incentives to improve childhood immunisation coverage and timeliness in Kenya (M-SIMU): a cluster randomised controlled trial. *Lancet Glob Health* 2017; **5:** e428–38.

170 Seth R, Akinboyo I, Chhabra A, et al. Mobile phone incentives for childhood immunizations in rural India. *Pediatrics* 2018; **141:** e20173455.

171 Ekhaguere OA, Oluwafemi RO, Badejoko B, et al. Automated phone call and text reminders for childhood immunisations (PRIMM): a randomised controlled trial in Nigeria. *BMJ Glob Health* 2019; **4:** e001232.

172 Bassani DG, Arora P, Wazny K, Gaffey MF, Lenters L, Bhutta ZA. Financial incentives and coverage of child health interventions: a systematic review and meta-analysis. *BMC Public Health* 2013; **13** (suppl 3)**:** S30.

173 Duvendack M, Mader P. Impact of financial inclusion in low-and middle-income countries. *Campbell Syst Rev* 2019; **15:** e1012.

174 Owusu-Addo E, Renzaho AMN, Smith BJ. The impact of cash transfers on social determinants of health and health inequalities in sub-Saharan Africa: a systematic review. *Health Policy Plan* 2018; **33:** 675–96.

175 Siddiqi A, Rajaram A, Miller SP. Do cash transfer programmes yield better health in the first year of life? A systematic review linking low-income/middle-income and high-income contexts. *Arch Dis Child* 2018; **103:** 920–26.

176 Glassman A, Duran D, Fleisher L, et al. Impact of conditional cash transfers on maternal and newborn health. *J Health Popul Nutr* 2013; **31** (suppl 2)**:** 48–66.

177 Owusu-Addo E, Cross R. The impact of conditional cash transfers on child health in low- and middle-income countries: a systematic review. *Int J Public Health* 2014; **59:** 609–18.

178 Ranganathan M, Lagarde M. Promoting healthy behaviours and improving health outcomes in low and middle income countries: a review of the impact of conditional cash transfer programmes. *Prev Med* 2012; **55** (suppl)**:** S95–105.

179 Durao S, Visser ME, Ramokolo V, et al. Community-level interventions for improving access to food in low-and middle-income countries. *Cochrane Database Syst Rev* 2020; **7:** CD011504.

180 Pega F, Liu SY, Walter S, Pabayo R, Saith R, Lhachimi SK. Unconditional cash transfers for reducing poverty and vulnerabilities: effect on use of health services and health outcomes in low-and middle-income countries. *Cochrane Database Syst Rev* 2017; **11:** CD011135.

181 Hunter BM, Harrison S, Portela A, Bick D. The effects of cash transfers and vouchers on the use and quality of maternity care services: a systematic review. *PLoS One* 2017; **12:** e0173068.

182 Bellows B, Bulaya C, Inambwae S, Lissner CL, Ali M, Bajracharya A. Family planning vouchers in low and middle income countries: a systematic review. *Stud Fam Plann* 2016; **47:** 357–70.

183 Stewart R, van Rooyen C, Dickson K, Majoro M, de Wet T. What is the impact of microfinance on poor people? A systematic review of evidence from sub-Saharan Africa. 2010. https://assets.publishing.service.gov.uk/media/57a08af4ed915d3cfd000a40/MicroFinance_ForWeb.pdf (accessed Feb 12, 2022).

184 Målqvist M, Yuan B, Trygg N, Selling K, Thomsen S. Targeted interventions for improved equity in maternal and child health in low- and middle-income settings: a systematic review and meta-analysis. *PLoS One* 2013; **8:** e66453.

185 GBD 2019 Universal Health Coverage Collaborators. Measuring universal health coverage based on an index of effective coverage of health services in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet* 2020; **396:** 1250–84.

186 Campisi SC, Carducci B, Akseer N, Zasowski C, Szatmari P, Bhutta ZA. Suicidal behaviours among adolescents from 90 countries: a pooled analysis of the global school-based student health survey. *BMC Public Health* 2020; **20:** 1102.

187 Mulaku M, Opiyo N, Karumbi J, Kitonyi G, Thoithi G, English M. Evidence review of hydroxyurea for the prevention of sickle cell complications in low-income countries. *Arch Dis Child* 2013; **98:** 908–14.

188 Fung A, Horton S, Zabih V, Denburg A, Gupta S. Cost and cost-effectiveness of childhood cancer treatment in low-income and middle-income countries: a systematic review. *BMJ Glob Health* 2019; **4:** e001825.