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Abstract: The Sustainable Development Goals (SDGs) provide a historic opportunity to implement at scale interventions to promote Early Childhood Development (ECD). While the evidence base for the importance of ECD has grown, the research is distributed across sectors, populations, and settings with diversity noted in the scope and focus. In this paper, we provide a comprehensive updated analyses of ECD interventions across five sectors: health; nutrition; education; child protection; and social protection. Our review concludes that to make interventions, successful, smarter and sustainable, they need to be implemented as multi-sectoral intervention packages anchored in "nurturing care". The recommendations emphasize that intervention packages should be applied at developmentally appropriate times during the life-course, target multiple risks, and build on existing delivery platforms for feasibility of scale-up. While interventions will continue to improve with the growth of developmental science, the evidence is now strong that parents, caregivers, and families need to be supported in providing nurturing care and protection for young children to achieve their developmental potential.

Nurturing Care: Science and Effective Interventions to Promote Early Childhood Development

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Paper 1

Black, M. et al. Early child development coming of age: From science to practice.

Paper 3

Richter, L.M. et al. Investing in the Foundations of Sustainable Development: Nurturing Care to Optimise Early Childhood Development

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PRB and SL conceptualised the review in consultation with the Early Child Development Series Steering Committee and wrote the first draft of the Series paper with substantial inputs from KP, ZB, RPE, MFG, and TV led the review of MCNH and nutrition interventions. NR, PI, and AKY led the review of early childhood education and parenting interventions. HM led the review of child maltreatment prevention interventions. LCHF led the review of social protection interventions. SGM, AC, AF, and VGM contributed to the scientific literature review of nurturing care and human development. TW and HY reviewed the literature on cumulative and protective risk factors. All authors and members of the review groups saw successive drafts of the paper and provided input. PRB, SL, and KP prepared the final version of the Series paper, which all authors approved and PRB is the overall guarantor.

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Conflicts of Interest

PRB is employed by UNICEF. JFL has received several contracts, gifts, and grants focused on the impact of early child development programmes from UNICEF, the Anne Çocuk Eğitim Vakfı (AÇEV, Mother-Child Education Foundation), the UBS Optimus Foundation, and the Open Road Alliance. The other authors declare that they have no conflicts of interest. The views expressed are those of the authors and not necessarily those of UNICEF, Bill & Melinda Gates Foundation, and Conrad N Hilton Foundation. As corresponding author, Pia Rebello Britto states that she had full access to all data and final responsibility to submit for publication.

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Abstract

The Sustainable Development Goals (SDGs) provide a historic opportunity to implement at scale interventions to promote Early Childhood Development (ECD). While the evidence base for the importance of ECD has grown, the research is distributed across sectors, populations, and settings with diversity noted in the scope and focus. In this paper, we provide a comprehensive updated analyses of ECD interventions across five sectors: health; nutrition; education; child protection; and social protection. Our review concludes that to make interventions, successful, smarter and sustainable, they need to be implemented as multi-sectoral intervention packages anchored in “nurturing care”. The recommendations emphasize that intervention packages should be applied at developmentally appropriate times during the life-course, target multiple risks, and build on existing delivery platforms for feasibility of scale-up. While interventions will continue to improve with the growth of developmental science, the evidence is now strong that parents, caregivers, and families need to be supported in providing nurturing care and protection for young children to achieve their developmental potential.

Abstract Word Count: 164 words

Key Messages

- Advances in basic and intervention science indicate that early childhood is a period of special sensitivity to promotive experiences and that critical time windows exist when the benefits of ECD interventions are amplified.
- The most fundamental promotive experiences in the early years come from nurturing care and protection received from parents, family and community, which have lifelong benefits including improved health and well-being and increased ability to learn and earn.
- Nurturing care and protection are supported by a range of interventions delivered pre-pregnancy through birth and the newborn period, infancy and early childhood, many of which exist with proven benefits for child development, including health, growth and learning.
- Interventions including nurturing care and protection can target multiple risks at developmentally appropriate times and can be integrated within existing preventative and promotive packages.
- These packages can build on existing platforms for delivering parental and child services at scale to vulnerable and difficult-to-reach populations, such as community-based strategies and social safety nets for enhanced effectiveness and sustainability.

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Nurturing Care: Science and Effective Interventions for Early Childhood Development

Introduction

Although global attention to early childhood development (ECD) has been established through its inclusion in the SDGs, 43% of children under 5 years of age in low- and middle-income countries (LMICs) are at risk of not achieving their developmental potential (Black et al., this issue). We suggest that this gap in human potential, at least in part, is due to the failure, to date, to apply the emerging scientific knowledge on how *Nurturing Care* shapes young children's development and to take action at scale using a multi-sector approach across key stages in the early life course.

We define *Nurturing Care* as a stable environment that is sensitive to children's health and nutritional needs, with protection from threats, opportunities for early learning, and interactions that are responsive, emotionally supportive, and developmentally stimulating. As an overarching concept, *Nurturing Care* is supported by a large array of social contexts – from home to parental work, child care, schooling, wider community, and policy influences.(1) It consists of a core set of inter-related functions, including: behaviours, attitudes, and knowledge of caregiving (e.g., health, hygiene care, feeding care); stimulation (e.g., talking, singing, playing); responsiveness (e.g., early bonding, secure attachment, trust, sensitive communication); and safety (e.g., routines, protection from harm).(2, 3) The single most powerful context for *Nurturing Care* is the immediate home and care settings of young children often provided by mothers, but also by fathers and other family members, as well as by child care services.

The brain has evolved to. *Nurturing Care* mediates the development of key brain regions and promotes developmental adaptations. These experiences have lifelong benefits, including an increased ability to learn, greater achievement in school and later life, citizenship, involvement in community activities, and overall quality of life.(4, 5) The period of early development is one of enormous change and is characterized by a high degree of plasticity in brain organization.(6, 7) Advances in developmental science have also provided an understanding of the multiple and overlapping critical windows of time when development of specific capacities and abilities is most powerfully enhanced.(8)(9) Nurturing, caring, enriching, and protective interactions provide the early environments needed for developmental progression to occur and protect infants and children from the negative impact of stress and adversity (See Panel 2). Prospective longitudinal studies from across the globe from Jamaica,(10-12) Pakistan,(13) Turkey(14, 15) and elsewhere have demonstrated that including elements of nurturing care in interventions significantly improves child development and later adult outcomes. The interplay between the elements of *Nurturing Care*, the timing of experiences, and complexity of risks requires action beyond single sector interventions.

Selection of interventions for review

This paper provides a comprehensive update of ECD interventions across key sectors. While progress has been made with ECD-related interventions, extant research is at different levels of maturity across sectors and distributed across numerous populations and settings. Experts from research communities in Reproductive Maternal, Newborn and Child Health (RMNCH), nutrition, parenting, early childhood education, maltreatment prevention, and social protection worked in teams using standard methods to critically appraise the available evidence that addressed child outcomes, including: (i) mortality, (ii) malformations, disability, and injury, (iii) nutrition and growth, and (iv) severe morbidity. The primary focus, however, was direct measures of child development outcomes (e.g., language, cognition, motor, social and emotional, learning, and psychosocial well-being). Together, these outcomes encompass those theorized to have an intermediate effect on child development, in addition to direct endpoints in child development. All reviews covered the period since publication of the last Lancet series on ECD - from 2011 to April 2015, and thereafter published individual studies, in each sector. Search strategies in each group were tailored to the existing evidence in each sector. The RMNCH and nutrition reviews relied on the most recent overviews of systematic reviews with good quality methods for all interventions and updated the evidence by incorporating newer studies, when available. The parenting and early childhood education, child protection, and social protection reviews relied on the most recent systematic reviews, and incorporating studies after April 2015, when available. From preconception to birth, the focus of the interventions is primarily on the maternal caregiver. From birth through infancy, interventions typically include both adult and child, and in the age period transitioning into primary school, we note a predominantly child-focused set of interventions with increasing emphasis on the importance of a nurturing environment provided by teachers. Details of the search methods used for selecting and screening reviews are described in Panel 1.

Panel 1: Methods and search strategy for selection of interventions for review

This article is based on peer-reviewed overviews, systematic reviews and individual studies that focusing primarily on child development outcomes. All reviews used established guidelines to search, evaluate, and synthesize the results of relevant research. The RMNCH and nutrition reviews relied primarily on six recent overviews of reviews, including the Lancet 2014 Every Newborn series,(16) the Lancet 2013 Maternal and Child Nutrition series,(17) the Lancet 2013 Child Pneumonia and Diarrhoea series,(18) the Reproductive Health 2014 supplement on essential MNCH interventions,(19) and the WHO/RMNCH/AKU 2011 Essential Interventions for RMNCH report,(20) and the Lancet 2016 Breastfeeding series.(21) The education review was based on four recent reviews, including the Lancet 2011 ECD series,(22) a 2015 Annual Review of Psychology systematic review of parenting interventions,(23) a DFID literature review of parenting and early childhood programmes,(24) and a UNICEF systematic review of parenting programmes.(25) A meta-analysis of education programmes was conducted to determine non-cognitive developmental benefits of parenting and early childhood education programmes, as this information was not available in existing systematic reviews. The maltreatment review updated the Lancet 2009 series article on prevention of child maltreatment(26) and a systematic review of child maltreatment prevention reviews,(27) by reviewing recent reviews of maltreatment prevention interventions (24-36)., including home visiting,(28-30), parenting-training programmes,(31, 32) sexual abuse prevention programmes,(33, 34) universal campaigns to prevent physical abuse,(35) behavioural and counseling interventions,(36) detection of child maltreatment,(37) and three review studies on prevention of child maltreatment.(38-40) The social protection review examined five systematic reviews that focused on the effects of social programmes, including conditional and unconditional cash transfers and microcredit schemes.(41-45) After examining the systematic reviews, the literature was searched for papers that had been published since the systematic reviews. Twenty-four new studies were included that investigated the effects of CCTs or UCTs on measures of health, nutrition, or developmental outcomes. Each review included overviews and systematic reviews published from 2011 to April 2015. The search focused on research conducted in LMICs, but systematic reviews based on evidence from high-income countries (HICs) were included for maltreatment prevention where evidence from LMICs was either unavailable or limited. Data were double-extracted using a standardized form. Methodological quality of systematic reviews was assessed using the AMSTAR criteria, where appropriate. More detailed information on the search strategies for each review can be found in the supplementary web appendices.

Panel 2: Co-occurrences among bio-ecological and/or contextual risk factors in LMICs

While there are parallels in the types of risk and promotive factors encountered by children in HICs and LMICs, the limited evidence indicates that children from LMICs are more likely to encounter a greater number and range of risk factors and fewer promotive influences than poor children in HICs.(46, 47) Toxins, chronic severe malnutrition, direct exposures to societal armed conflict and displacement, and refugee status are risk factors that occur in LMICs, but are rarely seen in HICs. Poor sanitation, severe childhood diarrhea, iron deficiency anemia, orphan status, substandard housing, domestic violence, harsh physical punishment, and maternal depression are risk factors that occur at a higher rate in LMICs than in HICs and can be frequently amplified by exposure to conflict and population displacement. Some evidence indicates that there may be a reduced availability of promotive factors in LMICs, such as routine neonatal screening for iodine deficiency,(48) childbirth attended by skilled health personnel,(49) and fewer learning resources in the home.(50) In addition to a greater range and prevalence, there are higher levels of co-occurrence among risk factors in LMICs compared to HICs. (51) Based on analysis of Multiple Indicator Cluster Survey data, multiple risk factors co-occur. For example, 85% of children aged 3 to 4 years in West and Central Africa and 56% in East Asia and Pacific experience multiple risks. Data estimating risks for the approximately 1 in 10 children living in conflict, crises, and insecure conditions are scant; however we estimate higher levels of co-occurrence of risk factors in such situations. The findings support the application of coordination or combining of interventions, within packages, to reduce exposure to multiple risk factors.

Other specific examples of co-occurrence are:

Nutritional deficiencies in infancy and early childhood likely to occur with:

- being born small for gestational age or preterm or both;
- parents who are less involved, sensitive or responsive;
- extreme poverty and food insecurity;
- suboptimal infant and young child feeding practices;
- high exposure to pathogens and corresponding burden of infectious disease in infancy and childhood;
- home environments characterized as less stimulating;
- exposure to domestic violence.

Maternal depression and anxiety likely to coexist with:

- pre-term birth;
- low birthweight;
- poor infant growth and lowered cognitive development;
- less adequate prenatal care;
- less adequate caregiving including:
 - suboptimal infant and child feeding practices (including exclusive breastfeeding);
 - insufficient communication and play to stimulate learning;
 - delayed and inappropriate care-seeking;
- increased child morbidity;
- increased use of harsh discipline;
- increased family stress.

Exposure to societal violence likely to occur with:

- child abuse and neglectful parenting;
- disruption of family or community support systems;
- disrupted and dysfunctional health systems;

- child nutritional deficiencies;
- child not receiving adequate health care (e.g. immunization)

Growing up in an overcrowded home likely to occur with:

- high burden of infections in infancy or childhood;
- inadequate health care (e.g. immunizations)
- malnutrition;
- spousal violence;
- parental use of harsh physical punishment;
- child ingestion of toxic substances;
- maternal depression.

Interventions encompassing the period before conception to birth

Maternal health

While nurturing care interventions usually begin at birth, established RMNCH interventions can reduce adverse growth and health outcomes including stunting, low birth weight and iron deficiency anaemia that are strongly related to early child development. In our review of LMICs, we identified six such RMNCH interventions during the period from preconception to birth and labour that have statistically significant effects on child development, in addition to growth, mortality, morbidity, or disability. These interventions include: iodine supplementation before or during pregnancy,(52) antenatal corticosteroids for women at risk of preterm birth,(53) magnesium sulphate for women at risk of preterm birth,(54) antiplatelet agents for women at risk of pre-eclampsia,(55, 56) and therapeutic hypothermia for hypoxic ischaemic encephalopathy (see web appendix for details). One review found mixed effects of delayed cord clamping on measures neurodevelopment at four months. Tobacco and alcohol use are viewed as an important threats to the health of pregnant women and their children. A review of 86 randomized control trials (RCTs) showed that psychosocial programmes have been successful during pregnancy for smoking cessation, reducing low birthweight and preterm births, but evidence is limited on such interventions in LMICs.(57)

Maternal nutrition, micronutrients and iodine supplementation

The ability of a mother to support the health and development of her children is critically dependent on her own health and well-being before, during, and after pregnancy. Intrauterine growth restriction (IUGR) influences multiple aspects of child development and has been linked to poorer neurodevelopmental outcomes, risks of prematurity, reduced school performance, and heightened behavioural problems in children.(58) Evidence suggests that linear growth is correlated across generations and short maternal stature is associated with low birth weight, stunting, childbirth complications, and increased child mortality.(59) The provision of a balanced energy and protein diet (60) as well as multiple micronutrients for women of childbearing age(58) and expectant mothers at risk of deficiencies show potential benefits in reducing the risk of IUGR, small for gestational age (SGA) births, and stillbirths. Iron and iron-folate supplementation during pregnancy reduces the risk of SGA and premature births,(61) while folic acid fortification is associated with prevention of neural tube defects and risk of adverse birth outcomes.(62) Iodine supplementation in moderate-to-severely iodine deficient areas is the only nutrition-related intervention during pregnancy with evidence of a significant impact on children's cognitive development scores (10-20%).(52)

Maternal stress, depression and mental disorders

The onset of caregiving in humans is triggered by hormonal signals beginning in pregnancy (e.g., oxytocin and lactogens).(63) Mental disorders and the timing of stress during pregnancy, can disrupt maternal programming that prepares women to respond towards their infants and have negative effects on the fetus.(64) The disruption to maternal programming might account for associations between maternal mental disorders, insecure mother-infant attachment and exposure to maltreatment. Antenatal mental disorders in women (including depression and anxiety) are among the commonest morbidities of pregnancy and are associated with a range of negative child outcomes, including SGA births, low levels of cognitive development; recent evidence is emerging that paternal mental health during pregnancy can also influence the socioemotional and behavioural development of children.(65) A systematic review of 13 trials of psychological interventions for women with antenatal depression in LMICs delivered by local community health workers showed positive effects on reducing maternal depression. Benefits to children included improved mother-infant interaction, better cognitive development and growth, reduced diarrhoeal episodes, and increased immunization rates.(66) Antidepressants for treatment of antenatal depression, on the other hand, have been associated with small but significant increases in preterm birth and reductions in birth weight.(67, 68) Persistence of depression (into the postnatal period and beyond) seems to be of particular importance in relation to cognitive development, including achievement of developmental milestones, and language development.(64) Recent trials from Bangladesh(69) and Uganda(70) suggest that group-based parenting programmes can improve maternal mental health in community settings and young children's cognitive and receptive language scores. However, more analysis is needed to determine which characteristics of maternal health interventions are associated with improved maternal wellbeing and issues of scalability.

Living in poverty is associated with a high degree of stress. Cash transfer programmes have increased rates of prenatal care, probability of in-facility birth and of having a skilled birth attendant(71) -- conditions often associated with improved birth and later developmental outcomes. During labour and childbirth, mothers who have continuous social support (e.g., emotional support, comfort measures, information, advocacy) show significant positive clinical

benefits for themselves and for their infants.(72)

Interventions from birth to five years

Parenting Support

Opportunities for stimulation, responsive parent-child interactions, child-directed/focused enrichment, early learning, and positive parenting are crucial for children's development.(22) Parenting programmes are operationally defined as interventions or services aimed at improving parenting interactions, behaviours, knowledge, beliefs, attitudes, and practices. Three recent reviews of parenting programmes in LMICs found positive effects on direct measures of children's cognitive and language development across diverse policy, service delivery, and social contexts.(23-25). We updated and expanded on the previous reviews by conducting a meta-analysis of non-cognitive outcomes and concluded that parenting programmes increased scores on measures of psycho-social development (SMD 0.35, 95% CI 0.14-0.56, 13 studies) and motor development (SMD 0.13, 95% CI 0.07-0.19, 9 studies), in addition to child cognitive development (SMD 0.36, 95% CI 0.22-0.49, 19 studies). The effect on child growth was not statistically significant.

Parenting programme implementation varied in relation to dose of intervention, setting, and curriculum. The total amount of contact with parents, which ranged from less than 10 hours to 120 hours, did not have a clear relationship to the size of effect.(24) Some programme models have used only home visits, e.g., Roving Caregivers in Jamaica (73) and others have used group sessions, e.g., Pastoral del Niño in Paraguay.(74) Combined group sessions and home visits in Bangladesh(75) and Brazil(76) produced better outcomes than home visits alone. The most effective parenting programmes used multiple behaviour change techniques, including small media such as posters and cards that illustrate enrichment practices, opportunities for parental practice of play and responsive talk with their child, guidance and support for changing practices and problem-solving strategies.(23) Examples include, the *Care for Child Development* package developed by UNICEF and WHO, and "Reach Up and Learn", which provide opportunities to use multiple strategies to strengthen nurturing care by parents.(10) A notable gap in the reviews is the role of fathers in promoting nurturing care and protection.(77) Parenting programmes that combine nutrition and stimulation have been effective in improving child outcomes. (19) Taken together, the results suggest that parenting support programmes that promotes nurturing care and protection can significantly augment the positive impacts of basic health and nutrition, education and protection interventions on early child development outcomes.

Attachment and bonding

Different brain systems enhance nurturing by supporting infant-mother attachment, as well as emotional wellbeing, learning and memory, attention, and executive functions.(78) Secure attachment forms with a caregiver who provides security, safety, affection and comfort. Aspects of *Nurturing Care* during birth and labour include early initiation of breastfeeding and interventions such as Kangaroo Mother Care (KMC) which promotes thermal sufficiency in preterm infants, and early bonding. KMC has been associated with an increase in bonding indicators such as mother-infant attachment (MD 6.24, 95% CI 5.57-6.91), infant growth, and rates of early initiation and continued exclusive breastfeeding (RR: 1.20, 95% CI 1.01-1.43).(79) Most of these evaluations were undertaken in health facilities; there is a need for research on focusing on effectiveness of KMC or variant thereof when delivered at scale in community settings.(80)

Breastfeeding

Breastfeeding has clear short-term benefits for child health, reducing mortality and morbidity from infectious diseases, healthy food preferences, and promotes the establishment of a healthy gut microbiome.(81) A recent review on 17 observational studies of breastfeeding presents evidence that optimal breastfeeding supports improved performance in intelligence tests in childhood and adolescence, demonstrating an IQ increase of 3.44 points (95% CI 2.30-4.58).(82). Findings from a recent analysis of the Pelotas birth cohort in Brazil also demonstrated a dose-response relationship between breastfeeding duration and increased intelligence, educational attainment, and income.(81, 83) The positive effect of breastfeeding has been observed in one RCT in Belarus, where duration of total and exclusive breastfeeding was higher in the intervention group that received the baby-friendly hospital initiative, as well as performance in intelligence tests at 6.5 years.(84) A cohort analysis from South Africa found that exclusive breastfeeding was associated with fewer than average conduct disorders.(85)

Micronutrients and child feeding

One high-quality review limited to four trials found that multiple micronutrient supplementation in children at risk of deficiencies has also been shown to improve academic performance among children 5-12 years of age (SMD: 0.30, 95% CI 0.01-0.58). (86). A review of iron supplementation in children aged 0-12 months found improvement in psychomotor development (MD 6.90, 95% CI 1.35-12.45), One review of iron supplementation found a decrease in IQ (MD: -3.00, 95% CI -5.96 to -0.04)(87); a second review found an improvement in mental development (SMD: 0.30, 95% CI 0.15-0.46) and IQ (SMD: 0.41, 95% CI 0.20-0.62).(88) One review focused on the effect of supplementary food given to socio-economically disadvantaged children 3 months to 5 years of age found that food supplements improved psychomotor development (SMD 0.41, 95% CI 0.10-0.72), but found mixed effects on measures of cognitive development in different trials (SMD -0.40, 95% CI -0.79,0; Bayley II: Mental Development), (SMD 0.58, 95% CI 0.17-0.98; cognitive development test battery).(89) Results from individual studies in Bangladesh(90) and India(91) suggest that responsive feeding can be effective in promoting child growth and developmental outcomes.

Prevention of child maltreatment

Family violence is increasingly recognized as a key public health problem in LMICs. Maltreatment during childhood is associated with reduced mid-sagittal area and hippocampal volume, which are brain regions involved in learning and memory.(92) Children who receive inadequate care, especially in the first 24 months of life, are more sensitive to the effects of stress and display more behavioural problems compared to children who receive nurturing care.(93) There is increasing evidence that one of the most powerful predictors of caregiving behaviour is how caregivers, especially mothers, were cared for themselves.(94) Children who grow up neglected or abused by their parents, or under conditions of extreme distress within their families, are at risk of developing a host of unhealthy behaviours that affect their own lives. When these children grow up, they tend to be less equipped to take on a parenting role and are more likely to perpetuate a cycle of adverse caregiving across generations. The maltreatment prevention interventions with the best evidence are selective programmes (e.g. Nurse Family Partnership) characterized by intensive visits by professional home visitors, beginning prenatally, but these programmes have not been evaluated in LMICs. The extent to which these findings are generalized beyond the specific HICs where they have been evaluated is unknown (see supplementary web appendix for maltreatment prevention interventions). A systematic review of 12 parenting interventions for reducing harsh/abusive parenting in LMICs found potentially positive results on a range of parenting measures, but the quality of included trials was generally low.(31) Early intervention that occurs prior to the onset of abusive and neglectful parenting is crucial to preventing maltreatment. One specific parenting programme (Triple P) has shown some promise in one HIC RCT. There is an urgent need for more rigorously evaluated maltreatment prevention interventions in LMICs, focusing on parenting and child outcomes, and adapted for low resource contexts. More recent reviews of ECD interventions in LMICs are suggesting associations with violence reduction and peace promotion (See web appendix).

Out of home interventions

Effects of early learning programmes, including quality childcare, kindergarten, preschool, and pre-primary are well established in LMICs.(22) Based on an update of an earlier published review,(24) we found that formal and non-formal or community-based preschools in LMICs improved scores on direct measures of children's cognitive development (SMD 0.67, 95% CI 0.43-0.91, 26 studies) and psychosocial development (SMD 0.23, 95% CI 0.06-0.4, 5 studies). Effects on child growth were non-significant and one study measuring motor development showed non-significant effects. The earlier review found that effects of non-formal preschools on child outcomes were typically weaker than the effects of formal preschools; yet some low-cost and innovative programmes such as home-based preschool(95) and a child-to-child approach improve developmental outcomes in comparison to non-participants. Regardless of type, programme quality is a key predictor of effectiveness; important factors of preschool quality include greater number, variety and challenging play materials,(96) interactive / dialogic reading, classroom organization and instructional support. Nurturing environments in the form of care and positive interactions and individualized attention appear to be important in early learning programmes. Positive center emotional climate, including individualized attention, positive affect, and reinforcement of children's behaviours, has shown associations with children's early-childhood cognitive as well as socioemotional skills in Chile(97) and Ecuador.(98)

Social safety net interventions

Our analysis of the systematic reviews(41, 42, 44, 45, 71) and the new literature (see Appendix) on social safety net interventions suggests positive effects of conditional cash transfer programs on some child outcomes, including birth weight and illness or morbidity. Outcomes with mixed or sub-group effects included height-for-age or stunting,

weight-for-age or underweight, and cognitive and language development. Conditional cash transfer programme participation consistently had no effects on hemoglobin concentration or prevalence of anemia in children. In terms of indirect effects of these programs, results were strong and significant for effects of participation on prenatal care, growth monitoring, micronutrient supplementation, and household food consumption. There were mixed effects, however, on the presence of a skilled birth attendant at child birth, and receipt of child vaccinations. It is difficult, however, to compare results across countries and contexts because programmes differ greatly. The impact of cash transfers on child development can be improved by combining social protection and ECD interventions. Cash transfer programmes try to address many issues at multiple levels (e.g. parental, community) that influence child development, but they do not directly change the factors that are linked with improving development outcomes. On the other hand, programmes promoting child development that have an educational or stimulation component have shown larger cognitive effects than cash-only or nutrition-only programmes in Columbia.(99) Bringing these two interventions together can address both economic and nurturing-care factors that impact developmental outcomes.

In summary: Nurturing care and protection can mediate risk factors in early childhood

We conducted a comprehensive review of 40 ECD-related interventions across diverse sectors and found 14 types of interventions that show benefit on multiple child outcomes including child development, based on high quality systematic reviews (**Table 1**). Many of those with effects on child development encompass aspects of *Nurturing Care* including parenting support and social protection, care for the caregiver, and early learning opportunities provided in or out of the home environment.

Table 1: Summary of effective interventions for improving child development, nutrition and growth, mortality, disability and morbidity in LMICS, based on high-quality systematic review evidence

Intervention type	Child Development	Nutrition & Growth	Mortality	Disability, Injury & Malformations	Severe Morbidity
Iodine supplementation before or during pregnancy	✓	✓	✓	✓	
Antenatal corticosteroids for women at risk of preterm birth	✓		✓		✓
Magnesium sulphate for women at risk of preterm birth	✓			✓	
Antiplatelet agents for women at risk of pre-eclampsia	✓	✓	✓		
Therapeutic hypothermia for hypoxic ischaemic encephalopathy	✓		✓	✓	✓
Psychological interventions for common perinatal mental disorders	✓	✓			✓
Iron supplementation in children	✓	✓			
Multiple micronutrient supplementation in children	✓	✓			
Supplementary feeding for disadvantaged children	✓	✓			
Parenting programmes	✓				
Integrated parenting and nutrition programmes	✓	✓			
Out of home interventions (pre-primary education)	✓				
Conditional cash transfer	✓				✓
Unconditional cash transfers					✓
Periconceptional folic acid fortification/supplementation				✓	
Birth interval <18 months vs. 36-60 months		✓	✓		
Preconceptional diabetes care			✓	✓	
Iron and iron-folate supplementation during pregnancy		✓			
Multiple micronutrient supplementation during pregnancy		✓	✓		
Balanced protein-energy supplementation during pregnancy		✓	✓		
Intermittent preventive therapy and bed nets for malaria in mothers and children		✓	✓		✓
Antibiotics for premature rupture of membranes		✓		✓	✓

Lower genital tract infection screening and treatment		✓			
Antibiotics for asymptomatic bacteriuria		✓			
Detection and treatment of syphilis		✓	✓		✓
Smoking cessation interventions		✓			
Delayed cord clamping (more placental transfusion)	✓	✓	✓		✓
Continuous support during childbirth					✓
Kangaroo mother care (KMC), skin-to-skin, cap/wrap (thermal care)		✓	✓		✓
Topical emollient therapy for preterm neonates		✓	✓		✓
Intramuscular vitamin K for neonates					✓
Handwashing behavior and water quality improvement (WASH)		✓	✓		✓
Rotavirus, HiB, & pneumococcal vaccinations			✓		✓
Vitamin A supplementation in children		✓	✓	✓	✓
Zinc supplementation + treatment for acute diarrhea in children		✓	✓		✓
Deworming drug treatment in children		✓			✓
Breastfeeding promotion, education, or support	✓	✓			
Complementary feeding education/provision		✓			✓
Treatment of moderate and severe acute malnutrition		✓			✓
Interventions to prevent child maltreatment (specific home-visiting and parenting programmes)*					

Notes. Checkmarks pertain to statistically significant pooled effect sizes. * Most rigorous trials of interventions to prevent child maltreatment have been conducted in HICs, with far fewer in LMICs, and are not uniformly effective in reducing injuries, physical abuse and neglect.

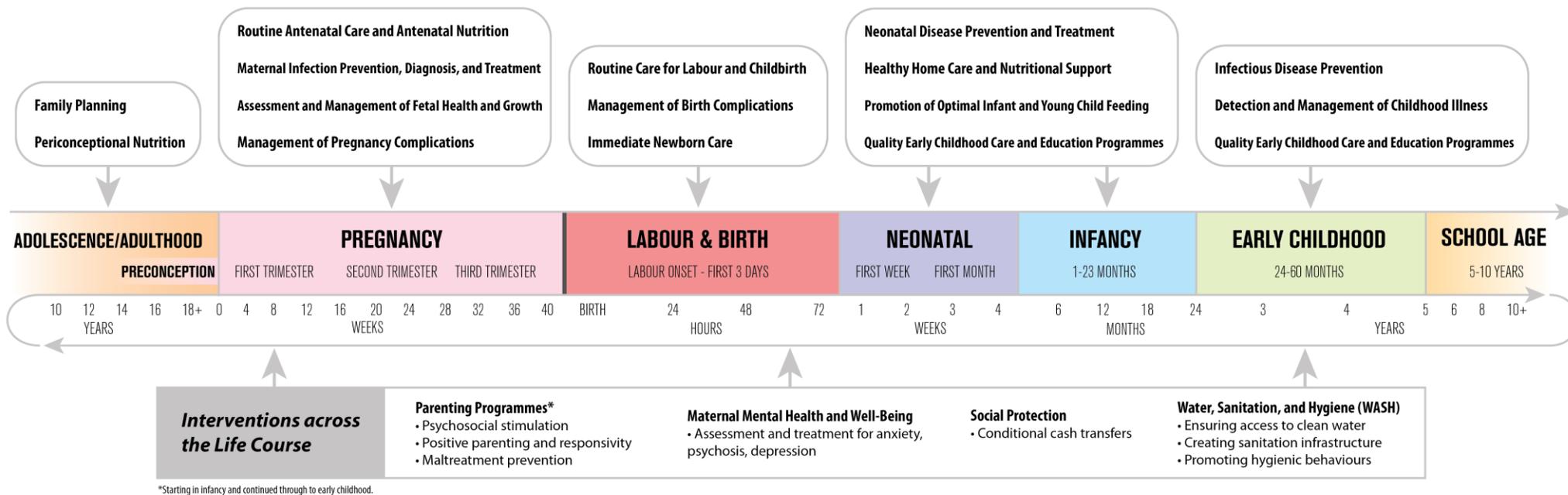


Figure 1: Evidence-based interventions that affect aspects of Nurturing Care

Intervention packages that integrate *Nurturing Care* with sector-specific programmes

Building on the earlier Lancet ECD series, the subsequent literature on early childhood interventions has expanded to include new longitudinal data and cohort data from LMICs. Most interventions during the period from preconception to birth focus on the physical and mental health of the mother to support a healthy pregnancy and improve birth outcomes. Interventions focusing on nurturing care and protection are usually introduced at birth, however, maternal programming for nurturing care begins during pregnancy and even earlier, with caregiver's own childhood experiences. Evidence-based interventions during infancy, which combine basic sectoral elements in health, nutrition, child and social protection, and child care and learning, with nurturing care and protection can synergistically improve child developmental outcomes. For example, including stimulation in nutrition programmes can improve developmental outcomes, which cannot be fully promoted through nutrition interventions alone.(23) Breastfeeding is an example of an intervention, which combines elements of nutrition with bonding.

Building on sectoral services

Multi-sector approaches include coordinated services across sectors, ideally with unifying policies. Integrated approaches refer to integration across services with shared messages and opportunities for synergy. (Black, et al., this series). Many sectoral interventions could serve as the basis for delivery of services that link policy level strategies of cash transfer, social policies, and income generation with programmatic interventions that could benefit child development, such as parenting support (See web appendix). Sectors, such as water and sanitation, were not included in this review, as further research is needed to examine their effects on developmental outcomes. However, associations have been noted between these sectoral interventions and such outcomes as child nutritional status, growth, and health. (73)(74)(75)

Delivering multi-sectoral intervention packages to improve child development

The impact of interventions could be improved by taking into consideration the major insights we have gained over the past decade about how human development is affected by complex and multi-faceted experiences, starting with previous generations. Based on the science of early human development, we need conceptualize meaningful integration of interventions through a coordinated approach. In instances where sectoral interventions were combined with elements of nurturing care and protection, the impact of the intervention on child outcomes increased significantly (See web appendix for established studies of ECD). This approach allows us to intervene with the family as a unit rather than the child alone. Further, there are increasing opportunities to improve interventions by combining them with nurturing care and protection, through parenting support and skills programmes.

Previous attempts at creating packages of effective interventions have focused either on the temporal relevance of the interventions, i.e., packaging interventions that co-occur during the same age period of the child,(100) or on the delivery of the programmes through the same system (e.g., MNCH). While important to consider these factors, we also need to incorporate nurturing care and protection into the packages and tailor them to unique sets of risks and adversities facing the young child population particular to the setting.

Based on our review, we propose three illustrative packages that build on these principles and the findings. These interventions affect different aspects of nurturing care and cover numerous domains and stages in the life course (**Figure 1**).

1. ***Family Support and Strengthening Package***: Three elements of family strengthening: (i) access to quality services (e.g., antenatal care, immunization, nutrition); (ii) skills building (e.g., positive and responsive parenting to reduce harsh discipline and promote stimulation); and (iii) support (e.g., social protection, safety networks, family support policies) increase the likelihood that families are better able to provide nurturing care for their children. Each of these elements - services, skills and support – have independent predictive effects, however significant positive effects are seen when they are combined with programmatic interventions (e.g., social protection interventions). By creating a package of the three elements of “Services, Support and Skill building”, based on the age of the child and nature of risks, developmental outcomes could be substantially improved.
2. ***‘Caring for the Caregiver’- Multi-Generational Nurturing Care Package***: This 2-generation package, emphasizes care and protection of the mother's and father's physical and mental health and well-being

while enhancing their capacity to provide nurturing care to their child. This package combines the essential interventions, of health and nutrition, from pre-conception, for the 1st 1,000 days, adding to them elements of care, responsivity, stimulation and protection, primarily delivered by the health system. This package can be further strengthened with parental leave policies as discussed in Richter et al, this series. While the reviews did not specifically cover situations of conflict and violence, this package is also relevant for humanitarian contexts (See Panel 3). Conflict, violence, and insecurity present a complex array of adversities. Families, parents and caregivers, in these settings, require a package of services that addresses their needs as well as the immediate and long-term needs of their children.

3. **Early Learning & Protection Package:** This set of interventions integrates support to young children, as well as parental support and facilitation of teachers' and caregivers' ability to create a nurturing environment in early childhood centers, classrooms, and community settings for learning. The package of interventions should include nurturing care and protection by enhancing teachers' capacities to providing a nurturing, safe, and positive emotional climate and should include greater attention to parental support. Long term gains have been noted when early learning packages have included parenting support and protection for young children.(14) This package needs to emphasize quality and family support through parental empowerment, guidance on nutrition and care, and child protection.

There are advantages of such integrated packages in terms of delivery; one location can be used for the provision of key services for young children. Platforms at community, clinic, and school levels can be identified to coordinate the delivery of the packages targeting population segments and families in greatest need. For example, community platforms that mobilize antenatal and postnatal home visits by community health workers complement facility-based care and promote family contact with the health system at crucial times. Social protection platforms provide the opportunity for identification of families and delivery of packages of services that link these policies with programmatic interventions. Factors that influence selection of package of interventions include: the age group being targeted, the expertise of the sector, coverage, or an analysis of the most efficient and effective use of resources within a service for a particular context. More evaluation is needed to codify the interventions to pull them together into essential packages, assess effectiveness, implementation quality and cost-benefits of integrated, inter-sectoral and multi-sectoral approaches for ECD packages. Delivery of multi-sectoral services involves challenges, including, limited workforce capacity, demonstration of value added for including programmatic interventions of nurturing care, and political will (some of these challenges are discussed in Richter et al., this series).

Panel 3: ECD for violence prevention and peace promotion

While the literature on implementing ECD interventions in contexts of conflict and fragility is limited, the theoretical and empirical underpinnings are strong. The biobehavioral systems that underlie the development of parent-child relationships are ancient and deeply rooted in our mammalian evolution and also highly adaptable to changes in the environment. For example, exposure to violence in the home environment and other adverse childhood experiences are associated with changes in brain structure and function. Unfortunately, these children are also at an increased risk to become perpetrators of violence as they grow older, so that violence can become self-perpetuating from generation to generation. The biological underpinnings of these phenomena are likely involve epigenetic mechanisms. Early parent-child programs aimed at enhancing responsive parenting and supporting can reduce adverse childhood experiences (poor nutrition, neglect, abuse, and exposure to violence in the home) and can positively impact the child's cognitive and socio-emotional development as well as their brain structure and function as well as their physical health. Despite an ever-growing body of research, we still have a long way to go before we fully understand the role of the epigenome in shaping human behavior across generations. If consistent findings emerge, this will provide a solid foundation for the hypothesis that interventions to strengthen families, promote nurturing care and protection, and to improve the cognitive and socioemotional well-being of children have trans-generational consequences for building a more peaceful world from the bottom-up. (See web appendix for details)

Future research areas

While we have made progress in understanding “what works”, there are major gaps in our knowledge. The particular set of risks faced by children in conflict is not well understood. We also lack knowledge about the effectiveness of ECD interventions operating in conflict-affected and fragile country contexts. We need to improve our understanding of (i) how to better combine interventions through robust assessment of intervention outcomes and evaluations of integrated parenting, responsive care, stimulation, mental health, education and protection interventions that could be delivered through community platforms; (ii) use of technology-based platforms to deliver effective interventions (See web appendix); and (iii) evidence-based approaches to scaling up.

Conclusion

We call for greater integration between sectoral interventions and those that promote nurturing care and protection to improve developmental outcomes. The results of the review suggest that “successful, smart and sustainable” interventions to improve developmental outcomes need to: (i) promote nurturing care and protection; (ii) be implemented as packages that target multiple risks; (iii) be applied at developmentally appropriate times during the life course; (iv) be of high quality; and (v) build on existing delivery platforms to enhance feasibility of scaling-up and sustainability. We have proposed illustrative packages that meet these requirements. The nature of these interventions will continue to improve as new understanding of early human development emerges. While question remains about scaling-up interventions at a population level (See Richter et al., this series) we are now at a historic juncture where the evidence is clear about what needs to be done to improve the well-being of future generations and the political commitment strong, as expressed in Agenda 2030. In this paper we call for meaningful integration across sectoral interventions through programmatic packages that promote nurturing care and protection to improve developmental outcomes, and also for better integration of evidence-based interventions within health and nutrition sectors. The science is clear and the evidence convincing that our earliest experiences matter; the SDGs provide a critical opportunity for implementation. We must draw on this knowledge to take action to support parents, caregivers, and families in providing the nurturing care and protection that young children deserve.

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Figure 1: Evidence-based interventions that affect aspects of Nurturing Care

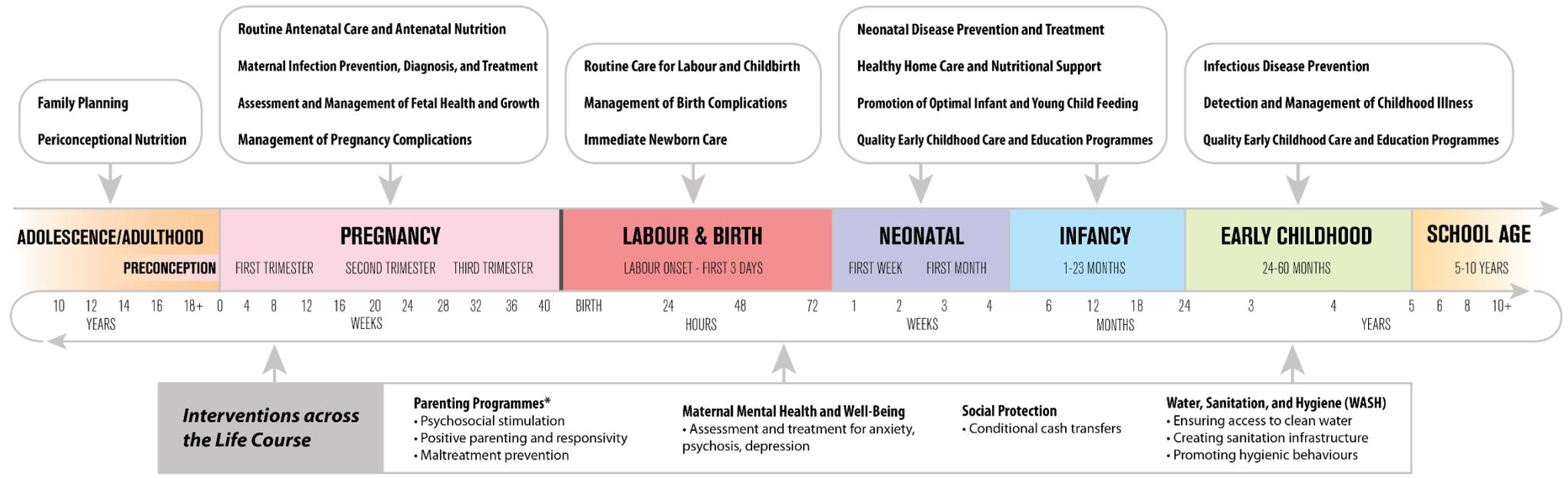


Table 1: Summary of effective interventions for improving child development, nutrition and growth, mortality, disability and morbidity in LMICS, based on high-quality systematic review evidence

Intervention type	Child Development	Nutrition & Growth	Mortality	Disability, Injury & Malformations	Severe Morbidity
Iodine supplementation before or during pregnancy	✓	✓	✓	✓	
Antenatal corticosteroids for women at risk of preterm birth	✓		✓		✓
Magnesium sulphate for women at risk of preterm birth	✓			✓	
Antiplatelet agents for women at risk of pre-eclampsia	✓	✓	✓		
Therapeutic hypothermia for hypoxic ischaemic encephalopathy	✓		✓	✓	✓
Psychological interventions for common perinatal mental disorders	✓	✓			✓
Iron supplementation in children	✓	✓			
Multiple micronutrient supplementation in children	✓	✓			
Supplementary feeding for disadvantaged children	✓	✓			
Parenting programmes	✓				
Integrated parenting and nutrition programmes	✓	✓			
Out of home interventions (pre-primary education)	✓				
Conditional cash transfer	✓				✓
Unconditional cash transfers					✓
Periconceptional folic acid fortification/supplementation				✓	
Birth interval <18 months vs. 36-60 months		✓	✓		
Preconceptional diabetes care			✓	✓	
Iron and iron-folate supplementation during pregnancy		✓			
Multiple micronutrient supplementation during pregnancy		✓	✓		
Balanced protein-energy supplementation during pregnancy		✓	✓		
Intermittent preventive therapy and bed nets for malaria in mothers and children		✓	✓		✓
Antibiotics for premature rupture of membranes		✓		✓	✓

Lower genital tract infection screening and treatment		✓			
Antibiotics for asymptomatic bacteriuria		✓			
Detection and treatment of syphilis		✓	✓		✓
Smoking cessation interventions		✓			
Delayed cord clamping (more placental transfusion)	✓	✓	✓		✓
Continuous support during childbirth					✓
Kangaroo mother care (KMC), skin-to-skin, cap/wrap (thermal care)		✓	✓		✓
Topical emollient therapy for preterm neonates		✓	✓		✓
Intramuscular vitamin K for neonates					✓
Handwashing behavior and water quality improvement (WASH)		✓	✓		✓
Rotavirus, HiB, & pneumococcal vaccinations			✓		✓
Vitamin A supplementation in children		✓	✓	✓	✓
Zinc supplementation + treatment for acute diarrhea in children		✓	✓		✓
Deworming drug treatment in children		✓			✓
Breastfeeding promotion, education, or support	✓	✓			
Complementary feeding education/provision		✓			✓
Treatment of moderate and severe acute malnutrition		✓			✓
Interventions to prevent child maltreatment (specific home-visiting and parenting programmes)*					

Notes. Checkmarks pertain to statistically significant pooled effect sizes. * Most rigorous trials of interventions to prevent child maltreatment have been conducted in HICs, with far fewer in LMICs, and are not uniformly effective in reducing injuries, physical abuse and neglect

Web Appendix

[Click here to download Web Appendix: Paper 2 Supplementary Web Appendix_Jul12.docx](#)

July 12, 2016

Dear Dr. Das

We would like to thank you (as editor) and the reviewers for their comments on our paper entitled "*Nurturing Care: Science and Effective Interventions for Early Childhood Development.*" We believe that your editorial comments and those the comments from the reviewers have been very helpful in allowing us to improve the manuscript.

Please see below our responses to the editorial comments and those of the reviewers.

We attached the revised copy of the paper for your consideration.

Sincerely,
Pia Britto & Stephen Lye

Editor/Review Comments	Author Response/Revisions
Authors need to lose the IMRAD format for the summary, and also in the main text. For example, the subheadings in the intro (breastfeeding, maternal nutrition, etc) can be combined with the sections about these risk factors in the results.	Revised – IMRAD format removed in abstract and main text. Background information on breastfeeding, maternal nutrition is combined with section on results.
Panel 2 is search strategy so we will keep but move to first page.	Revised - Panel 2 has been moved up in the paper.
Panel 5 can be summarised in main text and rest moved to web	Revised – Multi-sectoral services summarized in main text; panel removed; also discussed in Paper 1.
Panel 6 seems important so would keep.	Revised – We agree, the illustrative packages are important, so we have taken them out of a panel and included them in the main body of the paper.
Panels 7 and 8 can be briefly summarised in text and then moved to web (or referenced).	Revised – Panels on technology and emerging science moved to web appendix
Panels 3 and 4 I think are better on web.	Revised – Panels on social protection and peace promotion moved to web appendix. However have included a shorter panel on the scientific underpinnings of ECD interventions in emergency contexts, because the literature is sparse on this topic and we want to call out that gap in the literature
Overall word count should be 4500, and refs 150 (should be OK when panels move to web as a lot of refs in panels)	Revised – The word count of the paper is ~4625 word, excluding objects, references, and front matter.
Need statement in text (contributors, COI, acknowledgements)	Contributors, COI and acknowledgements are included on page 2.
The authors describe a section on MICS and some recent data analysis of MICS data linking poverty and risk - promotive factors	Revised – The MICS analysis on SES and risk factors has been removed. We are working on it for another individual paper where the issue can

Editor/Review Comments	Author Response/Revisions
<p>vs risk factors. I was not clear as to why this was put in the introduction as it looked like a new analysis and although very interesting and relevant, wasn't quite sure where this should sit within the article.</p>	<p>be given sufficient attention.</p>
<p>Identification of research areas: The authors define the term "nurturing care" in the introduction and break up the interventions into "nurturing care, health and nutrition and education" in the appendix. It would be really helpful for the reader if there was clarity as to what the authors define as "nurturing care" and how they classified topics for review into this vs. health and nutrition vs. education.</p>	<p>Revised – we have now included an elaborated definition on nurturing care and its relationship to the interventions that are delivered by the sectors of health, nutrition, education. This definition is aligned with the conceptual framing provided in paper 1.</p>
<p>The methodology for identifying research areas relating to "nurturing care and protection" was not entirely clear or transparent particularly as the research areas then generated included health and nutrition and education which are separated as different areas in the web appendix table. This maybe comes down to clarity of definitions.</p>	<p>Revised – see above</p>
<p>Although most topic areas seemed to have been covered there were some areas which were not and it was not entirely clear how a judgement was made on inclusion or exclusion of topics e.g. how come they did not include screening for PKU, hypothyroidism, hearing screening for example, or if they included "interventions at birth", why did that not include "quality obstetric care" or rates of cesarean sections or neonatal resuscitation. I imagine that you have to stop somewhere and can not include everything but was a little unsure as to how the topics were chosen and defined.</p>	<p>Revised – The focus of the paper is on child development outcomes. Interventions, such as health interventions were identified through overviews of essential MNCH services and those that showed developmental benefits. The interventions were identified by the sector specific review team using a set of standard protocols for data searching, screening, filters, and selection.</p>
<p>I also was not clear what their inclusion and exclusion criteria were for each of the study searches eg. Population, intervention, comparison group, outcomes. This may have been in a web appendix or may be too much detail but I wanted a bit of clarity. The authors do define (panel 2) that the studies pertained to LMICS (as much as possible) but do not define this and do not make it clear which studies</p>	<p>Revised – We have now clarified in Panel 2 the inclusion of HICS and LMIC. HICs are included for maltreatment prevention interventions only, as existing evidence was unavailable or limited from LMICs.</p>

Editor/Review Comments	Author Response/Revisions
<p>were from LMICs and which had data mainly from HIC settings. Could this be also in the table in the web appendix.</p>	
<p>I am sure the expert panel had reasons to include or not certain subject areas/interventions but it wasn't clear. For the topics that were chosen, were there PICO's done (as above), or how did the team define the reviews/questions that they chose to include? The authors describe that they looked up key words and search terms that this was in an appendix but I was unable to find this in the appendices that I reviewed.</p>	<p>Revised – we have now provided a series of papers in the web-appendix each one detailing the search strategy and methods for the sector specific reviews</p>
<p>The authors conducted a targeted web search of systematic reviews. Which databases did they use and how did they define systematic reviews? What were the exact dates of searching? Many of the references are systematic reviews but there are a number of topics where there is only a review paper by a few authors referenced. Could the authors describe within the article which topics had a systematic review already conducted and which ones did not - maybe in the table of topics in the appendix? I wasn't clear if these ones were a "de novo" review and if so, how that was done (maybe this is missing from the appendices).</p>	<p>Revised – we included reviews from 2011 to March 2015, and clarified this in description of the search strategies. Databases searched are available in web appendix papers. All topics had published, peer reviewed systematic reviews. Updated review/de novo and meta-analysis conducted for parenting and early childhood education only, as existing reviews focused on cognitive outcomes only – the updated analysis in this paper includes non-cognitive outcomes.</p>
<p>Outcomes: It is not entirely clear in the article what outcomes the authors are describing or looking at as an end result. In panel 2 the authors explain that the outcomes they considered were child health, growth, behavior, learning and psycho-social functioning but although I understand how this relates to "nurturing care", I wonder if it needed to be spelled out. Also, could the detail of what outcomes were included or not be placed somewhere in the appendix? It is clear that these are very variable in many of these studies and hard to tally. This is particularly the case when looking at the antenatal studies with outcomes which may be linked to neuro-development. Were the authors able to define outcomes in any way (as in what they included or analysed or did not</p>	<p>Revised – the paper reviews the available evidence that addressed child outcomes, including: (i) mortality, (ii) malformations, disability, and injury, (iii) nutrition and growth, and (iv) severe morbidity. The primary focus, however, was direct measures of child development outcomes (e.g., language, cognition, motor, social and emotional, learning, and psychosocial well-being). Together, these outcomes encompass those theorized to have an intermediate effect on child development, in addition to direct endpoints in child development.</p> <p>We have described in an above comment the definition of nurturing care and in the paper clarify what it means.</p>

Editor/Review Comments	Author Response/Revisions
within the reviews)?	
Figure 3 - this was a very useful diagram. I was not clear if the topics were the interventions considered by an expert panel or reviewed and how these were chosen (going back to the section before on identification of research areas).	Revised – Fig 1 moved to after the review to explain the inclusion of interventions
Conception to birth: The authors describe a number of key interventions in areas of pregnancy and describe adverse birth outcomes such as low birth weight and SGA as the outcomes in these studies. This makes sense to me as there is evidence that SGA and LBW are related to longer term neurodevelopmental outcomes although the authors do not make this entirely clear and it becomes a little confusing. This is similar in the section on maternal health and infection when the authors describe outcomes from syphilis in terms of stillbirths and mortality. I can see that on pp16 1st paragraph, the authors do link this better but I wonder if a sentence earlier on in the methods might be helpful.	Revised – we have streamlined the results to be able to describe better the patterns of findings. We have moved to the appendix the review of interventions that do not directly influence child development outcomes. We have presented a table of the interventions and called out the specific interventions linked to child development.
Panel 3: ECD and Peace-building - This is an interesting and important area however this panel seemed a little long and detailed in the discussion of Mother Child Education Foundation in paragraph 3.	Revised – we have moved the panel to a web appendix. However we have included a smaller panel on ECD interventions in conflict and fragile settings.
Page 18 - landmark studies - these studies were very helpful and interesting to read but I was not clear as to how the authors came to consensus on these being landmark studies.	Revised – we have changed the title from landmark to established studies, as the reviewer is correct, we do not have consensus on the landmark standing of these studies, but do have consensus on the validity of the results.
pp.12 4th line - Maternal health and infection: "Along with routine immunisations....." The authors describe HIV and IPT treatment and give a figure of 19%. Is this for IPTp or for HIV or for both? It is not clear from the sentence.	Revised – we have clarified this in the paper and the result has moved to the web appendix.
Ref 6 - separated over two lines,	Revised – done
Ref 18, 33 - no page number.	Revised – done
Ref 57 - #?	Revised – done
Ref 73 - Cochrane database number?	Revised – done
Ref 132, 175 – Formatting	Revised – done
Reference 87 and 88 are the same.	Revised – done
I found the paper not always easy to follow, and several times I got 'lost' as I was reading through the sections. I think this is	Revised - we have reformatted the paper slightly, with providing more prominent headings

Editor/Review Comments	Author Response/Revisions
<p>partly because of the way the headings are organised, and partly in the writing. I would suggest that attention should be paid to the hierarchy of headings. For example rather than introduce a major section with non-bold italics in small font (eg 'interventions during infancy; birth to two years') it would have been better to have a more prominent heading.</p>	
<p>I also think the paper would benefit from some editing to reduce the length and complexity of some of the sentences and make the language crisper. For example the last paragraph on page 18 (beginning with 'Previous attempts...') the second sentence runs to 5 lines and has 6 commas.</p>	<p>Revised – we have edited the paper to make the sentences simpler.</p>
<p>I am not sure that Figure 1 is necessary, and the information can be just as easily be represented in the text.</p>	<p>Revised Figure on CPI/CRI has been removed.</p>
<p>In the copy that I have that I downloaded from the lancet website, there was no table 2; the paper goes from table 1 to table 3.</p>	<p>Revised The revised paper has one table only.</p>
<p>Mother-infant attachment, which is severely affected by poor maternal mental health, has not been adequately covered. Please refer to the recent Lancet series on perinatal mental health published in November 2014, (especially Stein et al 2014) for a comprehensive coverage of the topic. This systematic review should be included in the synthesis.</p>	<p>Revised - New information included on Lancet 2014 paper and attachment on page 10</p>
<p>Recent evidence on the association of maternal depression with exclusive breastfeeding (Rahman et al 2015, Maternal and Child Nutrition) could also be mentioned in the section on co-occurrence of risk (page 6).</p>	<p>Revised – included in Panel 2</p>
<p>The review does not discuss implementation challenges in adopting multi-sectoral interventions - this is probably beyond the scope of the review but deserves a mention in the discussion section. The key challenge is to translate the evidence into actionable policy and programmes and deserves a few sentences.</p>	<p>Revised this comment has been addressed in the concluding section of the paper.</p>

Nurturing Care: Science and Effective Interventions to Promote Early Childhood Development

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Paper 1

Black, M. et al. Early child development coming of age: From science to practice.

Paper 3

Richter, L.M. et al. Investing in the Foundations of Sustainable Development: Nurturing Care to Optimise Early Childhood Development

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Contributors

PRB and SL conceptualised the review in consultation with the Early Child Development Series Steering Committee and wrote the first draft of the Series paper with substantial inputs from KP. ZB, RPE, MFG, and TV led the review of MCNH and nutrition interventions. NR, PI, and AKY led the review of early childhood education and parenting interventions. HM led the review of child maltreatment prevention interventions. LCHF led the review of social protection interventions. SGM, AC, AF, and VGM contributed to the scientific literature review of nurturing care and human development. TW and HY reviewed the literature on cumulative and protective risk factors. All authors and members of the review groups saw successive drafts of the paper and provided input. PRB, SL, and KP prepared the final version of the Series paper, which all authors approved and PRB is the overall guarantor.

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Conflicts of Interest

PRB is employed by UNICEF. SL has received several grants in relation to health and child development from xxx. The other authors declare that they have no conflicts of interest. The views expressed are those of the authors and not necessarily those of UNICEF, Bill & Melinda Gates Foundation, and Conrad N Hilton Foundation. As corresponding author, Pia Rebello Britto states that she had full access to all data and final responsibility to submit for publication.

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Abstract

The Sustainable Development Goals (SDGs), provide a historic opportunity to implement at scale interventions to promote Early Childhood Development (ECD). While the evidence base for the importance of ECD has grown, the research is distributed across sectors, populations, and settings with diversity noted in the scope and focus. In this paper, we provide a comprehensive update of ECD interventions across five sectors: health; nutrition; education; child protection; and social protection. Our review concludes that to make interventions, successful, smarter and sustainable, they need to be implemented as multi-sectoral intervention packages anchored in “nurturing care.” The recommendations emphasize that intervention packages should be applied at developmentally appropriate times during the life-course, target multiple risks, and build on existing delivery platforms for feasibility of scale-up. While interventions will continue to improve with the growth of developmental science, the evidence is now strong that parents, caregivers, and families need to be supported in providing nurturing care and protection that young children need to achieve their developmental potential.

Word Count: 164 words

Key Messages

- Advances in basic and intervention science indicate that early childhood is a period of special sensitivity to promotive experiences and that critical time windows exist when the benefits of ECD interventions are amplified.
- The most fundamental promotive experiences in the early years come from nurturing care and protection received from parents, family and community, which have lifelong benefits including an improved health and well-being and increased ability to learn and earn.
- Nurturing care and protection is supported by a range of interventions delivered pre-pregnancy through birth and the newborn period, infancy and early childhood, many of which exist with proven benefits for child development, including health, growth and learning.
- Interventions including nurturing care and protection can target multiple risks at developmentally appropriate times and can be integrated within existing preventative and promotive packages.
- These packages can build on existing platforms for delivering parental and child services at scale to vulnerable and difficult to reach populations, such as community-based strategies and social safety nets for enhanced effectiveness and sustainability

Nurturing Care: Science and Effective Interventions for Early Childhood Development

Introduction

Even though global attention to early childhood development (ECD) has been established through its inclusion in the SDGs, 43% of children under 5 years of age in low- and middle-income countries (LMICs) are at the risk of not achieving their developmental potential (Black et al., this issue). We suggest that our failure to enable these children to do so is, at least in part, due to our failure to utilize fully the emerging scientific knowledge on how *Nurturing Care* shapes young children's development and can be applied to take action at scale and narrow this large gap in human potential using a multi-sector approach across key stages in the early life course.

We define *Nurturing Care* as a stable environment that is sensitive to children's health and nutritional needs, with protection from threats, opportunities for early learning, and interactions that are responsive, emotionally supportive, and developmentally stimulating. As an overarching concept, *Nurturing Care* is supported and enhanced by a large array of social contexts – from home to parental work, child care, schooling, wider community, and policy influences. (1) It consists of a core set of inter-related functions, including: behaviours, attitudes, and knowledge of caregiving (e.g., health, hygiene care, feeding care); stimulation (e.g., talking, singing, playing); responsiveness (e.g., early bonding, secure attachment, trust, sensitive communication); and safety (e.g., routines, protection from harm).(2, 3) The single most powerful and proximal context for *Nurturing Care* is the immediate home and care settings of young children often provided by mothers, but also by fathers, siblings, grandparents, extended family, and other child care services.

The brain has evolved to adapt in response to a wide range of early experiences, which supports the rapid acquisition of language, cognitive skills, and socio-emotional competencies. *Nurturing Care* mediates the development of key brain regions and promotes developmental adaptations. These experiences have lifelong benefits, including an increased ability to learn, greater achievement in school and later life, citizenship, involvement in community activities, and overall quality of life.(4, 5) The period of early development is one of enormous change and is characterized by a high degree of plasticity in brain organization. (10, 11) Advances in developmental science have also provided an understanding of the multiple and overlapping critical windows of time when development of specific capacities and abilities is most powerfully enhanced.(8) (9) Nurturing, caring, enriching, and protective interactions provide the early environments needed for developmental progression to occur and protect infants and children from the negative impact of stress and adversity (See Panel 2). Prospective longitudinal studies from across the globe from Jamaica,(7-9) Pakistan,(10) Turkey(11, 12) and elsewhere have demonstrated that including elements of nurturing care into ECD interventions significantly improves child development and later adult outcomes. The interplay between the elements of *Nurturing Care*, the timing of experiences, and complexity of risks requires action beyond single sector interventions.

Selection of interventions for review

This paper provides a comprehensive update of ECD interventions across key sectors. While ~~much good~~ progress has been made with studies and systematic reviews on ECD-related interventions, ~~extant the~~ research is at different levels of maturity across sectors and distributed across numerous populations and settings. ~~EE~~ Experts ~~were selected to review and synthesize available evidence, from representing~~ research communities in ~~Reproductive M~~maternal, ~~N~~ewborn and ~~C~~hild ~~H~~health (RMNCH), nutrition, parenting, ~~and~~ early childhood education, maltreatment prevention, and social protection ~~worked in teams to review and synthesize available evidence~~. Each ~~review~~ team used standard methods to do a comprehensive review of interventions ~~and reviews~~ that addressed ~~five~~ child outcomes, including: (i) mortality, (ii) malformations, disability, ~~and injury~~, (iii) nutrition and growth, and (iv) ~~severe~~ morbidity. The primary focus, however, was ~~direct measures of~~ child development outcomes (e.g., language, cognition, motor, social and emotional, learning, and psychosocial well-being). ~~Together, these outcomes encompass those that are theorized to have an intermediate effect on child development, in addition to direct measures of progress or endpoints in child development. All reviews covered the period since publication of the last Lancet series on ECD - from 2011 to March 2015.~~ Search strategies ~~in each group~~ -were tailored ~~to-by each review team depending on~~ the scope, quality, and focus of existing evidence in each sector. The ~~RMNCH~~ and nutrition reviews identified and relied on the most recent overviews of systematic reviews with good quality methods for all interventions and updated the evidence by incorporating newer studies, when available. The parenting and early childhood education, child protection, and social protection reviews relied on the most recent systematic reviews in each sector. ~~From preconception to birth, the focus of the interventions is primarily on the mother or caregiver. From birth through infancy, interventions typically include both adult and child, and in the age period transitioning into primary school we note a predominantly child-focused set of interventions with increasing evidence on the importance of a nurturing environment provided by teachers.~~ Details of the search methods used for selecting and screening reviews are described in Panel ~~2.1~~

Comment [PB1]: Kerrie for the panel below on methods – are nirmala’s references added:

These are the three reviews that informed the review of ECE programmes for this paper

1. Aboud, F. E., & Yousafzai, A. K. (2015). Global Health and Development in Early Childhood. *Annual Review of Psychology*, 66, 433-457.

2. Brown, T. W., van Urk, F. C., Waller, R., & Mayo-Wilson, E. (2014). Centre-based day care for children younger than five years of age in low-and middle-income countries. The Cochrane Library. <http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010543.pub2/abstract:jsessionid=E3BEDDA47DD4271336478C85444338D1.f02t03?deniedAccessCustomisedMessage=&userIsAuthenticated=false>

Rao, N., Sun, J., Wong, J.M.S., Weekes, B.S., Ip, P., Shaeffer, S., Young, M.E., Bray, M., Chen, E., & Lee, D. (2014). *Early Childhood Development and Cognitive Development in Developing Countries: A Rigorous Literature Review DFID*, UK Government. <http://epi.ioe.ac.uk/cms/Default.aspx?tabid=3465>

Panel 12: Methods and search strategy for selection of interventions for review

This article is based on overviews and systematic reviews that were published and peer reviewed focusing on numerous child outcomes, but primarily on child development outcomes. All reviews used established guidelines to search, evaluate, and synthesize the results of relevant research. The RMNCH and nutrition reviews relied primarily on five recent overviews of reviews, including the Lancet 2014 Every Newborn series,(13) the Lancet 2013 Maternal and Child Nutrition series,(14) the Lancet 2013 Child Pneumonia and Diarrhoea series,(15) the Reproductive Health 2014 supplement on essential MNCH interventions,(16) and the WHO/RMNCH/AKU 2011 Essential Interventions for RMNCH report.(17) The education review was based on four recent reviews, including the Lancet 2011 ECD series,(18) a 2015 Annual Review of Psychology systematic review of parenting interventions(19), a DFID literature review of parenting and early childhood programmes,(20) and a UNICEF systematic review of parenting programmes.(21) A meta-analysis of education programmes was conducted to determine non-cognitive developmental benefits of parenting and early childhood education programmes, as this information was not available in existing systematic reviews. The maltreatment review updated the Lancet 2009 series for prevention of child maltreatment(22) and a systematic review of reviews of interventions to reduce child maltreatment,(23) in addition to a review of 14 recent reviews of maltreatment prevention interventions, including home visiting,(24-26), parenting-training programmes,(27, 28) sexual abuse prevention programmes,(29, 30) universal campaigns to prevent physical abuse,(31) behavioural and counseling interventions,(32) detection of child maltreatment,(33) and three review studies on prevention of child maltreatment.(34-36) The social protection review examined five systematic reviews that focused on the effects of social programmes, including conditional and unconditional cash transfers and microcredit schemes.(37-41)

After examining the systematic reviews, the literature was searched for papers that had been published since the systematic reviews. 24 new studies were included that investigated the effects of CCTs or UCTs on measures of health, nutrition, or developmental outcomes. Each review included overviews and systematic reviews published from 2011 to April 2015. The search focused on research conducted in LMICs, but systematic reviews based on evidence from high-income countries were included for maltreatment prevention where evidence from LMICs was either unavailable or limited. The reviews were double data extracted using a standardized form and methodological quality of systematic reviews was assessed using the AMSTAR criteria, where appropriate. More detailed information on the search strategies for each review can be found in the supplementary web appendix.

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Nurturing care can mediate risk factors in early childhood

In Conclusion, Wwe conducted a comprehensive review of 40 ECD related interventions across diverse sectors and found 13 interventions have available evidence of statistically significant effects on multiple child outcomes including child development, based on high quality systematic reviews (See Table 1). Many of the interventions with effects on child development encompass aspects of *Nurturing Care* including parenting support and social protection, care for the caregiver, and early learning opportunities provided in or out of the home environment. Human infant development anticipates and relies on care by adults that is nurturing, caring, enriching, and protective. These nurturing interactions provide the early environments needed for developmental progression to occur and to protect infants. Nurturing interactions and can mediate the deleterious effects of poverty and other risk factors,(42) which have greater variety and prevalence in LMICS and have higher levels of co-occurrence (Panel 3); children from the negative impact of stress and adversity (See Panel 2). Advances in developmental science have also provided an understanding of windows of time when development of specific capacities and abilities is nurtured. A critical period is a maturational stage, or window, in the lifespan when the nervous system is especially sensitive to environmental stimuli. Critical periods are more clearly defined in the development of animal brains; in humans, there are multiple and overlapping sensitive and vulnerable periods with significant implications for greatest sensitivity to interventions.(43) The period of early human development is one of enormous change and is characterized by a high degree of plasticity in brain organization. (44, 45)

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Panel 2: Co-occurrences among bio-ecological and/or contextual risk factors in LMICs

While there are parallels in the types or risk and promotive factors encountered by children in high-income countries (HICs) and LMICs, the limited comparative evidence indicates that children from LMICs are more likely to encounter a greater number and variety of risk factors and fewer promotive influences than poor children in HICs.(1, 2) Toxins, chronic severe malnutrition, direct exposures to societal armed conflict and displacement, and refugee status are risk factors that occur in LMICs but are rarely seen in HICs. Poor sanitation, severe childhood diarrhea, iron deficiency anemia, orphan status, substandard housing, domestic violence, harsh physical punishment, and maternal depression are risk factors that occur at a higher rate in LMICs than in high-income countries. Some evidence indicates that there may be a reduced availability of promotive factors in LMICs, such as routine neonatal screening for iodine deficiency,(3) childbirth attended by skilled health personnel,(4) and fewer learning resources in the home.(5) In addition to a greater variety and prevalence, there are higher levels of co-occurrence among risk factors in LMICs compared to high-income countries (49) Our own analysis based on Multiple Indicator Cluster Survey data indicates that risk factors in early childhood co-occur. For example, 85% of children aged 3 to 4 years in West and Central Africa and 56% in East Asia and Pacific experience multiple risks. The findings support the application of coordination or combining of interventions, within packages, to reduce exposure to multiple risk factors. Data estimating risks for the approximately 1 in 10 children living in conflict, crises, and insecure conditions are scant; however we estimate higher levels of co-occurrence of risk factors in such situations. Children living in poverty are at greater risk for exposure to disadvantaged social and material environments. (50) Young children are particularly vulnerable to the effects of contaminants, household/ambient air pollution, and heavy metals due to the rapid growth and development of their organ and physiological systems, the immature state of their blood-brain barrier, and their increased likelihood of exposure to contaminated objects and foods.(50)

Other specific examples of co-occurrence are:

Nutritional deficiencies in infancy and early childhood likely to occur with:

- being born small for gestational age or preterm or both;
- parents who are less involved, sensitive or responsive;
- extreme poverty and food insecurity;
- suboptimal infant and young child feeding practices;
- high exposure to pathogens and corresponding burden of infectious disease in infancy and childhood;
- home environments characterized as less stimulating;
- exposure to domestic violence.

Maternal depression and anxiety likely to coexist with:

- pre-term birth;
- low birthweight;
- poor infant growth and lowered cognitive development;
- less adequate prenatal care;
- less adequate caregiving including:
 - suboptimal infant and child feeding practices (including exclusive breastfeeding);
 - insufficient communication and play to stimulate learning;
 - delayed and inappropriate careseeking;
- increased child morbidity;
- increased use of harsh discipline;
- increased family stress.

Exposure to societal violence likely to occur with:

- child abuse and neglectful parenting;
- disruption of family or community support systems;
- child nutritional deficiencies;

child not receiving adequate health care (eg immunization)

• _____

Growing up in an overcrowded home likely to occur with:

- high burden of infections in infancy or childhood;
- inadequate health care (eg immunizations)
- malnutrition;
- spousal violence;
- parental use of harsh physical punishment;
- child ingestion of toxic substances;
- maternal depression.

while there are parallels in the types or risk and promotive factors encountered by children in high-income countries (HICs) and LMICs, children from LMICs are more likely to encounter a greater number, variety and covariance of risk factors and fewer promotive influences than children in HICs.(43) Our analysis based on Multiple Indicator Cluster Survey data indicates that risk factors in early

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Table 1: Summary of effective interventions for improving child development, nutrition and growth, child development, mortality, disability and morbidity in LMICS, based on high-quality-rigorous systematic review evidence (NOTE: TABLE IS STILL BEING UPDATED)

Intervention type	Child Development	Nutrition & Growth	Mortality	Disability, Injury & Malformations	Severe Morbidity
Iodine supplementation before or during pregnancy	✓	✓	✓	✓	
Antenatal corticosteroids for women at risk of preterm birth	✓		✓		✓
Magnesium sulphate for women at risk of preterm birth	✓			✓	
Antiplatelet agents for women at risk of pre-eclampsia	✓	✓	✓		
Therapeutic hypothermia for hypoxic ischaemic encephalopathy	✓		✓	✓	✓
Psychological interventions for women with antenatal mental disorders	✓	✓			✓
Iron supplementation in children	✓	✓			
Multiple micronutrient supplementation in children	✓	✓			
Supplementary feeding for disadvantaged children	✓	✓			
Parenting programmes	✓				
Integrated parenting and nutrition programmes	✓	✓			
Out of home interventions (pre-primary education)	✓				
Conditional cash transfer	✓				✓
Unconditional cash transfers					✓
Periconceptual folic acid fortification/supplementation				✓	
Birth interval <18 months vs. 36-60 months		✓	✓		
Periconceptual Preconception diabetes care			✓	✓	
Iron and iron-folate supplementation during pregnancy		✓			
Multiple micronutrient supplementation during pregnancy		✓	✓		
Balanced protein-energy supplementation during pregnancy		✓	✓		
Intermittent preventive therapy and bed nets for malaria in mothers and children		✓	✓		✓

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Antibiotics for premature rupture of membranes		✓		✓	✓
Lower genital tract infection screening and treatment		✓			
Antibiotics for asymptomatic bacteriuria		✓			
Detection and treatment of syphilis		✓	✓		✓
Smoking cessation interventions		✓			
Delayed cord clamping (more placental transfusion)	✓	✓	✓		✓
Continuous support during childbirth					✓
Kangaroo mother care (KMC), skin-to-skin, cap/wrap (thermal care)		✓	✓		✓
Topical emollient therapy for preterm neonates		✓	✓		✓
Intramuscular vitamin K for neonates					✓
Handwashing behavior and water quality improvement (WASH)		✓	✓		✓
Rotavirus, HiB, & pneumococcal vaccinations			✓		✓
Vitamin A supplementation in children		✓	✓	✓	✓
Zinc supplementation + treatment for acute diarrhea in children		✓	✓		✓
Deworming drug treatment in children		✓			✓
Breastfeeding promotion, education, or support	✓	✓			
Complementary feeding education/provision		✓			✓
Treatment of moderate and severe acute malnutrition		✓			✓
Interventions to prevent child maltreatment (<u>specific e.g., home-visiting, and parenting programmes, counseling interventions</u>)*					

Notes. [Checkmarks pertain to statistically significant pooled effect sizes.](#) * Most rigorous trials of interventions to prevent child maltreatment have been conducted in HICs, with far fewer in LMICs, and are not uniformly effective in reducing injuries, physical abuse and neglect.

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Interventions encompassing the period before conception to birth

Maternal and newborn health

While nurturing care interventions usually begin after birth, established MNCH interventions, can reduce adverse growth and health outcomes including stunting, low birth weight and iron deficiency anaemia that are strongly related to early child development. While interventions involving nurturing care are noted at birth onwards, established interventions encompassing the period before birth, are precursors to reduced adverse growth and health outcomes including stunting, low birth weight, and iron deficiency anaemia. In our review of LMICs, we identified six such eight MNCH interventions during the period from preconception to birth and labour that have statistically significant effects on child development, in addition to growth, mortality, morbidity, or disability. These interventions include: iodine supplementation before or during pregnancy, (44) ~~diabetes care during preconception~~, antenatal corticosteroids for women at risk of preterm birth, (45) magnesium sulphate for women at risk of preterm birth, (46) antiplatelet agents for women at risk of pre-eclampsia, (47, 48) ~~delayed cord clamping~~, and therapeutic hypothermia for hypoxic ischaemic encephalopathy (see web appendix for details). ~~One review found mixed effects of delayed cord clamping on measures neurodevelopment at four months. Tobacco use is viewed as an important threat to the health of pregnant women and their children. Smoking and alcohol consumption are associated with poor child development outcomes.~~ A review of 86 randomized control trials (RCTs) showed that psychosocial intervention programmes have been successful during pregnancy ~~for in-smoking and alcohol cessation~~, ~~reducing low birthweight and preterm births, but although~~ evidence is limited on such interventions in LMICs. (49) ~~Nurturing Care begins to emerge through interventions provided at birth. These include early initiation of breastfeeding, thermal care, Kangaroo Mother Care, infant massage, and skin and cord care. (64) Most notably, skin-to-skin contact at birth through interventions such as Kangaroo Mother Care promotes thermal sufficiency and early bonding. Moreover, Kangaroo Mother Care is associated with increased early and continued breastfeeding which leads to improved child developmental outcomes. (65) For low birthweight infants, kangaroo care has been associated with an increase in bonding indicators such as mother-infant attachment (MD 6.24, 95% CI 5.57-6.91), infant growth, and rates of exclusive breastfeeding (RR: 1.20, 95% CI 1.01-1.43). (66, 67) The trials included in these analyses were undertaken in health facilities. Future research studies should focus on effectiveness of skin-to-skin care when delivered at scale in community settings. (16)~~

Comment [MP2]: I think diabetes care was a typo in the health review notes. I can't find these results in the paper..

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Comment [MP3]: This review that we have on file relates to tobacco only, not alcohol

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Maternal nutrition, micronutrients and iodine supplementation

The importance of optimal nutrition and healthy body composition for young women during preconception and pregnancy on child outcomes is well established. (45) Maternal nutrition (both under- and overnutrition) influences fertility, oocyte development/maturation, pre-implantation development as well as fetal growth and development, and the health and cognitive development of offspring in later life. (45) (Lancet, 2015, Peri-conception parental obesity', reproductive health', and transgenerational impacts) ~~Evidence suggests that linear growth is correlated across generations (46) and short maternal stature is associated with low birth weight, stunting, childbirth complications, and increased child mortality. (46) There is also strong empirical evidence supporting a link between maternal obesity and offspring obesity as a result of epigenetic mechanisms affecting the fetus and young child. (47) The ability of a mother to support the health and development of her children is critically dependent on her own health and well-being before, during, and after pregnancy. Exposure to infections, environmental toxins, and physical and mental health issues not only negatively impact her own long-term well-being, but that of her children. (48-25)~~

Intrauterine growth restriction (IUGR) influences multiple aspects of child development and has been linked to poorer neurodevelopmental outcomes, reduced school performance, and ~~heightened~~ behavioural problems in children. (50) ~~Evidence suggests that linear growth is correlated across generations and short maternal stature is associated with low birth weight, stunting, childbirth complications, and increased child mortality. (51) Maternal malnutrition leading to IUGR has been shown to modify gene expression in the offspring and future generations through epigenetic mechanisms. (44)(48) The provision of a balanced energy (52) and protein diet as well as multiple micronutrients for women of childbearing age (50) and expectant mothers at risk of deficiencies show potential benefits in reducing the risk of IUGR, small for gestational age (SGA) births, and stillbirths. Iron and iron-folate supplementation during pregnancy reduces the risk of SGA and premature births. (53) while feta support optimal child growth and development both in utero, at birth, and post-partum. Folic acid fortification is or supplementation, iron, iodine, and additional micronutrient supplementation during pregnancy have been associated with prevention of neural tube defects and risk of adverse birth outcomes. (54) Iodine supplementation in moderate-to-severely iodine~~

deficient areas is the only nutrition-related intervention during pregnancy with evidence of a significant impact on children's cognitive development scores (10-20%).(44)

-, improvement in cognitive development scores for children, reduction in underweight and stunting, and risk of adverse birth outcomes. Several individual studies of multiple micronutrients and iron-folate supplementation show potential benefits in reducing the risk of IUGR and small-for-gestational-age (SGA) births, but the potential benefits for mental and motor development during childhood are mixed.(51)

Maternal stress, depression and mental disorders

The onset of caregiving in humans is triggered by hormonal signals beginning in pregnancy (e.g., oxytocin and lactogens).(55) Mental disorders during pregnancy, and the timing of stress during pregnancy, can disrupt maternal programming that prepares women to respond towards their infants. (56) The disruption to maternal programming might account for associations between maternal mental disorders and insecure mother-infant attachment and exposure to maltreatment. Antenatal Non-psychotic mental disorders in women (including depression and anxiety) are among the commonest morbidities of pregnancy and the postnatal period are associated with a range of negative child outcomes, including SGA births, low levels of cognitive development, and (51) impacting fertility, pregnancy complications, and fetal/child development. (52) Most recently, recent evidence is emerging that paternal mental health during pregnancy stress can also influence the socioemotional and behavioural development of children pregnancy and neurological outcomes in. (57) A systematic review of 13 trials of psychological through the benefit of interventions for women with antenatal depression in LMICs, including inter-personal and cognitive behavioural therapies, delivered by local community health workers showed positive effects on reducing maternal depression. Benefits to children included improved mother-infant interaction, better cognitive development and growth, reduced diarrhoeal episodes, and increased immunization rates.(58) is well recognized (54), antidepressants for treatment of antenatal depression have been associated with small but significant increases in preterm birth and reductions in birth weight.(54, 55). A cluster-randomized trial of integrating cognitive-behavioral therapy with home visits by community health workers for mothers with postpartum depression in rural Pakistan showed that this strategy is both feasible and acceptable, with the intervention group having a 78% reduced odds (adjusted OR: 0.22, 95% CI 0.15-0.36) of major depression after 6 months and non-significant increases in WAZ and HAZ after 12 months.(52, 53) The study also increased rates of immunization, exclusive breastfeeding, and parental play with children.(53) A meta-analysis of 13 studies, primarily in LMICs, concluded that the most effective interventions for mothers with depression included infant massage and support groups. Antidepressants for treatment of antenatal depression, on the other hand, have been associated with small but significant increases in preterm birth and reductions in birth weight.(59, 60) Persistence of depression (into the postnatal period and beyond) seems to be of particular importance in relation to cognitive development, including achievement of developmental milestones, and language development.(56) Recent trials from Bangladesh(61) and Uganda(62) suggest that group-based parenting programmes can improve maternal mental health in community settings and young children's cognitive and receptive language scores. However, more analysis is needed to determine which characteristics of maternal health interventions are associated with improved maternal wellbeing and issues of scalability.

Living in poverty is associated with a high degree of stress. Cash transfer programmes have increased rates of prenatal care.(81) Participation in a conditional cash transfer (CCT) also significantly increased both the probability of in-facility birth and the probability of having a skilled birth attendant. While these conditions were associated with improved birth outcomes and later developmental outcomes, this is not always the case. During labour and childbirth, mothers who have continuous social support (e.g., emotional support, comfort measures, information, advocacy) show significant positive clinical benefits for themselves and for their infants.(82)

A recent review of perinatal mental disorders emphasizes the need to both treat the parent's disorder and help with associated caregiving difficulties, and for early identification of those parents at high risk (ref, Lancet 2014).

Living in poverty is associated with a high degree of stress. Indirect positive benefits of cash transfer programmes were noted for prenatal care.(59) Participation in a conditional cash transfer (CCT) also significantly increased both the probability of in-facility birth and the probability of having a skilled birth attendant. While these conditions were associated with improved birth outcomes and later developmental outcomes, this is not always the case. During labour and childbirth, mothers who have continuous social support (e.g., emotional support, comfort measures, information, advocacy) show significant positive clinical benefits for themselves and for their infants.(57)

Comment [MP4]: Replace with "nurturing care"

Kangaroo mother care

Aspects of Nurturing Care during birth and labour include early initiation of breastfeeding and interventions such as Kangaroo Mother Care (KMC) which promotes thermal sufficiency in preterm infants and early bonding. KMC has been associated with an increase in bonding indicators such as mother-infant attachment (MD 6.24, 95% CI 5.57-6.91), infant growth, and rates of exclusive breastfeeding (RR: 1.20, 95% CI 1.01-1.43).(63) The trials included in the review were undertaken in health facilities. Future research studies should focus on effectiveness of KMC when delivered at scale in community settings.

Interventions birth from birth to five years

Parenting Support

Opportunities for stimulation, early learning, and positive parenting within the home environment are crucial for children's development.(18) Parenting programmes are operationally defined as interventions or services aimed at improving parenting interactions, behaviours, knowledge, beliefs, attitudes, and practices. Three recent reviews of parenting programmes in LMICs found positive effects on direct measures of children's cognitive and language development across diverse policy, service delivery, and social contexts.(19-21) Parenting programmes focused on providing parenting support, including the promotion of responsive parent-child interactions, child-directed/focused enrichment and early childhood education. For this paper, We updated and expanded on the previous three parenting reviews by conducting a meta-analysis of including non-cognitive outcomes and concluded that parenting programmes increased scores on measures of psycho-social development (SMD 0.35, 95% CI 0.14-0.56, 13 studies) and motor development (SMD 0.13, 95% CI 0.07-0.19, 9 studies),— in addition to child cognitive development (SMD 0.36, 95% CI 0.22-0.49, 19 studies). The effect on child growth was not statistically significant.

Across the reviews, Parenting programme implementation varied in relation to dose of intervention, setting, and curriculum. The total amount of contact with parents, which ranged from less than 10 hours to 120 hours, did not have a clear relationship to the size of effect.(20) Some programme models have used only home visits, e.g., Roving Caregivers in Jamaica, (64) (60) and others have used group sessions, e.g., Pastoral del Niño in Paraguay.(65) Combined group sessions and home visits in Bangladesh(66) and Brazil(67)(62) produced better outcomes than home visits alone, (63) but not in Jamaica.(63) The most effective parenting programmes used multiple behaviour change techniques, including small media such as posters and cards that illustrate enrichment practices, opportunities for parental practice of play and responsive talk with their child, guidance and support for changing practices and problem-solving strategies.(19)(64) One such example include, the Care for Child Development package developed by UNICEF and WHO, and "Reach Up and Learn", which provides opportunities to use multiple strategies to strengthen nurturing care by parents.(10) Other examples include "Reach up and learn." A notable gap in the reviews is the role of fathers in promoting nurturing care psychosocial stimulation, nurturance, and protection.(68) Taken together, the results suggest that parenting support programmes that promote nurturing care and protection can significantly augment the positive impacts of basic health and nutrition, education and protection interventions on early childhood outcomes. Parenting programmes that combine nutrition and stimulation have been effective in improving child outcomes,(19) but (69, 73) However, the extent to which these combinations result in synergistic outcomes it is not clear.

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Attachment Kangaroo mother care

Different brain systems enhance nurturing by supporting infant-mother attachment, as well as emotional wellbeing, learning and memory, attention, and executive functions.(17) Secure attachment forms with a caregiver who provides security, safety, affection and comfort. Aspects of Nurturing Care during birth and labour include early initiation of breastfeeding and interventions such as Kangaroo Mother Care (KMC) which promotes thermal sufficiency in preterm infants, and and early bonding. KMC has been associated with an increase in bonding indicators such as mother-infant attachment (MD 6.24, 95% CI 5.57-6.91), infant growth, and rates of early initiation and continued exclusive breastfeeding (RR: 1.20, 95% CI 1.01-1.43).(63) The trials included in the review were Most of these evaluations were undertaken in health facilities. Future research studies should focus on effectiveness of KMC when delivered at scale in community settings. (19)

Comment [LR7]: or

Comment [PB8]: Kerrie could we add this citation – either here is space, if not in the web-appendix, please Feldman R, Rosenthal Z, Eidelman AI. Maternal-preterm skin-to-skin contact enhances child physiologic organization and cognitive control across the first 10 years of life. Biol Psychiatry. 2014 Jan 1;75(1):56-64

Breastfeeding and child feeding

Breastfeeding has clear short-term benefits for child health, reducing mortality and morbidity from infectious diseases, healthy food preferences, and promotes the establishment of a healthy microbiome.(69) ~~The benefits of early initiation and continued exclusive breastfeeding on neonatal survival and infant neurodevelopmental and cardiometabolic outcomes are well established. (10) Studies also suggest that exclusive breastfeeding may protect against elevated body mass index (BMI) in children through mechanisms that include alterations in early growth trajectories and leptin signaling.(66) In addition to its nutritional properties and role in maternal-child bonding, new evidence shows that breast milk promotes the establishment of a healthy microbiome(65) and the development of taste preferences in infants.(14, 66) A recent review on 17 observational studies of breastfeeding presents evidence that optimal breastfeeding supports improved performance in intelligence tests in childhood and adolescence, demonstrating an IQ increase of 3-44 points (95% CI 2.30-4.58),(70)-(67). Findings from a recent analysis of the Pelotas birth cohort in Brazil also demonstrated a dose-response relationship between breastfeeding duration and increased intelligence, educational attainment, and income.(69, 71) The positive effect of breastfeeding has been observed in one RCT in Belarus, where duration of total and exclusive breastfeeding was higher in the intervention group that received the baby-friendly hospital initiative, as well as performance in intelligence tests at 6.5 years.(72)(66)~~

Micronutrients and child feeding

One high-quality review limited to four trials found that mMultiple micronutrient supplementation in children at risk of deficiencies has also been shown to improve academic performance among children 5-12 years of age (SMD: 0.30, 95% CI 0.01-0.58),(73) ~~and a single study also found an effect on motor development. A r~~Reviews of iron supplementation in children aged 0-12 months consistently found improvement in psychomotor development (MD 6.90, 95% CI 1.35-12.45), One review of iron supplementation, but mixed effects on cognitive development. Some studies found a decrease in IQ (MD: -3.00, 95% CI -5.96 to -0.04),(74)(70, 71) and another review finds an improvement in mental development (SMD: 0.30, 95% CI 0.15-0.46) and IQ (SMD: 0.41, 95% CI 0.20-0.62).(75) (67) ~~One high quality review focused on the effect of supplementary food given to socio-economically disadvantaged children 3 months to 5 years of age found that providing food supplements improved psychomotor development (SMD 0.41, 95% CI 0.10-0.72), but found mixed effects on measures of cognitive development in different trials (SMD -0.40, 95% CI -0.79,0; Bayley II: Mental Development), (SMD 0.58, 95% CI 0.17-0.98; cognitive development test battery).(76) Programmes that combine nutrition and stimulation have been effective in improving child outcomes.(69, 73) However, the extent to which these combinations result in synergistic outcomes it is not clear. Results from individual studies in Bangladesh(77) and India(78) suggest that responsive feeding can be and sensitive care are effective in promoting child growth and developmental outcomes. Parents who are supported through coaching and modeling of behaviours tend to remember the information provided to them and engage in better responsive feeding and care practices.~~

Prevention of child maltreatment

Family violence is increasingly recognized as key public health issues in LMICs. Maltreatment during childhood is associated with reduced mid-sagittal area and hippocampal volume, which are brain regions involved in learning and memory.(79) Children who receive inadequate care, especially in the first 24 months of life, are more sensitive to the effects of stress and display more behavioural problems compared to children who receive nurturing care.(80) There is a growing literature showing that one of the most powerful predictors of caregiving behaviour is how caregivers, especially mothers, were cared for themselves.(81) Children who grow up neglected or abused by their parents, or under conditions of extreme distress within their families, are at risk of developing a host of unhealthy behaviours that affect their own lives. When these children grow up, they tend to be less equipped to take on a parenting role and are more likely to perpetuate a cycle of adverse caregiving across generations. The maltreatment prevention interventions with the best evidence are selective programmes (e.g. Nurse Family Partnership) characterized by intensive visits by professional home visitors for a period of at least one year, but these programmes have not been evaluated in LMICs and the extent to which these findings are generalized beyond the specific HICs where they have been evaluated is not clear (see supplementary web appendix for maltreatment prevention interventions). A systematic review of 12 parenting interventions for reducing harsh/abusive parenting in LMICs found potentially positive results on a range of parenting measures, but the quality of included trials was generally low.(27) Early intervention that occurs prior to the onset of abusive and neglectful parenting is crucial to preventing maltreatment. There is an urgent need for more rigorously evaluated maltreatment prevention interventions in LMICs, focusing on parenting and child outcomes, and adapted for low resource contexts. Reviews are limited in their coverage of interventions that respond to violence against children, in and out of emergencies, including gender-based violence, prevention of injuries, and harmful practices. More recent reviews of early child

Comment [PB9]: Recommendation for citation from Linda - could be included in web appendix: Rochat, Tamsen J., et al. "Exclusive breastfeeding and cognition, executive function and behavioural disorders in primary school-aged children in rural South Africa: a cohort analysis." *PLoS Medicine* (2016): 1-51.

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development ECD interventions in LMICs are suggesting associations with violence reduction and peace promotion (See supplementary web appendix).

Out of home interventions

Effects of early learning programmes, including quality childcare, kindergarten, preschool, and pre-primary are well established in LMICs. (18) (78) We updated and expanded on an earlier published review (20) and found formal and non-formal or community-based preschools in LMICs improved scores on direct measures of children's cognitive development (SMD 0.67, 95% CI 0.43-0.91, 26 studies) and psychosocial development (SMD 0.23, 95% CI 0.06-0.4, 5 studies). Effects on child growth were non-significant and one study measuring motor development showed non-significant effects. The earlier review found that effects of non-formal preschools on child outcomes were typically weaker than the effects of formal preschools: yet some low-cost and innovative programmes such as home-based preschool (148) and a child-to-child approach improve developmental outcomes in comparison to non-participants. Regardless of type, P and programme quality is a key predictor of programme effectiveness. Effective interventions to enhance preschool quality include greater number, variety and challenging play materials, (149) interactive / dialogic reading, (150) classroom organization and instructional support. (151) Some low-cost and innovative programmes such as home-based preschool (82) and a child-to-child approach resulted in better developmental outcomes compared with non-participants. Programme quality is a key predictor of programme effectiveness. (79-81) Effective interventions to enhance preschool quality include greater number, variety and challenging play materials, (82) dialogic reading, (78) classroom organization and instructional support. (82) Nurturing environments in the form of care and positive interactions and individualized attention appear to be important in early learning programmes. Positive center Observational measures of preschool quality have begun to emphasize the notion of emotional climate, which includes individualized attention, positive affect, and positive reinforcement of children's behaviours. One measure, for example, takes as its conceptual basis attachment theory and applies it to classroom interactions. (83) The Emotional climate and nurturing interactions scale has shown positive associations with children's early-childhood cognitive as well as socioemotional skills in Chile (83) (84) and Ecuador. (83, 85) Two experimental trials in Jamaica and Chile showed that promoting teachers' provision of positive emotional climate and behaviour management also improved children's self-regulation and attention, and reduced aggressive behaviours. (80).

Social safety net interventions

Our analysis of the systematic reviews¹⁵⁻¹⁹ and the new literature (see Appendix) on social safety net interventions suggests positive effects of conditional cash transfer programs on some child outcomes, including birth weight and illness or morbidity. Outcomes with mixed or sub-group effects included height-for-age or stunting, weight-for-age or underweight, and cognitive and language development. Conditional cash transfer programme participation consistently had no effects on hemoglobin concentration or prevalence of anemia in children. In terms of indirect effects of these programs, results were strong and significant for effects of participation on prenatal care, growth monitoring, micronutrient supplementation, and household food consumption. There were mixed effects, however, on the presence of a skilled birth attendant at child birth, and receipt of child vaccinations.. It is difficult, however, to compare results across countries and contexts because programmes differ greatly. The impact of cash transfers on child development can be improved by combining social protection and ECD interventions. Cash transfer programmes try to address many issues at multiple levels (e.g. parental, community) that influence child development, but they do not directly work to change the factors that are linked with improving development outcomes. On the other hand, programmes promoting child development that have an educational or stimulation component have shown larger cognitive effects than cash-only or nutrition-only programmes, in both in the US (79) and Columbia Latin America. (92) Bringing these two interventions together can address both economic and nurturing-care factors that impact developmental outcomes. Bringing these two interventions together can address both the direct and indirect factors that impact developmental outcomes.

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In summary: Nurturing care can mediate risk factors in early childhood

We conducted a comprehensive review of 40 ECD-related interventions across diverse sectors and found 13 interventions have available evidence of statistically significant effects on multiple child outcomes including child development, based on high quality systematic reviews (Table 1). Many of the interventions with effects on child development encompass aspects of Nurturing Care including parenting support and social protection, care for the

caregiver, and early learning opportunities provided in or out of the home environment. Human infant development anticipates and relies on care by adults that is nurturing, caring, enriching, and protective. These nurturing interactions provide the early environments needed for developmental progression to occur and to protect infants. Nurturing interactions can mediate the deleterious effects of poverty and other risk factors,(42) which have greater variety and prevalence in LMICS and have higher levels of co-occurrence (Panel 2). Advances in developmental science have also provided an understanding of windows of time when development of specific capacities and abilities is nurtured. A critical period is a maturational stage, or window, in the lifespan when the nervous system is especially sensitive to environmental stimuli. Critical periods are more clearly defined in the development of animal brains; in humans, there are multiple and overlapping sensitive and vulnerable periods with significant implications for greatest sensitivity to interventions.

Intervention packages that integrate *Nurturing Care* with sector-specific programmes

The review demonstrates that compared to the Lancet ECD series in 2007 and 2011, the literature on early childhood interventions has expanded to include new ~~intervention studies and new~~ longitudinal data ~~and cohort data from~~ LMICs (89, 90). Most interventions during the period from preconception to birth focus on the physical and mental health of the mother to support a healthy pregnancy and improve birth outcomes, given the associations between preterm birth, low birth-weight, birth complications, and poorer developmental outcomes for young children. At birth is when interventions focusing on nurturing care and protection are ~~usually introduced~~ ~~noted, however,~~ ~~maternal programming for nurturing care begins during pregnancy and even earlier, with their own childhood experiences of caregiver behavior.~~ During infancy, ~~our reviews indicate~~ ~~the synthesis of reviews of interventions~~ indicates that evidence-based interventions combining basic sectoral ~~intervening in health, nutrition, child and social protection, and child care and learning~~ ~~interventions~~ with nurturing care and protection can synergistically improve child developmental outcomes. For example, inclusion of stimulation in nutrition interventions increases effectiveness, as developmental outcomes cannot be fully promoted through nutrition interventions alone(19, 93) or ~~through then holistic interventions, such as~~ breastfeeding, ~~which~~ ~~has a strong impact because it~~ ~~have strong impact as they~~ combines elements of nutrition with bonding. ~~although further evidence is needed on the efficacy and effectiveness of breastfeeding promotion, education, and support, interventions in LMICs, in addition to feasible approaches to support breastfeeding in working mothers. (86).~~

Building on sectoral services

~~Some sectoral interventions, such as social protection, are not so differentiated across the life course. However, they could also serve as the basis for delivery of services that link policy level strategies of cash transfer, social policies, and income generation with programmatic interventions. Multi-sector approaches include coordinated services across sectors, ideally with unifying policies. Integrated approaches refer to integration across services with shared messages and opportunities for synergy. (Black, et al., this series). Many sectoral interventions could serve as the basis for delivery of services that link policy level strategies of cash transfer, social policies, and income generation with programmatic interventions that could benefit child development, such as parenting support. (See web appendix). For other sectors, such as water and sanitation, while the review indicated impact on child's nutritional status, growth, and health (73)(74)(75), further research is needed to examine effects on associations for developmental outcomes.~~

Delivering multi-sectoral ~~ECD~~ ~~intervention~~ packages to improve child development

~~Across the review,~~ ~~T~~ the degree of effectiveness of interventions varies with respect to improving child development outcomes. The impact of these interventions could be improved by taking into consideration the major insights we have gained over the past decade about how human development, ~~growth, genes, and caregiver behaviour are~~ ~~is~~ molded by complex and multi-faceted experiences ~~and environments, starting with previous generations.~~ The science of ~~tife~~ ~~understanding of~~ early human development encourages us to conceptualize interventions acting together in a meaningful manner, through a coordinated approach, so as to increase their benefits and address child outcomes more holistically.

In instances where sectoral interventions were combined with elements of nurturing care and protection, the impact of the intervention on child outcomes increased significantly (See web appendix for established studies of ECD). Combining interventions with elements of nurturing care and protection allows us to support families as the most proximal environment for early development by intervening with the family as a unit, as opposed to addressing the child as an isolated beneficiary. Further, the established and emerging science continues to offer opportunities to

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improve and better target interventions to improve their efficacy by combining them with nurturing care and protection, through parenting support and skills programmes.

Previous attempts at creating packages of effective interventions have focused either on the temporal relevance of the interventions, i.e., packaging interventions that co-occur during the same age period of the child (~~XX~~e.g., World Bank), or ~~then-on the are~~ delivery of the programmes through the same system (e.g., MNCH). In addition to taking into consideration ~~the temporal relevance to the age of the child, any consensus on the effectiveness and quality of the intervention, quality of the intervention, and feasibility of delivery at scale~~ the characteristics of the above mentioned packages, ~~in creating packages~~ we also need to incorporate nurturing care and protection into the packages and tailor the ~~me~~ packages to unique sets of risks and adversities facing the young child population particular to the setting that characterize complex environments.

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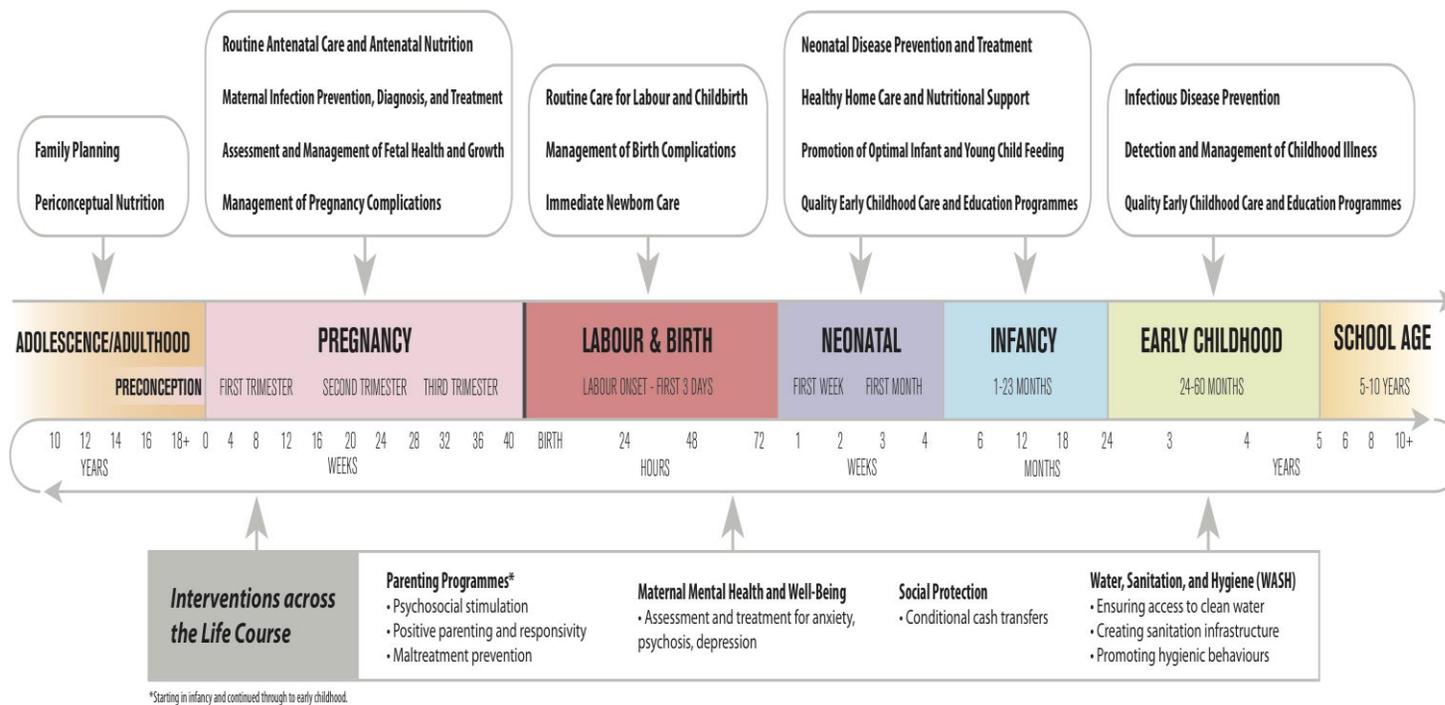


Figure 1: Evidence-based interventions that affect aspects of *Nurturing Care*

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Based on our review, we propose ~~three~~ illustrative packages that build on these principles and the findings. ~~These interventions affect different aspects of nurturing care and cover numerous domains and stages in the life course (Figure 1).~~

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1. **Family Support and Strengthening Package:** Three elements of family strengthening: (i) access to quality services (e.g., antenatal care, immunization, nutrition); (ii) skills building (e.g., positive and responsive parenting to reduce harsh discipline and promote stimulation); and (iii) support (e.g., social protection, safety networks, family support enabling policies) increase the likelihood that families are better able to provide nurturing care for their children. ~~As presented in the review, Each of these elements – services, skills and support – have independent predictive effects tend to operate independently.~~ As indicated in the review of the social protection interventions, significant positive effects are seen when they are combined with programmatic interventions. By creating a package of the ~~three~~ elements of Services, Support and Skill building, based on the age of the child and nature of risks, developmental outcomes could be substantially improved.
2. **“Caring for the Caregiver”- Multi-Generational Nurturing Care Package:** This ~~2-generation package, set of interventions~~ emphasizes care and protection of the mother’s and father’s physical and mental health and well-being while enhancing their her capacity to provide nurturing care to their child. This package combines the set of essential interventions, of health and nutrition, from pre-conception, for the 1st 1,000 days, adding to them elements of care, responsivity, stimulation and protection, integrates key elements across adolescent health, preconception, pregnancy, childbirth, post-natal, and newborn health. These interventions are primarily delivered by the health system. The main recipient of the services and skills is the parent, or adolescent as defined above. However, starting at childbirth, service involves two generations. This package can be further strengthened with parental leave policies as discussed in Richter et al, this series. While the reviews did not specifically cover situations of conflict and violence ~~(See Web appendix for details)~~, this package is also relevant for humanitarian contexts. ~~Conflict, violence,~~ and insecurity present a complex array of adversities. Families, parents and caregivers, in these settings, require a package of services that addresses their needs as well as the immediate and long term needs of their children.
3. **Early Learning & Protection Package:** This set of interventions integrates support to young children, of parents in learning programmes, as well as parental support and facilitation of teachers’ and caregivers’ ability to create a nurturing environment in early childhood centers, classrooms, and community settings for learning. ~~For young children, the existing set of services typically includes community based child care, preschool, kindergarten, and other early learning programmes. However,~~ the package of interventions should include nurturing care and protection by enhancing teachers’ capacities to providing a nurturing, safe, and positive emotional climate and should include greater attention to parental support. A parenting The ACEV programme in Turkey has demonstrated long-term gain when early learning packages have included protection and addressed both the child and the parent as target beneficiaries, (11) ~~(See Web appendix)~~ This package needs to emphasize quality and family support through parental empowerment, guidance on nutrition and care, and child protection.

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The advantages of such integrated packages from a delivery perspective is that one location for the provision of key services for young children, can be leveraged efficiently. Platforms, at community, clinic, and school levels, need to be identified to coordinate the delivery of the packages targeting population segments and families in greatest need. For example, community platforms that mobilize antenatal and postnatal home visits by community health workers complement facility-based care and promote family contact with the health system at crucial times. Social protection platforms could also serve as the basis for identification of families and delivery of packages of services that link ~~these policies~~ level strategies of cash transfer, social policies and income generation with programmatic interventions. The strategy selected to deliver a package of interventions might be determined by the age group being targeted, the expertise of the sector, coverage, or and an analysis of the most efficient and effective use of resources within a service for a particular context. More evaluations are needed to codify the interventions to pull them together into essential packages, assess effectiveness, implementation quality and cost-benefits of integrated, inter-sectoral and multi-sectoral approaches for ECD child health, growth and development packages. However delivering multi-sectoral services is not without its challenges of limited capacity of the workforce, requiring a clear case for the value add of including programmatic interventions of nurturing care, and political will (some of these challenges are discussed in Paper 3).

Future research areas

While we have made progress in our understanding of “what works”, we also note gaps in our knowledge. The particular set of risks faced by children in conflict are not well understood. Notable gaps in our understanding are evaluations and reviews of early childhood ECD interventions operating in conflict-affected and fragile country contexts. A recent set of reviews examining the association between preschool-aged interventions in LMICs and HICs high income countries and reduction of violence, note that while there are gaps in our knowledge, the trends noting the positive association between early care and later positive social outcomes for children are positive (94, 95) (88, 90). While we know that makes more sense to combining interventions supports, because of holistic caregiver and child development and the opportunity to provide multiple services, in one instance, to a family, a gap in our knowledge is that most interventions are still delivered through single sector approaches. We need to understand how to better combine interventions, through robust assessment of intervention outcomes, evaluations of integrated parenting, responsive care, stimulation, mental health, education and protection interventions that could be delivered through community and platforms. We also need to understand better how to use technology-based platforms to deliver effective interventions (See web appendix). We also need a range of evaluations, in addition to outcome evaluation, that focus on implementation evaluations to inform scale up and. Another set of gaps notes in the review was that further research is also needed to establish the validity of child development measures in LMICs. (7, 96)

Conclusion

On the basis of our review of recent evaluations, we call for greater integration between sectoral interventions and those that promote nurturing care and protection to improve developmental outcomes. We have reviewed the scientific basis for interventions to improve the health and well-being development of our world’s most valuable asset—our children. We have documented the effectiveness of interventions across domains of health and nutrition, education, and protection from violence, maltreatment, and poverty. The results of the review suggest that “smart and sustainable” interventions to improve developmental outcomes need to: (i) promote include nurturing care and protection behaviours; (ii) be implemented as packages that target multiple risks; (iii) be applied at developmentally appropriate times during the life course; (iv) be of high promote quality; and (v) build on existing delivery platforms to enhance feasibility of scaling-up and sustainability. We have proposed illustrative packages that meet these requirements. The nature of these interventions will continue to be improved as new understanding of early human development emerges. While question remains about scaling-up interventions at a population level (See Richter et al., this series) However, we are now at a historic juncture where the evidence is clear about what needs to be done to improve the future health and well-being of future generations and the political commitment strong, as expressed in Agenda 2030. The question remains about the means to scale up interventions at a population level and the commitment of nations to enable all children everywhere to reach their developmental potential (See Richter et al., this series). In this paper we call for meaningful greater integration between sectoral interventions through programmatic packages and those that promote nurturing care and protection to improve developmental outcomes. The science is clear and the evidence convincing that our earliest experiences matter and the SDGs are unique opportunity for implementation. Let us draw on this knowledge to take action to support parents, caregivers, and families in providing the nurturing care and protection that young children deserve.

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