

Chapter 13

Very Early Childhood Development

Frances E. Aboud and Aisha K. Yousafzai



INTRODUCTION

Developmental potential is the ability to think, learn, remember, relate, and articulate ideas appropriate to age and level of maturity, and an estimated 39 percent of the world's children under age five years do not attain this potential (Grantham-McGregor and others 2007).

The main reason for giving prominent attention to mental development from conception through the first 24 months of life is that early unfavorable conditions can impair the normal development of the brain. The impairment is often incremental and unnoticed until schooling begins. The most striking example of impairment is the gradual deletion of unused brain synapses. The lack of use may be due to the absence of stimulation in the family environment or lack of available energy for brain activity. Regenerating those lost synapses may occur at an older age but with additional costs. For example, children who do not acquire a good vocabulary in the early years will have difficulty learning how to read; children who do not acquire simple problem-solving strategies in the first 24 months will have difficulty understanding math concepts; children who do not develop secure emotional attachments to adults will have difficulty coping with stresses and challenges throughout life. The plasticity of the brain diminishes with age, but greater plasticity in the very early years suggests that brain development has a greater chance of being modified by protective interventions than by interventions later in life (Werker and Hensch 2015).

A second reason for attending to early mental development is that individuals, communities, and societies are healthier and more productive if they have mature mental skills. More educated adults are healthier and wealthier than less educated adults. Educated mothers have healthier children and are more likely to recognize symptoms of illness, follow medical advice, feed their children nutritious foods, and keep their homes clean (Boyle and others 2006; Cleland and van Ginneken 1988). Educated husbands are less likely to condone or use violence to resolve domestic conflicts (Abraham and others 2006). Follow-up data of adults who participated in early psychosocial stimulation programs demonstrate some of these long-term benefits (Gertler and others 2014).

This chapter discusses mental development from birth to age 24 months in low- and middle-income countries (LMICs). We include recent literature published since the 2011 child development series in *The Lancet*. Although we focus on cognitive and language domains, we touch on socioemotional, fine motor, and gross motor development. First, a description of how these domains are measured provides an operational definition of the term *mental development*. Second, conditions that derail early child development are examined. These conditions arise during the prenatal period and continue throughout the next 24 months; they include psychosocial stimulation, prenatal and postnatal nutrition, the physical environment, and

maternal mental health. Finally, the results of several systematic reviews and meta-analyses are presented to show the effects of stimulation and nutrition, along with disease-related interventions to promote mental development. Maternal interventions related to nutrition and mental health are also reviewed. A framework of critical components to include in programs is outlined.

PREVALENCE AND MEASUREMENT: WHAT DOES MENTAL DEVELOPMENT ENTAIL AT THIS AGE?

In the absence of well-validated international indicators, the Ten Questions Survey was used in 18 countries as part of the Multiple Indicator Cluster Survey 2005–06. Included were countries in the Caribbean, west Asia, southeast Asia, and Sub-Saharan Africa. The survey screens for disabilities by asking mothers of children ages 2–9 years two cognitive questions (for example, does your child learn to do things like other children his or her age?) and four language questions (for example, can your child name at least one object?). Results indicate that 7 percent of children had a cognitive disability, and 21 percent had a language disability. Overall, 27 percent of children screened positive for one of the sensory-motor-mental-social disabilities (Gottlieb and others 2009). However, because the answers depend on the ability of the mothers to notice disabilities, screening is likely to reveal only the tip of the iceberg (Yousafzai, Lynch, and Gladstone 2014). Also, because the items address disabilities rather than expected development, measurement experts are working to create a list of 30 or so mental milestones specific to the under-24-month age group to be asked of mothers (see, for example, Prado and others 2014).

The mental competencies of children during the first 24 months can now be directly assessed with behavioral tests and brain recordings. Both tools show that by the end of the first month, newborns respond to language more than to other sounds; they like looking at bright contrasts, movement, and color. The Brazelton Neonatal Behavioral Assessment Scale (Brazelton and Nugent 1995) assesses these competencies through observations of newborns interacting with others. Healthier newborns show better regulation of physiological states by self-soothing; better habituation to repeated sensory inputs, such as ringing bells; and greater response to social speech. The measured competencies are expected to facilitate engagement with physical and social environments in ways that will promote mental development. Impairments during the neonatal period

due to fetal lead contamination and deficits in iodine can be detected with this early assessment (Kooistra and others 2006; Patel and others 2006).

The most common measures of mental development after the newborn period are standardized behavioral tests, such as the Bayley Scales of Infant and Toddler Development, Third Edition (Bayley 2006) and the Griffiths Mental Development Scales (Griffiths and Huntley 1996). Both measure cognitive, receptive language, expressive language, fine motor, and gross motor development from birth to age 3.5 years using a number of items of increasing difficulty. The cognitive items mainly concern the ability to solve small problems. Receptive language items test the ability to understand the meaning of words, sentences, and abstract categories. Expressive language items assess the ability to use sounds, gestures, and the spoken word to communicate. Fine motor items include eye-hand coordination tasks. Gross motor development, such as sitting and walking, is not strongly related to mental development (Hamadani and others 2013) and so is not addressed here.

Social and emotional skills are an important domain of mental development, but measures for this age are not commonly applied in research, and determinants are not widely known. The Griffiths Scales include items that address personal-social skills, such as recognition of one's mother, enjoying playmates, and feeding and dressing oneself. The Bayley Scales also include a social-emotional subscale, with questions for parents that reveal the purposeful and social expression of emotions and interactive behaviors. However, secure attachment is the most important capability acquired in the first two years (Sroufe 2005). It is measured by the Strange Situation, in which observers note how much emotional security children derive from parents when under some stress due to the presence of strange people and objects. Malnourished children and those who receive less responsive warmth appear to be less emotionally secure than well-nourished and supported children (Cooper and others 2009; Isabella 1993; Valenzuela 1990).

CONDITIONS THAT AFFECT CHILD DEVELOPMENT

Many of the conditions that affect the health and growth of children in the first 1,000 days could affect mental development. These factors include the preconception and pregnancy nutritional status of the mother, birth weight and linear growth of the infant, and conditions of labor and delivery; maternal mental health; and

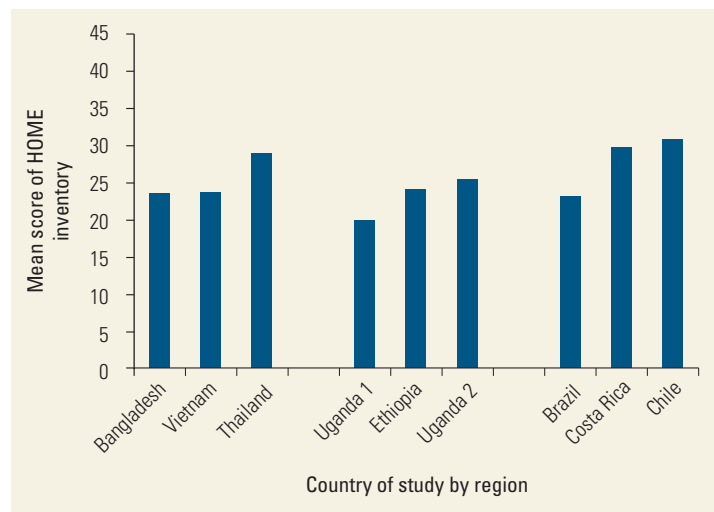
environmental conditions. However, we start with the condition most specific to mental development, namely, psychosocial stimulation. Many of these conditions co-occur, as will the impairments they cause.

Psychosocial Stimulation

Psychosocial stimulation refers to an external object or event that elicits a physiological and psychological response in the child. A specific measure of psychosocial stimulation is the Home Observation for Measurement of the Environment (HOME) Inventory (Bradley and Corwyn 2005). The infant and toddler version for children younger than age 24 months includes 45 items that are assessed through observation and interview. The essence of stimulation is observed in mother-child interaction that is verbal and responsive to the child's state, and in play materials that can be manipulated in different ways by the child. The caregiver is also questioned about activities that expose the child to places, people, and conversation. The focus is on opportunities to play and converse in ways that stretch thinking and understanding of speech. Scores on the HOME Inventory from around the world have ranged from a low of 20 (Boivin and others 2013) to a high of 31 (Lozoff and others 2010); in other words, the scores satisfied less than half to two-thirds of the items (figure 13.1). All studies showed very strong correlations between HOME scores and children's mental development, with low HOME scores associated with poor mental development.

A brief version of the inventory called the Family Care Indicators is available for use in national surveys. Consisting of 10 interview questions for the caregiver, it has been validated in South Asia and Sub-Saharan Africa (Hamadani, Tofail, and others 2010; Kariger and others 2012) and used to evaluate responsive and stimulating caregiving in 28 LMICs (Bornstein and Putnick 2012). Mothers (caregivers) were asked what they had done with their children under age five years in the past three days. Items largely focus on the variety of play materials available for the child (for example, things for making music, things for pretending, things for drawing) and play activities (for example, reading or looking at pictures, telling stories, singing songs). Only 25 percent of mothers said they had read to their children in the past three days, 25 percent had sung songs, and 35 percent had told stories. Scores did not vary by child's gender but were lower in families with more children. Thus, the presence of more children does not necessarily mean more of the right kind of stimulation. It is often mistakenly believed that older siblings provide sufficient stimulation and supervision. However, older

Figure 13.1 Mean HOME Inventory Score and Study

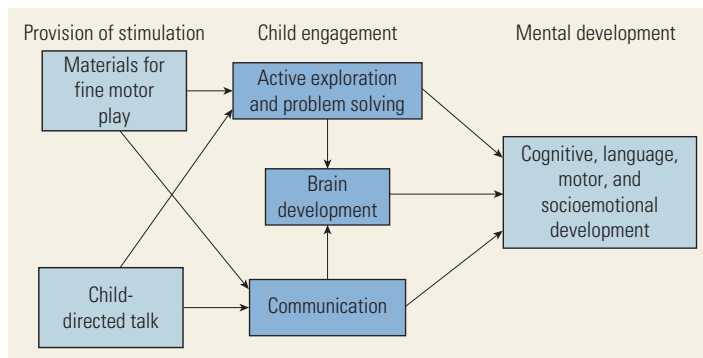


Sources: Bangladesh: 23.5 (Aboud and Akhter 2011); Vietnam: 23.6 (Williams and others 2003); Thailand: 28.9 (Williams and others 2003); Uganda 1: 19.8 (Boivin and others 2013); Ethiopia: 24.0 (Bougma 2014); Uganda 2: 25.4 (Singla, Kumbakumba, and Aboud 2015); Brazil: 23.1 (Eickmann and others 2003); Costa Rica: 29.8 (Lozoff and others 1987); Chile: 30.8 (Lozoff and others 2010).
Note: HOME = Home Observation for Measurement of the Environment.

siblings are not able to deliver the sophisticated language of adults or accurately perceive when young children are in danger (Morrongiello, Schell, and Schmidt 2010). Across all 28 LMICs surveyed, the average number of caregiving practices out of six performed in the past three days with a child under age five years was 3.03. Many parents from countries in South Asia and Sub-Saharan Africa practiced only one or two. Although no threshold score is available to identify inadequate levels of stimulation, low levels such as these are unlikely to support expected levels of mental development (Bradley and Corwyn 2005).

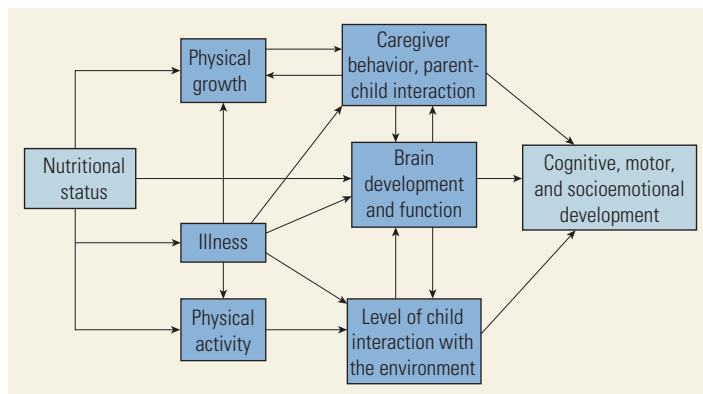
Both the HOME Inventory and its briefer version are highly correlated with children's mental development, ranging from $r = 0.20$ to $r = 0.46$ (Aboud and others 2013; Boivin and others 2013; Hamadani, Tofail, and others 2010; Tofail and others 2012). These correlations and the theoretical framework presented here (figure 13.2) support the design of stimulation interventions to enhance mental development. One hypothesized pathway proposes that an adult's child-directed conversation stimulates speech perception sites in the brain, thereby maintaining neural connections throughout language sites in the brain. Also, if the conversation is directly related to children's current state, it is expected to expand the children's receptive language and grammar. This interaction helps children translate their own thoughts and actions into speech and later into writing and reading. Play materials that children enjoy manipulating and combining in multiple ways help them learn about mass

Figure 13.2 Framework Illustrating Pathways from Psychosocial Stimulation to Mental Development



Source: Larson and Yousafzai 2014.

Figure 13.3 Framework Illustrating Pathways from Nutritional Status to Mental Development



Source: Brown and Pollitt 1996; Prado and Dewey 2014.

and weight, as well as problem solving. The material must be challenging so that children have opportunities to construct the material in new ways.

Child Nutrition

One of the strongest risk factors for poor mental development is short length- or height-for-age (for cross-sectional studies, see Olney and others 2009; Servili and others 2010; for longitudinal studies, see Grantham-McGregor and others 2007). Stunting is a commonly used indicator of chronic undernutrition, defined as more than two standard deviations below the age- and gender-specific norm, that increases rapidly after age six months; by 24 months, 50 percent of children in LMICs are stunted (Victora, de Onis, and Hallal 2010). Children rarely catch up after this age.

It is not clear why length and height are so strongly related to cognitive and language development, except

that linear growth may be a proxy for other critical nutrition processes related to brain and behavioral development. A model of how nutrition contributes to mental development is presented in figure 13.3 (Brown and Pollitt 1996; Prado and Dewey 2014). One pathway is direct in the sense that nutrients support the structure and activity of brain sites responsible for mental development. Other pathways are indirect in that nutrition enhances health and engagement with the environment, which promote mental development. Evidence from nutrition interventions showing effects on growth and health are described here. The next section presents intervention effects on mental development.

Macronutrients

Sufficient macronutrients, such as carbohydrates, proteins, and fats, are important to linear growth and mental development. In the first six months, exclusive breastfeeding provides sufficient nutrients to support healthy rates of growth and immunity (Kramer and others 2001) (see chapter 5 in this volume, Stevens, Finucane, and Paciorek 2016). After age six months, the quality of diet is captured by the term *dietary diversity* and measured as the number of seven different food categories in a daily diet (Daelmans, Dewey, and Arimond 2009). Dietary diversity was positively related to linear growth in five of the nine countries for which these data were analyzed (Jones and others 2014). Improving dietary diversity, especially with animal-source foods, is a critical message in nutrition education interventions (Neumann and others 2007). In eight studies, nutrition education alone for mothers of children ages 6–24 months, usually about foods to feed and number of meals, led to gains in length, with an effect size of $d = 0.21$, where effect size d refers to the number of standard deviations by which intervention children's length exceeded that of control children (Dewey and Adu-Afarwuah 2008; Imdad, Yakoob, and Bhutta 2011). Agricultural improvements at the household level are also being implemented and evaluated (Iannotti and others 2014).

Micronutrients

Micronutrients such as iron and iodine are considered to be important for mental development in the first 24 months (see chapter 11 in this volume, Lenters, Wazny, and Bhutta 2016; and chapter 12, Das and others 2016). Numerous studies have demonstrated high levels of anemia in young children, especially in South Asia and Sub-Saharan Africa, where 20 percent of children younger than age five years are anemic (Black and others 2013). Both an iron-deficient diet and hookworm in contaminated soil are responsible for low

levels of hemoglobin. Anemic children are consistently found to have lower levels of mental development than non-anemic children in case-control studies, and differences persist over the long term (Lozoff and others 2006). Anemic children also show a number of socially isolating behaviors, such as wariness and lethargy. However, the nutritional and mental consequences of providing young children with iron are mixed and generally weak (Pasricha and others 2013). In many cases, iron therapy has not sufficiently raised their hemoglobin levels; even when it has, children's mental development scores frequently have not improved. Alternative explanations are being sought for the longitudinal findings, such as low levels of stimulation in the home environment, where the mother may be anemic. Brain functioning, such as speed of processing auditory and visual information, may be a more sensitive measure of the mental effects, especially if iron is an important element in the myelin sheath around neuronal axons (Lozoff and others 2006).

Iodine deficiency is consistently associated with poor school achievement, but much less is known about its effect on the mental development of children younger than age 24 months (Zimmermann 2012; Zimmermann, Jooste, and Pandav 2008). Many countries lack naturally occurring iodine in the soil and water and therefore must fortify a product such as salt. Most of the data on prevalence has been collected from children ages 6–12 years whose urinary iodine levels tend to match that of their parents. Based on these data, an estimated 40 percent of the Sub-Saharan African population and 31.6 percent of the population of East Asia and Pacific and South Asia are iodine deficient (Black and others 2013). Four prospective studies find that mental development scores of children with inadequate iodine levels at birth were half a standard deviation less than those with healthy levels (Bougma and others 2013); this finding translates into a development quotient difference of 8 points on a standard mental test—a meaningful difference.

Multiple Vitamin and Mineral Supplements

Multiple micronutrients constitute the common nutritional supplement provided to young children. Children are often deficient in many minerals, such as iron and zinc, as well as vitamins. All are critical for health and growth, and their effects on mental development are becoming clear. The rationale for studying multiple micronutrients is that they work together to improve health, they appear to be necessary for linear growth, and they are found in many sites in the brain. Most of what is known about the effects of combining multiple micronutrients comes from evaluations of trials in which various combinations are provided in a powder sprinkled on the food daily at mealtime. Alternatively,

researchers weigh meal foods and calculate quantities of different nutrients in each food item.

Linear growth is still the strongest correlate of mental development, so it is important to evaluate the effects of macro- and micronutrient interventions on children's height. The section on Interventions for Mental Development reports effects on cognitive and language outcomes. Systematic reviews have consistently shown that the effect sizes of nutrition interventions on linear growth gains were lowest for micronutrient fortification (about 0.12), and better for energy alone (about 0.25) and the provision of food with extra proteins and nutrients (about 0.28) (Bhutta and others 2013; Dewey and Adu-Afarwuah 2008). The effect sizes for nutrition education were 0.20, especially those programs emphasizing dietary diversity and animal-source foods. Although nutrition education is insufficient on its own, especially in food-insecure sites, it is necessary if benefits from short-term supplementation and fortification are to be sustained, and in some cases leads to better mental development (Vazir and others 2013).

Environmental Conditions

Environmental conditions encompass a broad array of vectors, including contaminated razors used to cut the umbilical cord and leading to tetanus, viruses and bacteria that follow a fecal-oral transmission route starting from poor home sanitation and leading to diarrhea, parasites carried by the female *Anopheles* mosquito leading to malaria, and *Chlamydia trachomatis* brought by moisture-seeking flies to children's eyes that can lead to blindness. Despite a resurgence in some places, deaths due to neonatal tetanus, and sensory-motor disabilities due to polio and measles, are being reduced with the help of vaccines. However, trachoma, diarrhea, and cerebral malaria continue to have major impacts on early mental development.

Trachoma

Trachoma, active in 40.6 million people worldwide, is responsible for blindness in 8.2 million people (Mariotti, Pascolini, and Rose-Nussbaumer 2009). It is endemic in 57 countries, but 80 percent of the cases are in 15 countries, most in Sub-Saharan Africa. One study of southern Sudan found that 64 percent of children ages 1–9 years had active trachoma; 46.2 percent of infants had signs of active trachoma (Ngondi and others 2005). The condition begins in early childhood when the *Chlamydia trachomatis*, passed by hand or flies, leads to inflammation of the conjunctiva of the upper eyelid. The infection may disappear, but repeated reinfection leads to blindness. Although surgery is needed for cases of blindness

among adults, the more common approach has been mass azithromycin antibiotic treatment as a primary and secondary prevention (Ogden and Emerson 2012).

Diarrhea

Diarrhea becomes most prevalent between 6 and 24 months of age; children have on average four to five episodes a year (Kosek, Bern, and Guerrant 2003). The most common cause of severe diarrhea is rotavirus, for which vaccines are being given to infants in many countries in East Asia and Pacific and South Asia and Sub-Saharan Africa (Armah and others 2010). Other common causes are bacteria, such as salmonella, shigella, and pathogenic *E. coli*. The main route of transmission is fecal-oral, so the risk is high if families do not use a latrine or improved sources of water. Children become exposed to contaminated soil and water, typically after age six months when they start to crawl and share family meals. Hookworm, one of the geohelminths found in contaminated soil, is responsible for half of the anemia in children, and diarrhea is a common cause of malnutrition and stunting (Checkley and others 2008). Although there is little evidence that worms and diarrhea directly impede mental development, they may diminish important determinants, such as growth and activity (Fischer Walker and others 2012; Taylor-Robinson, Jones, and Garner 2007) (see chapter 9 in this volume, Keusch and others 2016).

Enteropathy

Recent attention has focused on tropical or environmental enteropathy, which results from constantly ingested fecal bacteria, as a subclinical condition. In several studies, fecal bacteria contamination was very high in children's food and in soil and chicken feces found around the home where children play (Ngure and others 2014); these levels are correlated with microbiological data from the children and high levels of inflammation. Constantly high levels of pathogenic bacteria lead to chronic changes in the villi of the small intestines (Humphrey 2009; McKay and others 2010; Weisz and others 2012). The effect of enteropathy is to increase absorption of bacterial products, such as endotoxins, into the system and allow for leakage of nutrients, such as proteins. Consequently, young children experience recurrent infections, with associated loss of appetite and diversion of nutrients to fight infections and inflammation, resulting in inactivity and growth faltering. Jiang and others (2014) find a direct association between mental development scores and the number of days during which an infant experienced fever and elevated levels of pro-inflammatory cytokines. Although preliminary, the work suggests a connection between inflammation and mental development. If enteropathy is as

prevalent and severe as feared, how to eliminate sources of contamination in the environment without restricting children's access to psychosocial stimulation around the home must be seriously reconsidered.

Cerebral Malaria

Cerebral malaria has clear but variable consequences for early childhood mental development. There are 104 malaria-endemic countries in the world; most are in Sub-Saharan Africa. The parasite *Plasmodium falciparum*, in particular, is most strongly associated with cerebral malaria leading to high fever, coma, and organ failure. Contracted by pregnant women or young children, malaria is a serious cause of death and disability among children. In one Ugandan study, approximately 10 percent of survivors had severe neurological deficits; the majority had moderate problems that were detected only with psychological testing when the children were older (Bangirana and others 2006). Disabilities are evident in auditory or visual processing, as well as in memory and attention; language problems were not as severely affected. Because impairments vary, many researchers report the number of subtests on which cerebral malaria survivors show deficits compared with controls. For example, a prospective study with children ages 5–9 years in Kampala, Uganda, finds that on several tests of attention, working memory, and learning, 36.4 percent showed deficits on at least one measure at hospital discharge; 21.4 percent maintained deficits at six-month and two-year follow-ups, compared with 5.7 percent of healthy controls (Boivin and others 2007; John and others 2008). Deficits in attention and memory were most common and were related to the number of seizures and duration of coma.

Most of this research has been conducted in urban hospitals, although the larger burden of malaria is likely found in rural sites. Consequently, the evidence is strong that a large proportion of children with cerebral malaria and its associated brain complications will show long-term cognitive and perceptual problems.

Maternal Nutrition

The optimum body mass index (BMI) for women at the start of pregnancy is 18.5 to 24 kilograms per meter squared. In LMICs, more than 10 percent of women are less than 18.5, with the highest levels of low BMI found in South Asia and Sub-Saharan Africa (Black and others 2013). BMI is an important benchmark because it highlights the undernutrition of many women before they become pregnant. The failure to meet the benchmark indicates increased risk of difficult deliveries for mothers and children; short maternal stature, defined as less than

145 centimeters, is also problematic. Although the rate of low BMI is declining, the prevalence of unattended home deliveries remains high. Consequently, birth injuries, such as asphyxia, are untreated and leave lasting effects on mental development.

Mothers with low BMI, short stature, or both put their children at risk of being small-for-gestational-age (SGA). SGA, defined as having birth weight less than the 10th percentile for gestational age, includes newborns who are at term (37–40 weeks) but small—less than 2,500 grams at 37 weeks and less than 2,900 grams at 40 weeks, as well as those who are preterm and small. In 2010, an estimated 32.4 million newborns in LMICs, or 27 percent of the 120 million births, were SGA; of these, 30 million were born at term with intrauterine growth restriction (Lee and others 2013). South Asia makes the highest contribution to this figure; 42 percent of its births are SGA. Prematurity tends to be consistent at 18 percent for Sub-Saharan Africa and 12 percent for South Asia (Lawn and others 2014), although very few born younger than 32 weeks survive in LMICs. The group most at risk for neurological and developmental disabilities is the combined group of premature infants and term SGA infants, who together make up 43.3 million or 36 percent of live births (Lee and others 2013). Some experts identify only SGA infants (preterm and term) as high risk.

Increased Risk of Neurodevelopmental Disabilities

Although the first hurdle for SGA and premature newborns is surviving respiratory distress, hypothermia, and infections during the first month, the second hurdle is early neurodevelopmental disabilities (Blencowe and others 2013). These issues include cognitive impairment, hearing and vision problems, and motor and behavioral problems. A systematic review of surviving preterm children, mainly from high-income countries (HICs), indicates that approximately 7 percent showed mild or moderate-to-severe impairment in one of these areas. Those with very short gestational age fared worse: 24.5 percent of those with less than 32 weeks' gestation had moderate-to-severe impairment, whereas 1.8 percent of those between 32 and 37 weeks had impairments (Blencowe and others 2013; Platt 2014). One hospital-based assessment of surviving preterm Bangladeshi infants with gestational age of less than 33 weeks finds that 73 percent had mild or serious impairments when tested at younger than age two years; 66 percent were reported as having impairments between ages two and four years (Khan and others 2009); most of the impairments were cognitive. Although most data come from studies in HICs, conclusions and applications to East Asia and Pacific and South Asia and Sub-Saharan Africa

are clear, especially for the 12.6 million children born at ages 32–37 weeks who need facility and family care but not necessarily a high-technology intensive care unit. More research is needed to identify the range of disabilities they may experience related to sensory development, learning, mental health, and executive function. Programs to prevent and treat these disabilities have received little attention in LMICs.

Increased Risk of Delayed Mental Development

The third hurdle for SGA and premature newborns is linear growth restriction, an important determinant of mental development. SGA newborns have experienced fetal growth restriction and are unlikely to catch up because of problems starting breastfeeding and the usual decline in growth rates found in the first 24 months (Christian and others 2013). In 19 longitudinal cohort studies from LMICs that followed children from birth to between ages 12 and 60 months, low birth weight (LBW) children were almost three times more likely to be stunted (< -2.00 height-for-age z-score) than normal birth weight children, but this likelihood varied according to gestational age. The risks were highest for preterm SGA newborns (odds ratio: 4.51), next for term-SGA (odds ratio: 2.43), and lowest for preterm average-for-gestational-age (odds ratio: 1.93). Accordingly, although prematurity was the stronger determinant of neonatal mortality, weight-for-gestational-age had more lasting effects on linear growth. The mental development of SGA newborns may be compromised in the short term, but their longer-term prospects in LMICs are unclear. For example, Tofail and others (2012) find that at age 10 months, LBW Bangladeshi infants, most of whom were term, had lower mental and motor Bayley scores than normal birth weight children, after controlling for a range of covariates, such as weight, length, and gestational age. Similarly, Walker and others (2004) find lower Griffiths scores at ages 15 and 24 months on cognitive and motor subscales for term-LBW Jamaican children compared with normal-weight peers. Thus, preterm- and term-SGA babies are likely to have lower mental development if they continue to have poor health and growth, and inadequate nutrition during fetal growth may be partly responsible.

Maternal Mental Health

Maternal depression is increasingly recognized as an important risk factor for poor child development (Tomlinson and others 2014; Walker and others 2011) (see chapter 3 in this volume, Filippi and others 2016). A systematic review reports that the prevalence of maternal depression among pregnant women in low-income and lower-middle-income countries was 15.9 percent,

and in the postpartum period was 19.8 percent; these rates are higher than those for women in HICs, which are, on average, 10 percent and 13 percent, respectively (Fisher and others 2012). Prevalence is higher in many South Asian countries, for example, in Pakistan, where one study reports a 25 percent prevalence of maternal depression in the antenatal period and 28 percent in the postnatal period (Rahman, Iqbal, and Harrington 2003). Recognizing that depression may not be confined to the prenatal and postnatal periods, many researchers monitoring maternal depression for 24 months after birth and beyond find it to be high in South Asia and Sub-Saharan Africa, from 20 percent to 30 percent, using the WHO's 20-item Self-Reporting Questionnaire (Harpham and others 2005; Servili and others 2010; Weobong and others 2009).

Important determinants of maternal mental health include intimate partner violence (Ludermir and others 2008); social support (Rahman and Creed 2007); the quality of her relationships with her husband (Oweye, Aina, and Morakinyo 2006) and other close relatives, such as in-laws (Chandran and others 2002); and her coping strategies (Faisal-Cury and others 2003). Nutritional status may be implicated. Evidence suggests that iron-deficiency anemia contributes to a depressed mood at levels lower than required for a diagnosis of depression, as might iodine deficiency (Beard and others 2005). Illness, fatigue, and lethargy are likely to reduce a mother's ability to cope as well as to care for her young child. Infants with special needs requiring higher levels of care have been linked to higher levels of maternal distress (Yousafzai, Lynch, and Gladstone 2014).

Studies from South Asia have shown that young children of depressed mothers are at risk of poor health, growth, and development outcomes. Rural Pakistani children of depressed mothers were twice as likely to have five or more episodes of diarrhea per year than children of nondepressed mothers (Rahman, Bunn, and others 2007). Studies from India and Pakistan have shown that infants born to depressed mothers are 2.3 to 7.4 times more likely to be underweight (Patel and others 2004); in India, they were more likely to be stunted, but not in Vietnam, Ethiopia, or Peru (Harpham and others 2005). Evidence for the effect of maternal depression on mental development is mixed in LMICs. Some hospital samples show a link (for example, Hamadani and others 2012), but in rural Ethiopia, maternal depression was not associated with poor mental development in children (Servili and others 2010). In Bangladesh, maternal depression was found to be linked to poor mental development outcomes only if depressed mothers perceived their children as irritable (Black and others 2007). Maternal depression has a

potentially detrimental impact on children and needs to be examined more carefully.

INTERVENTIONS TO ENHANCE MENTAL DEVELOPMENT

This section describes key protective interventions that promote healthy early child development. We consider each intervention's outcome (figure 13.4), organizing the interventions into development-specific interventions that focus on the child, including psychosocial stimulation, child nutrition, and reduction of infections, followed by development-sensitive interventions that focus on the mother, including maternal nutrition and maternal mental health, that might indirectly affect the child.

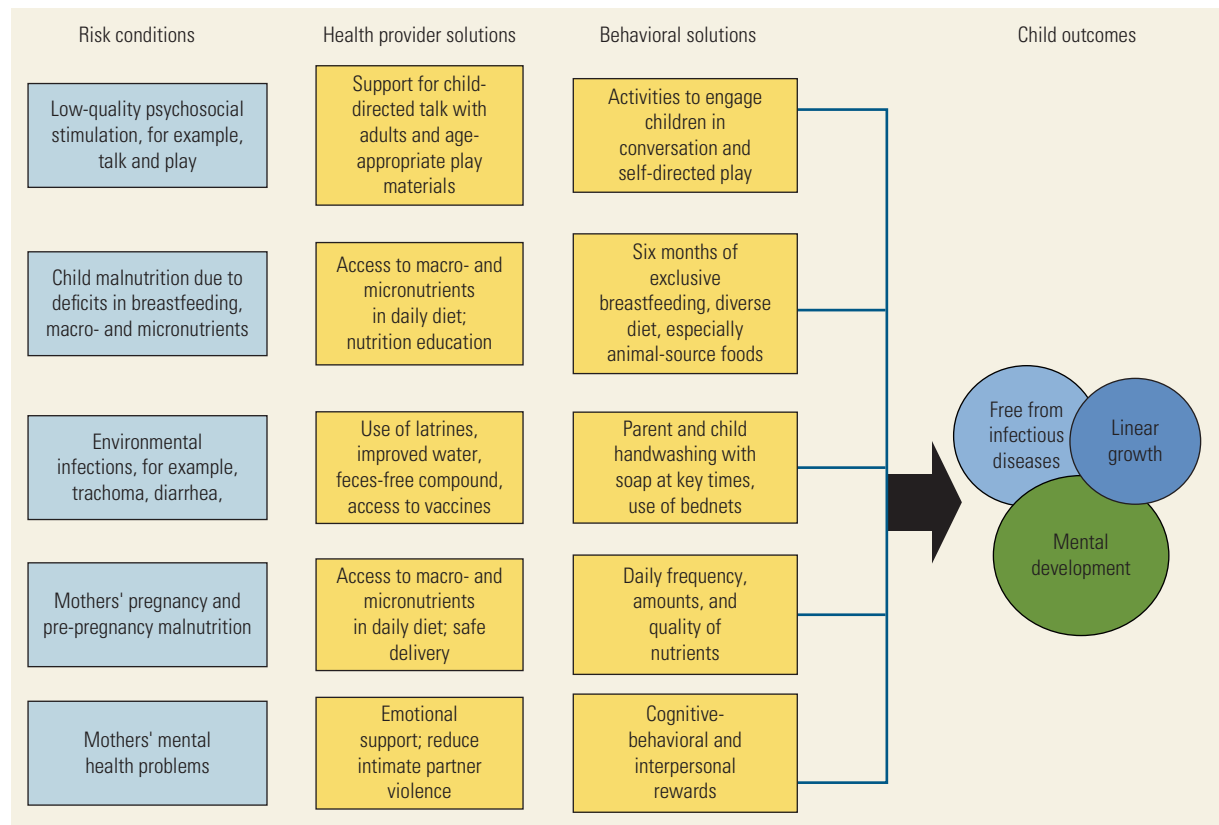
Development-Specific Interventions

Psychosocial Stimulation

One of the strongest protective factors for mental development is the amount and quality of psychosocial stimulation provided in the home. A systematic review and meta-analysis of stimulation intervention outcomes from 21 studies finds positive effects: the mean effect size for cognitive outcomes was $d = 0.420$ and for language outcomes was $d = 0.468$ (Aboud and Yousafzai 2015). These effects are considerably higher than for other interventions, such as nutrition and hygiene. However, stimulation programs require considerably more manpower, training, and supervision. Four models of delivery have been implemented and evaluated (box 13.1), but all require special training of professionals or paraprofessionals and a method of instruction that encourages parents to actively learn new practices and be able to generalize what they learn as their children grow.

Changing behavior is difficult, but one review identifies several techniques that are more successful than others (Aboud and Yousafzai 2015). The traditional technique of simply educating or informing parents about what to do and why has not worked (Aboud 2007). Behavior change requires more than communication; it requires active learning techniques, such as demonstrations, practicing with children and receiving coaching and feedback, identifying and solving problems with enacting the practice, providing visual reminders, and engaging social support from peers and family members. Actual changes to parents' behavior can be evaluated using the HOME Inventory; effect sizes for better HOME scores in intervention groups tend to be higher whenever mental scores are high, thus confirming a strong relationship between changes to stimulation

Figure 13.4 Conditions That Put Children at Risk of Poor Mental Development, and Solutions Entailing Health Provider Support and Parental Behavior Changes



Source: Compilation based on sources cited in this chapter.

and mental development (figure 13.5). Typically changes are small, although significantly greater than changes in the control group. There are too few longitudinal studies yet to confirm that parents are able to sustain the new practices and adapt them as children age.

Overall, stimulation interventions, regardless of their delivery strategy, successfully improved mental development. This success may be partly attributed to the effect of the interventions on raising parental stimulation practices, which, in addition to linear growth, is one of the strongest correlates of mental development.

Child Nutrition

Exclusive breastfeeding from birth to six months is known to support healthy rates of growth and immunity. Correlational evidence argues that breastfed babies also have better mental development (Anderson, Johnson, and Remley 1999). This claim was affirmed by a trial in Belarus, in which half of the hospitals were randomly assigned to start the World Health

Organization–supported Baby-Friendly Hospital Initiative activities sooner than others. Mothers who delivered in these hospitals breastfed longer, and their children had higher verbal intelligence at age six years (Kramer and others 2008).

One important nutrient in breast milk, fatty acids, has been studied in relation to mental development but mainly in HICs. Long-chain polyunsaturated fatty acids (PUFA), particularly n-3, that are present in the brain and breast milk are considered to be a promising candidate to support mental development. Multiple trials, conducted mainly in HICs where it is possible to provide infants with formula milk with varying amounts of fatty acids, found no effects on Bayley mental or motor scores (Beyerlein and others 2010; Qawasmi and others 2012; Smithers and others 2008). Similar tests of fatty acids found in fish and fish oil have shown no advantage to Bangladeshi children whose mothers received fish oil during pregnancy (Tofail and others 2006). However, research on fatty acids continues to follow children as

Box 13.1

Four Models of Stimulation Program Delivery

Four delivery formats for stimulation programs are most common: home visits, group sessions, clinic appointments, and one of these three piggybacked onto conditional cash transfer (CCT) programs. A fifth, combining group with home visits, has become increasingly common. All delivery models require a curriculum manual for providers. Those employing paraprofessionals require more training and supervision.

Home visits entail weekly or fortnightly visits by a paraprofessional to the children's homes. The home visitors engage in specific age-appropriate play activities with the children, demonstrate these activities to watching mothers, and leave play materials that will be replaced at the next session. Interventions based on home visits usually entailed more than 24 visits over 12 months (Lozoff and others 2010; Tofail and others 2013; Vazir and others 2013).

Group sessions consist of meetings with 8 to 20 mothers, and sometimes fathers, with their children at convenient locations in communities. Paraprofessionals from the community or local community health workers conduct the sessions. Group leaders demonstrate specific activities and coach mothers as they practice with their children. Groups could engage in discussions and general problem solving. Interventions using groups usually had fewer sessions than those using home visits (Aboud and Akhter 2011). Many interventions combined home visits with group sessions (Aboud and others 2013; Eickmann and others 2003; Yousafzai and others 2014). Informational and social needs

common to all parents are addressed during group sessions, and family-specific problems are addressed during home visits. These combined interventions usually had more than 15 contacts over 12 or 24 months.

The third model uses well- or sick-baby clinic visits to inquire about what mothers know about stimulating their children with toys and talk and counseling them on improved practices. This advice is usually provided by professionals, sometimes with two to four contacts (Jin and others 2007; Potterton and others 2010) and with at most 12 monthly contacts (Nair and others 2009). Group and clinic models explicitly aim to change parents' behavior, particularly the opportunities that parents provide for play and conversation.

The final model is the scale up of stimulation interventions using the infrastructure of a CCT program. One example is the home-visiting program attached to Colombia's Familias en Acción program. Mother Leaders from the community were trained to make weekly visits to the homes of children ages 12–24 months to provide guidance on play (Attanasio and others 2014). Another Colombian example is the home-based group care offered to CCT beneficiaries, whereby mothers were trained to provide stimulation weekdays to 15 children (most under age three years) in their homes (Bernal and Fernández 2013). Both large-scale effectiveness evaluations showed positive effects on the order of 0.2 to 0.3 standard deviation difference on children's cognitive and language abilities.

they age (Colombo and others 2013). Supplementation with a milk lipid, ganglioside, was found to have positive effects on early mental development in Indonesia (Gurnida and others 2012). Furthermore, research has found mental development benefits of fatty acids in colostrum; 14-month-old children whose mothers had high levels of n-3 PUFA in colostrum and who were breastfed with greater intensity or duration had higher mental development scores (Guxens and others 2011). Thus, the clear cognitive benefits to breastfeeding appear to stem from high levels of n-3 PUFA and cumulative amounts of ingested breast milk.

Research is being conducted on multiple micronutrients with and without lipids. Some studies use vitamin A as the baseline and compare it with five other micronutrients (Black and others 2004); others provide a porridge with carbohydrates and add micronutrients (Manno and others 2012; Rosado and others 2011). Pollitt and others (2000) gave all children eight micronutrients (vitamins and minerals) with high-energy milk added to the diet of intervention children only. The fortification in many cases was available for a period of six to eight months; the effects on mental development scores were small. A review of 21 interventions examining the effects of

multiple micronutrients on mental development yielded a very small overall effect size of $d = 0.082$ (Larson and Yousafzai in press). In many cases, children showed benefits, such as reduced anemia, but no benefits in linear growth. Motor development improved in some cases. Currently multiple micronutrients are being combined with a lipid base that provides macronutrients to examine their combined effects on linear growth. This combination has the potential to enhance mental development in food-insecure sites.

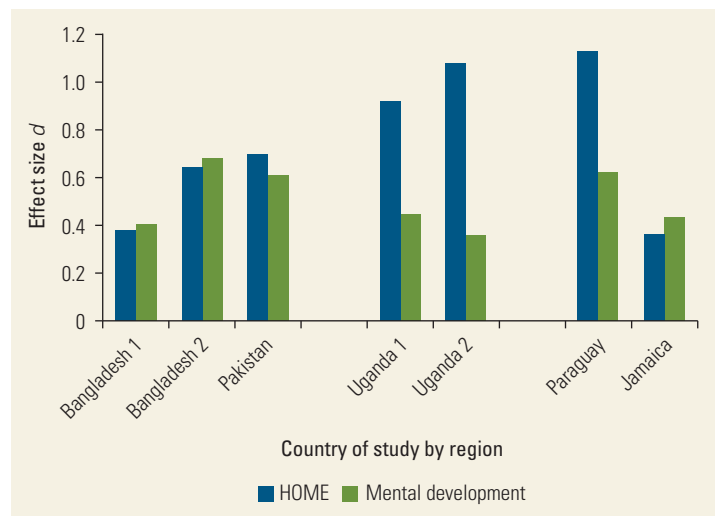
Integrated Packages of Psychosocial Stimulation and Child Nutrition

Researchers and program implementers are paying closer attention to optimizing integrated packages of stimulation and nutrition care given the independent and potentially additive benefits to promoting mental development. Although most small- and large-scale interventions have found little added benefit to mental development from integrating nutrition with stimulation (Attanasio and others 2014; Grantham-McGregor and others 2014; Yousafzai and others 2014), other benefits of integration, such as cost and task-sharing, are being examined. This combination is illustrated in a completed stimulation and nutrition trial in Pakistan (box 13.2).

Reducing Infection Transmitted by Ground Contamination, Mosquitoes, and Flies

The most commonly implemented solutions to environmental causes of infection are constructing and using latrines, improving access to clean drinking water, promoting facewashing and handwashing with soap, cleaning up animal feces around the home, immunizing all infants with the rotavirus vaccine, and deworming children starting at age 12 months (Dangour and others 2013; Ejemot and others 2008; Fewtrell and others 2005). Places where piped water and sewerage systems are installed have experienced an immediate reduction in diarrheal diseases (Fewtrell and others 2005). However, widespread provision of water and sanitation infrastructure is unrealistic in the near future, especially in rural areas of LMICs. Although 68 percent of urban dwellers in LMICs have latrines, only 40 percent of rural people have them (UNICEF 2013). Improved sources of water are commonly provided at the community level or preferably at point of use, so that the urban-rural gap for improved water is narrower than that for sanitation (94 percent of urban dwellers have access to improved sources of water compared with 76 percent of rural dwellers). Concern about the effects of very high levels of arsenic in drinking water is supported by evidence of fetal loss and infant mortality

Figure 13.5 HOME Effect Size, Mental Development Effect Size, and Study



Sources: Bangladesh 1: HOME 0.38, Language Development 0.40 (Aboud and Akhter 2011); Bangladesh 2: HOME 0.64, Cognitive Development 0.67 (Aboud and others 2013); Pakistan: HOME 0.69, Cognitive Development 0.60 (Yousafzai and others 2014); Uganda 1: HOME 0.91, Language Development 0.44 (Boivin and others 2013); Uganda 2: HOME 1.07, Cognitive Development 0.35 (Singla, Kumbakumba, and Aboud 2015); Paraguay: HOME 1.12, Mental Development 0.62 (Pearson and others 2008); Jamaica: HOME 0.36, Cognitive Development 0.42 (Walker and others 2004).

Note: HOME = Home Observation for Measurement of the Environment.

(Rahman, Vahter, and others 2007), but arsenic in water appears to have little effect on mental development in the first 24 months and up to age five years (Hamadani, Grantham-McGregor, and others 2010; Hamadani and others 2011).

Immunization with rotavirus vaccine as part of the national immunization schedule has begun in more than 35 countries, with support from the Global Alliance for Vaccines and Immunization. The rotavirus vaccine has been effective in reducing severe cases of diarrhea, mortality, and hospital and clinic visits, and it provides protection for several years. Mass treatment of children with deworming medication and azithromycin for trachoma can be attached to outreach services that deliver vitamin A drops. However, these are short-term solutions. The WHO's recommended SAFE (surgery, antibiotics, facial cleanliness, and environmental improvements) strategy for trachoma elimination also includes hygiene (facewashing) and environmental management (along with surgery and antibiotics) as the more sustainable approaches (Mecaskey and others 2003).

Environmental management of stagnant water is only one of the means by which to control malaria. Bednets, intermittent preventive treatment, and vaccines are the most studied preventive interventions (Cissé and others 2006; Gies and others 2009). The provision of free insecticide-treated bednets led to high coverage and protection (Alaii and others 2003); and three

Box 13.2

Pakistan Early Child Development Scale-Up Trial: Case Study of a Successful Program

The Pakistan Early Child Development Scale-Up Trial successfully enhanced the cognitive, language, and motor development of children whose parents received counseling in psychosocial stimulation for their children, with or without enhanced nutrition education and multiple micronutrient fortification (Yousafzai and others 2014). The program showed clear benefits from parenting practices that improved mother-child interactions and the quality of home stimulation. Lady Health Workers (LHWs), who every month deliver basic maternal and child health services to rural and remote households as part of the government health system, added counseling on psychosocial stimulation and nutrition to their activities for families with children under age two years.

Psychosocial Stimulation Intervention

The psychosocial stimulation intervention, using the Care for Child Development messages and materials developed by the United Nations Children's Fund (UNICEF) and the World Health Organization, encouraged mother-child play and communication activities (UNICEF and WHO 2009). The LHWs provided information about recommended practices and benefits, suggested developmentally appropriate activities for caregivers to try with their young children, and coached caregivers by providing prompts and encouragement to respond to children's efforts and communication. The goal of the intervention was to enhance the quality of caregiver-child interactions and promote children's cognitive, language, motor, and social-emotional skills.

The intervention was delivered through a combination of home visits and group sessions. The group sessions offered opportunities for problem solving and social support through encouragement, praise, and peer-to-peer learning.

Nutrition Intervention

The nutrition intervention was designed to enrich the existing basic nutrition education curriculum in the LHW program delivered through home visits. This goal was achieved by the addition of responsive feeding messages and the distribution of a multiple micronutrient powder for young children ages 6–24 months. The LHWs were trained to move away from a traditional didactic approach to a counseling strategy for delivering nutrition education. During the home visits, the LHWs provided information about recommended practices and benefits, engaged in problem solving, and provided encouragement.

Critical to the success of the program was the use of supportive supervision, on-the-job coaching, and mentorship for LHWs. It was important for them to integrate the new practices with existing health messages without burdening mothers. Group delivery strategies combined with home visits permitted the LHWs to reach a greater proportion of the community, and the demand for community-based services increased. The cost of integrating the interventions into the existing LHW services was US\$4 per month per child.

Source: Gowani and others 2014; Yousafzai and others 2014.

intermittent doses of an antimalarial medication at the time of routine immunization reduced the incidence of malaria by 20 percent (Macete and others 2006). Neither hemoglobin levels nor future immunity were compromised with these preventive antimalarial measures. Psychosocial stimulation interventions appear to be effective at overcoming some of the deficits caused by cerebral malaria.

Latrine use and handwashing habits are very difficult to change. Interventions to increase latrine use and handwashing have met with success mainly in

controlled experimental settings (Briscoe and Aboud 2012); they have been less successful when implemented at the community level (Huda and others 2012; Hutton and Chase, forthcoming; Luby and others 2008).

Development-Sensitive Interventions

Maternal Nutrition

Strategies to address the growing number of premature births (Lawn and others 2014) have not yet been identified. High stress during pregnancy is a correlate

among African-American women, many of whom deliver preterm-LBW babies (Lobel and others 2008). SGA is thought to be associated with maternal infection (malaria) and malnutrition (Black and others 2013), and preventable through intermittent preventive anti-malarial treatment (Gies and others 2009) and maternal nutrition, respectively.

Raising birth weights by providing supplements to pregnant women has received mixed reviews. Iron and folic acid supplementation are clearly beneficial, the latter in reducing neural tube defects that result in mental development impairments. Reviews of studies providing micronutrient supplements, energy-protein supplements, or both found small reductions in the number of SGA newborns (Haider and Bhutta 2012; Imdad, Yakoob, and Bhutta 2011). However, a large study in Bangladesh examined the effects of a daily energy-protein supplement starting either in the first trimester or later in the second trimester, and the effects of an additional 13 micronutrients, compared with the usual iron and folic acid (Persson and others 2012). Gestational age with a mean of 39 weeks was similar across groups, indicating that prematurity was not affected. Birth length and birth weight were not affected, with 31 percent LBW. Infant mortality was lowest among children whose mothers received multiple micronutrients and started energy-protein supplements early. A follow-up on the children from this study, using two items from the Bayley Scale at age seven months, found minimal differences on one item benefiting only those with low BMI mothers who received early energy-protein supplements (Tofail and others 2008). The nonsignificant findings of this study are supported by a preliminary meta-analysis of 10 randomized controlled trials (RCTs) in which pregnant women were given micronutrient or other fortified foods and their children tested before age 24 months. The overall mental development effect size was $d = 0.042$ (Larson and Yousafzai in press). Many scientists conclude that providing nutrition supplements during pregnancy is too late to significantly benefit birth outcomes and mental development, and that maternal nutritional status at conception is critical. More attention needs to be given to nutrition among children and adolescent girls.

Iodine is so important for reproductive and mental development that governments legislate the fortification of salt for general use. Interventions designed to study the effects of iodine on mental development in iodine-deficient areas typically randomize pregnant women to receive capsules that provide sufficient iodine for one year. Ten existing interventions, two of which were RCTs, found a moderate effect size for mental development of $d = 0.50$ (Bougma and others 2013).

Iodine provided during pregnancy was more beneficial than iodine supplementation given to children after birth. Another strategy is to provide the lactating mother with iodine supplements; this indirect supplementation maintained healthy urine and serum levels in the infant better than direct supplementation of the infant (Bouhouch and others 2014). An important test is whether iodine delivered through salt in the diets of mothers and children improves the mental development of children. Careful scrutiny of RCTs in which school-age children were given an iodine capsule or a placebo reveals that the large majority of verbal and nonverbal tests yielded no positive outcomes (Huda, Grantham-McGregor, and Tomkins 2001; van den Briel and others 2000). However, iodized salt had a consistently small but positive effect on the mental development scores of children under age 24 months in Ethiopia (Bougma and others 2014). In short, iodine will have maximum effect on children's mental development if available to women during pregnancy and lactation.

Maternal Mental Health

Integrated packages supporting mothers and children are receiving increasing attention (Tomlinson and others 2014). The postnatal period up to 24 months after birth might be a suitable time to address maternal depression along with child feeding and stimulation practices. This broader focus might benefit children's development and can be provided in a context that does not stigmatize mothers. The available handful of evaluated interventions suggests that alleviating maternal depression may help mothers better meet their children's needs. In Pakistan, the Thinking Healthy program was developed using principles of cognitive-behavioral therapy, although it also includes elements of interpersonal therapy. Cognitive-behavioral and interpersonal therapies are the two therapies for which there is sound evidence in North America and Europe; it is valuable to know that their principles can be adapted for use in LMICs. In Pakistan, community health workers were trained in a structured form of dialogue that covered empathic listening, family engagement, guided discovery using pictures, behavioral activation, and problem solving.

The integration of the Thinking Healthy program in a community-based maternal and child health service resulted in significant reduction of maternal depression in Pakistan. Additional positive benefits in the intervention group were lower rates of infant and young child diarrheal illness, higher rates of young child immunization, higher reported use of contraceptives among women, and increased parental time spent playing with their young children (Rahman and others 2008). It is reasonable that countries with a high

prevalence of maternal depression should implement preventive programs for all women by combining risk-reducing skills for depression with child stimulation and nutrition skills. In Uganda, a combined 12-session group program to address maternal depression, child stimulation, and nutrition was effective in preventing depressive symptoms and enhancing children's cognitive and language development (Singla, Kumbakumba, and Aboud 2015).

COST-BENEFIT OF EARLY CHILDHOOD INTERVENTIONS

Recognition of the beneficial societal returns of investing in early childhood is increasing (Kilburn and Karoly 2008). Many of the interventions discussed in this chapter are cost-effective and cost information is available (further detail can be found in chapter 17 in this volume, Horton and Levin 2016). This section focuses on literature not covered elsewhere specific to psychosocial stimulation and maternal depression. Generally, cost analyses are more readily available on the benefits of preschool programs for children ages three years and older (Engle and others 2011); less information is available on the costs of early stimulation interventions for children younger than age two years. There may be several reasons for the meager available data on costs for early stimulation interventions; for example, Alderman and others (2014) highlight the many challenges in calculating cost-benefits of health and nutrition services with integrated early stimulation, including synergies between the fixed costs (existing costs linked to service delivery) and the additional costs of implementing the new intervention. A recent attempt at a cost and cost-effectiveness analysis points to the challenges that contribute to this lack of data on LMICs (Batura and others 2015). One challenge is that the follow-up is short, and outcomes do not focus on productivity.

One short-term cost-effectiveness analysis compared the costs and benefits of a nutrition education-plus-supplement package with one that counseled psychosocial stimulation (Gowani and others 2014). The former provided micronutrient fortification whereas the latter provided some play and book materials, costing approximately US\$4.50 per child per month (approximately US\$55¹ per year) using group and home visits. More psychosocial stimulation intervention studies need to conduct cost analyses, as do programs that combine nutrition and hygiene with stimulation and maternal mental health. One cost-benefit study analyzing labor market returns for

a Jamaica cohort studied by Grantham-McGregor and others (1991) finds that adults age 22 years who received early psychosocial stimulation earned 25 percent more than control counterparts (Gertler and others 2014).

Cash transfer or CCT programs that target the most economically disadvantaged families provide a delivery platform that shows promising returns to investment in short- and medium-term outcomes. The two Colombian studies described in this chapter (box 13.1) showing benefits to children who received home visits or home-based group care under three years of age estimated a cost per child of US\$516 per year (Attanasio and others 2014) and US\$347 per 16 months (Bernal and Fernandez 2013). Evaluations of large-scale and long-running programs in Ecuador (Fernald and Hidrobo 2011; Paxson and Schady 2010), Mexico (Fernald, Gertler, and Neufeld 2008), and Nicaragua (Macours, Schady, and Vakis 2012) have demonstrated benefits to child outcomes in the preschool years. Cash transfers of US\$70 monthly, for example, are linked to conditions such as attending health clinics, providing good nutrition, and school enrollment (Fernald, Gertler, and Neufeld 2008). Evaluations of CCT programs show that benefits are greater for the poorest children. Two pathways have been proposed to explain how CCT programs result in benefits to children's development. First, families might invest more in better nutrition for young children and in learning and play materials. For example, mothers who received a cash transfer (non-conditional) in Ecuador were more likely to purchase a toy for their young children (Fernald and Hidrobo 2011). Second, reduced financial pressure and stress may lead to improved psychosocial well-being in the family, leading to improved early child care. These models are primarily from Latin America and the Caribbean, but hold promise for other regions.

CONCLUSIONS

The risk factors of greatest importance concern low-quality psychosocial stimulation at home; inadequate child nutrition; infections from environmental vectors, such as trachoma and malaria; and maternal nutrition and mental health during the first 1,000 days.

- **Psychosocial stimulation.** Programs to promote mental development through stimulation are very effective, especially if they use techniques of active learning to help parents and community paraprofessionals adopt the recommended practices.
- **Child nutrition.** The effects of macro- and micronutrients on development are increasingly clear as the

pathways through health, behavior, and brain development have been clarified.

- **Infectious illnesses.** Significant advances have been made in vaccines, preventive medications, and treatment; access remains a major obstacle. Further research is required to understand how repeated infections, particularly diarrheal illness, affect child nutrition and development outcomes.
- **Maternal nutrition.** Nutrients available to children from the pregnant and lactating mother are being examined. These include iodine, iron, and PUFA.
- **Maternal mental health.** Given the high levels of depressive symptoms among mothers of young children beyond the postnatal period, mental health can no longer be neglected in health and development services. Effective strategies are likely to benefit all mothers with young children in these settings.

Recommendations for future directions include the following:

- Government, community-based, and private organizations can adopt and adapt successful context-specific programs that address four or five critical practices related to stimulation, nutrition, hygiene, and maternal care. Evaluations of outcomes, acceptability, costs, and task-sharing among personnel can clarify whether there are benefits to integrating services.
- Program planners and implementers can adopt a social-ecological approach that improves access to food, a clean environment, and availability of play materials, as well as promotes parent practices that support child development.
- Programs can incorporate a multimode communication strategy of supportive practices so they are seen as normative and approved by respected authorities. The communication modes could include community groups, home visits, clinic visits, and mass media.
- Policy makers and partners can implement cost-effectiveness analyses in LMICs.
- Researchers and other stakeholders can develop and provide advocacy materials for effective programs and disseminate them to government officials, policy makers, health and education professionals, media, and civil society organizations.

NOTE

World Bank Income Classifications as of July 2014 are as follows, based on estimates of gross national income (GNI) per capita for 2013:

- Low-income countries (LICs) = US\$1,045 or less

- Middle-income countries (MICs) are subdivided:
 - a) lower-middle-income = US\$1,046 to US\$4,125
 - b) upper-middle-income (UMICs) = US\$4,126 to US \$12,745
 - High-income countries (HICs) = US\$12,746 or more.
1. For comparability across chapters, we present economic data in U.S. dollars, adjusted to 2012.

REFERENCES

- Aboud, F. E. 2007. "Evaluation of an Early Childhood Parenting Program in Rural Bangladesh." *Journal of Health, Population and Nutrition* 25: 3–13.
- Aboud, F. E., and S. Akhter. 2011. "A Cluster Randomized Evaluation of a Responsive Stimulation and Feeding Intervention in Bangladesh." *Pediatrics* 127: e1191–97.
- Aboud, F. E., D. R. Singla, M. I. Nahil, and I. Borisova. 2013. "Effectiveness of a Parenting Program in Bangladesh to Address Early Childhood Health, Growth and Development." *Social Science and Medicine* 97: 250–58.
- Aboud, F. E., and A. K. Yousafzai. 2015. "Global Health and Development in Early Childhood." *Annual Review of Psychology* 66: 433–57.
- Abraham, N., R. Jewkes, R. Laubscher, and M. Hoffman. 2006. "Intimate Partner Violence: Prevalence and Risk Factors for Men in Cape Town, South Africa." *Violence and Victims* 21 (2): 247–64.
- Alaii, J. A., H. W. van den Borne, S. P. Kachur, H. Mwenesi, J. M. Vulule, and others. 2003. "Perceptions of Bed Nets and Malaria Prevention before and after a Randomized Controlled Trial of Permethrin-Treated Bed Nets in Western Kenya." *American Journal of Tropical Medicine and Hygiene* 68: 142–48.
- Alderman, H., J. R. Behrman, S. Grantham-McGregor, F. Lopez-Boo, and S. Urzua. 2014. "Economic Perspectives on Integrating Early Child Stimulation with Nutritional Interventions." *Annals of the New York Academy of Sciences* 1308: 129–38.
- Anderson, J. W., B. M. Johnson, and D. T. Remley. 1999. "Breast-Feeding and Cognitive Development: A Meta-Analysis." *American Journal of Clinical Nutrition* 70 (4): 525–35.
- Armah, G. E., S. O. Sow, R. F. Breiman, M. J. Dallas, M. D. Tapia, and others. 2010. "Efficacy of Pentavalent Rotavirus Vaccine against Severe Rotavirus Gastroenteritis in Infants in Developing Countries in Sub-Saharan Africa: A Randomised, Double-Blind, Placebo-Controlled Trial." *The Lancet* 376: 606–14.
- Attanasio, O. P., E. O. A. Fitzsimons, S. M. Grantham-McGregor, C. M. Douglas, and M. Rubo-Codina. 2014. "Using the Infrastructure of a Conditional Cash Transfer Program in Colombia: Cluster Randomized Controlled Trial." *British Medical Journal* 349: g5785.
- Bangirana, P., R. Idro, C. C. John, and M. J. Boivin. 2006. "Rehabilitation for Cognitive Impairments after Cerebral Malaria in African Children: Strategies and Limitations." *Tropical Medicine and International Health* 11 (9): 1341–49.

- Batura, N., Z. Hill, H. Haghparast-Bidgoli, R. Lingam, T. Colburn, and others. 2015. "Highlighting the Evidence Gap: How Cost Effective Are Interventions to Improve Early Childhood Nutrition and Development?" *Health Policy and Planning* 30 (6): 813–21. doi:10.1093/heapol/czu055.
- Bayley, N. 2006. *Bayley Scales of Infant Development Manual*. 3rd ed. Antonio, TX: The Psychological Corporation.
- Beard, J. L., M. K. Hendricks, E. M. Perez, L. E. Murray-Kolb, A. Berg, and others. 2005. "Maternal Iron Deficiency Anemia Affects Postpartum Emotions and Cognition." *Journal of Nutrition* 135: 265–72.
- Bernal, R., and C. Fernández. 2013. "Subsidized Child Care and Child Development in Colombia: Effects of *Hogares Comunitarios de Bienestar* as a Function of Timing and Length of Exposure." *Social Science and Medicine* 97: 241–49.
- Beyerlein, A., M. Hadders-Algra, K. Kennedy, M. Fewtrell, A. Singhal, and others. 2010. "Infant Formula Supplementation with Long-Chain Polyunsaturated Fatty Acids Has No Effect on Bayley Developmental Scores at 18 Months of Age—IPD Meta-Analysis of 4 Large Clinical Trials." *Journal of Pediatric Gastroenterology and Nutrition* 50 (1): 79–84.
- Bhutta, Z. A., J. K. Das, A. Rizvi, M. F. Gaffey, N. Walker, and others. 2013. "Evidence-Based Interventions for Improvement of Maternal and Child Nutrition: What Can Be Done and at What Cost?" *The Lancet* 382 (9890): 452–77.
- Black, M. M., A. H. Baqui, K. Zaman, S. W. McNary, K. Le, and others. 2007. "Depressive Symptoms among Rural Bangladeshi Mothers: Implications for Infant Development." *Journal of Child Psychology and Psychiatry* 48 (8): 764–72.
- Black, M. M., A. H. Baqui, K. Zaman, L. A. Persson, S. El Arifeen, and others. 2004. "Iron and Zinc Supplementation Promote Motor Development and Exploratory Behavior among Bangladeshi Infants." *American Journal of Clinical Nutrition* 80 (4): 903–10.
- Black, R. E., C. G. Victora, S. P. Walker, Z. A. Bhutta, P. Christian, and others. 2013. "Maternal and Child Undernutrition and Overweight in Low-Income and Middle-Income Countries." *The Lancet* 382 (9890): 427–51.
- Blencowe, H., A. C. C. Lee, S. Cousens, A. Bahalim, R. Narwal, and others. 2013. "Preterm Birth-Associated Neurodevelopmental Impairment Estimates at Regional and Global Levels for 2010." *Pediatric Research* 74 (Suppl. 1): 17–34.
- Boivin, M. J., P. Bangirana, J. Byarugaba, R. O. Opoka, R. Idro, and others. 2007. "Cognitive Impairment after Cerebral Malaria in Children: A Prospective Study." *Pediatrics* 119 (2): e360–66.
- Boivin, M. J., P. Bangirana, N. Nakasujja, C. F. Page, C. Shohet, and others. 2013. "A Year-Long Caregiver Training Program to Improve Neurocognition in Preschool Ugandan HIV-Exposed Children." *Journal of Developmental and Behavioral Pediatrics* 34 (4): 269–78.
- Bornstein, M. H., and D. L. Putnick. 2012. "Cognitive and Socioemotional Caregiving in Developing Countries." *Child Development* 83 (1): 46–61.
- Bougma, K., F. E. Aboud, K. B. Harding, and G. S. Marquis. 2013. "Iodine and Mental Development of Children 5 Years Old and Under: A Systematic Review and Meta-Analysis." *Nutrients* 5 (4): 1384–416.
- Bougma, K., G. S. Marquis, F. E. Aboud, H. Mohammed, D. Singla, and others. 2014. "Iodine and Other Nutritional Predictors of Infant and Preschoolers' Development: Results from a Cluster Randomized Trial in Ethiopia." Micronutrient Forum Conference, Addis Ababa, June 5.
- Bouhouch, R. R., S. Bouhouch, M. Cherkaoui, A. Aboussad, S. Stinca, and others. 2014. "Direct Iodine Supplementation of Infants versus Supplementation of their Breastfeeding Mothers: A Double-Blind, Randomized, Placebo-Controlled Trial." *The Lancet Diabetes and Endocrinology* 2: 197–209.
- Boyle, M. H., Y. Racine, K. Georgiades, D. Snelling, S. Hong, and others. 2006. "The Influence of Economic Development Level, Household Wealth and Maternal Education on Child Health in the Developing World." *Social Science and Medicine* 63 (8): 2242–54.
- Bradley, R. H., and R. F. Corwyn. 2005. "Caring for Children around the World: A View from HOME." *International Journal of Behavioral Development* 29 (6): 468–78.
- Brazelton, T. B., and J. K. Nugent. 1995. *Neonatal Behavioral Assessment Scale*. 3rd ed. London: McKeith Press.
- Briscoe, C., and F. E. Aboud. 2012. "Behaviour Change Communication Targeting Four Health Behaviours in Developing Countries: A Review of Change Techniques." *Social Science and Medicine* 75 (4): 612–21.
- Brown, J. L., and E. Pollitt. 1996. "Malnutrition, Poverty and Intellectual Development." *Scientific American* 274 (2): 38–43.
- Chandran, M., P. Tharyan, J. Muliylil, and S. Abraham. 2002. "Post-Partum Depression in a Cohort of Women from a Rural Area of Tamil Nadu, India: Incidence and Risk Factors." *British Journal of Psychiatry* 181: 499–504.
- Checkley, W., G. Buckley, R. H. Gilman, A. M. O. Assis, R. L. Guerrant, and others. 2008. "Multi-Country Analysis of the Effects of Diarrhoea on Childhood Stunting." *International Journal of Epidemiology* 37 (4): 816–30.
- Christian, P., S. E. Lee, M. D. Angel, L. S. Adair, S. E. Aifeen, and others. 2013. "Risk of Childhood Undernutrition Related to Small-for-Gestational Age and Preterm Birth in Low- and Middle-Income Countries." *International Journal of Epidemiology* 42 (5): 1340–55.
- Cissé, B., C. Sokhna, D. Boulanger, J. Milet, E. H. Bâ, and others. 2006. "Seasonal Intermittent Preventive Treatment with Artesunate and Sulfadoxine-Pyrimethamine for Prevention of Malaria in Senegalese Children: A Randomised, Placebo-Controlled, Double-Blind Trial." *The Lancet* 367 (9511): 659–67.
- Cleland, J., and J. K. van Ginneken. 1988. "Maternal Education and Child Survival in Developing Countries: The Search for Pathways of Influence." *Social Science and Medicine* 27 (12): 1357–68.
- Colombo, J., S. E. Carlson, C. L. Cheatham, D. L. Shaddy, E. H. Kerling, and others. 2013. "Long-Term Effects of LCPUFA Supplementation on Childhood Cognitive Outcomes." *American Journal of Clinical Nutrition* 98 (2): 403–12.

- Cooper, P. J., M. Tomlinson, L. Swartz, M. Landman, C. Molteno, and others. 2009. "Improving Quality of Mother-Infant Relationship and Infant Attachment in Socioeconomically Deprived Community in South Africa: Randomised Controlled Trial." *British Medical Journal* 338: b974.
- Daelmans, B., K. Dewey, and M. Arimond. 2009. "New and Updated Indicators for Assessing Infant and Young Child Feeding." *Food and Nutrition Bulletin* 30 (2): S256–62.
- Dangour, A. D., L. Watson, O. Cumming, S. Boisson, Y. Che, and others. 2013. "Interventions to Improve Water Quality and Supply, Sanitation and Hygiene Practices, and Their Effects on the Nutritional Status of Children." *Cochrane Database of Systematic Reviews* 8: CD009382. doi:10.1002/14651858.
- Das, J. K., R. A. Salam, A. Imdad, and Z. A. Bhutta. 2016. "Infant and Young Child Growth." In *Disease Control Priorities* (third edition): Volume 2, *Reproductive, Maternal, Newborn, and Child Health*, edited by R. Black, R. Laxminarayan, M. Temmerman, and N. Walker. Washington, DC: World Bank.
- Dewey, K., and S. Adu-Afarwuah. 2008. "Systematic Review of the Efficacy and Effectiveness of Complementary Feeding Interventions in Developing Countries." *Maternal and Child Nutrition* 4 (Suppl. 1): 24–85.
- Eickmann, S. H., A. Lima, M. Guerra, M. Lima, P. Lira, and others. 2003. "Improved Cognitive and Motor Development in a Community-Based Intervention of Psychosocial Stimulation in Northeast Brazil." *Developmental Medicine and Child Neurology* 45 (8): 536–41.
- Ejemot, R., J. Ehiri, M. Meremikwu, and J. Critchley. 2008. "Hand Washing for Preventing Diarrhoea." *Cochrane Database Systematic Review* (1): CD004265.
- Engle, P. L., C. H. Fernald, J. R. Behrman, C. O'Gara, A. K. Yousafzai, and others. 2011. "Strategies for Reducing Inequalities and Improving Developmental Outcomes for Young Children in Low-Income and Middle-Income Countries." *The Lancet* 378 (9799): 1339–53.
- Faisal-Cury, A., J. J. A. Tedesco, S. Kahhale, P. R. Menezes, and M. Zugaib. 2003. "Postpartum Depression: In Relation to Life Events and Patterns of Coping." *Archives of Women Mental Health* 7: 123–31.
- Fernald, L. C. H., P. J. Gertler, and L. M. Neufeld. 2008. "Role of Cash in Conditional Cash Transfer Programmes for Child Health, Growth, and Development: An Analysis of Mexico's Oportunidades." *The Lancet* 371 (9615): 828–37.
- Fernald, L. C. H., and M. Hidrobo. 2011. "Effect of Ecuador's Cash Transfer Program (*Bono de Desarrollo Humano*) on Child Development in Infants and Toddlers: A Randomized Effectiveness Trial." *Social Science and Medicine* 72 (9): 1437–46.
- Fewtrell, L., R. B. Kaufmann, D. Kay, W. Enanoria, L. Haller, and others. 2005. "Water, Sanitation, and Hygiene Interventions to Reduce Diarrhoea in Less Developed Countries: A Systematic Review and Meta-Analysis." *The Lancet Infectious Diseases* 5 (1): 42–52.
- Filippi, V., D. Chou, C. Ronsmans, W. Graham, and L. Say. 2016. "Levels and Causes of Maternal Morbidity and Mortality." In *Disease Control Priorities* (third Edition): Volume 2, *Reproductive, Maternal, Newborn, and Child Health*, edited by R. Black, R. Laxminarayan, M. Temmerman, and N. Walker. Washington, DC: World Bank.
- Fischer Walker, C. L., L. Lamberti, L. Adair, R. L. Guerrant, A. G. Lescano, and others. 2012. "Does Childhood Diarrhea Influence Cognition beyond the Diarrhea-Stunting Pathway?" *PLoS One* 7 (10): e47908.
- Fisher, J., M. Cabral de Mello, V. Patel, A. Rahman, T. Tran, and others. 2012. "Prevalence and Determinants of Common Perinatal Mental Disorders in Women in Low- and Lower-Middle-Income Countries: A Systematic Review." *Bulletin of the World Health Organization* 90 (2): 139–49G.
- Gertler, P., J. Heckman, R. Pinto, A. Zanolini, C. Vermeersch, and others. 2014. "Labour Market Returns to an Early Childhood Stimulation Intervention in Jamaica." *Science* 344: 998–1001.
- Gies, S., S. O. Coulibaly, C. Ky, F. T. Ouattara, B. J. Brabin, and others. 2009. "Community-Based Promotional Campaign to Improve Uptake of Intermittent Preventive Antimalarial Treatment in Pregnancy in Burkina Faso." *American Journal of Tropical Medicine and Hygiene* 80 (3): 460–69.
- Gottlieb, C. A., M. J. Maenner, C. Cappa, and M. S. Durkin. 2009. "Child Disability Screening, Nutrition, and Early Learning in 18 Countries with Low and Middle Incomes: Data from the Third Round of UNICEF's Multiple Indicator Cluster Survey (2005–06)." *The Lancet* 374 (9704): 1831–39.
- Gowani, S., A. K. Yousafzai, R. Armstrong, and Z. A. Bhutta. 2014. "Cost Effectiveness of Responsive Stimulation and Nutrition Interventions on Early Child Development Outcomes in Pakistan." *Annals of the New York Academy of Sciences* 1308: 149–61.
- Grantham-McGregor, S. M., Y. Cheung, S. Cueto, P. Glewwe, L. Richter, and others. 2007. "Developmental Potential in the First 5 Years for Children in Developing Countries." *The Lancet* 369 (9555): 60–70.
- Grantham-McGregor, S. M., L. C. H. Fernald, R. M. C. Kagawa, and S. Walker. 2014. "Effects of Integrated Child Development and Nutrition Interventions on Child Development and Nutritional Status." *Annals of the New York Academy of Sciences* 1308: 1–22.
- Grantham-McGregor, S. M., C. A. Powell, S. P. Walker, and J. H. Himes. 1991. "Nutritional Supplementation, Psychosocial Stimulation, and Mental Development of Stunted Children: The Jamaican Study." *The Lancet* 338 (8758): 1–5.
- Griffiths, R., and M. Huntley. 1996. *GMDs 0-2. Griffiths Mental Development Scales-Revised: Birth to 2 Years*. Oxford: Hogrefe.
- Gurnida, D. A., A. M. Rowan, P. Idradinata, D. Muchtadi, and N. Sekarwa. 2012. "Association of Complex Lipids Containing Gangliosides with Cognitive Development of 6-Month-Old Infants." *Early Human Development* 88 (8): 595–601.
- Guxens, M., M. A. Mendez, C. Molto-Puigmarti, J. Julvez, R. Garcia-Esteban, and others. 2011. "Breastfeeding, Long-Chain Polyunsaturated Fatty Acids in Colostrum, and Infant Mental Development." *Pediatrics* 128 (4): e880.
- Haider, B. A., and Z. A. Bhutta. 2012. "Multiple-Micronutrient Supplementation for Women during Pregnancy." *Cochrane Database of Systematic Reviews* 11: CD004905. doi:10.1002/14651858.CD004905.pub3.

- Hamadani, J. D., S. M. Grantham-McGregor, F. Tofail, B. Nermell, B. Fangstrom, and others. 2010. "Pre- and Postnatal Arsenic Exposure and Child Development at 18 Months of Age: A Cohort Study in Rural Bangladesh." *International Journal of Epidemiology* 39 (5): 1206–16.
- Hamadani, J. D., F. Tofail, T. Cole, and S. Grantham-McGregor. 2013. "The Relation between Age of Attainment of Motor Milestones and Future Cognitive and Motor Development in Bangladeshi Children." *Maternal and Child Nutrition* 9 (Suppl. 1): 89–104.
- Hamadani, J. D., F. Tofail, A. Hilaly, S. N. Huda, P. Engle, and others. 2010. "Use of Family Care Indicators and Their Relationship with Child Development in Bangladesh." *Journal of Health, Population and Nutrition* 28 (1): 23–33.
- Hamadani, J. D., F. Tofail, A. Hilaly, F. Mehrin, S. Shiraji, and others. 2012. "Association of Postpartum Maternal Morbidities with Children's Mental, Psychomotor and Language Development in Rural Bangladesh." *Journal of Health, Population, and Nutrition* 30 (2): 193–204.
- Hamadani, J. D., F. Tofail, B. Nermell, R. Gardner, S. Shiraji, and others. 2011. "Critical Windows of Exposure for Arsenic-Associated Impairment of Cognitive Function in Pre-School Girls and Boys: A Population-Based Cohort Study." *International Journal of Epidemiology* 40 (6): 1593–604.
- Harpham, T., S. Huttly, M. J. De Silva, and T. Abramsky. 2005. "Maternal Mental Health and Child Nutritional Status in Four Developing Countries." *Journal of Epidemiology and Community Health* 59: 1060–64.
- Horton, S., and C. Levin. 2016. "Cost-Effectiveness of Interventions for Reproductive, Maternal, Neonatal, and Child Health." In *Disease Control Priorities* (third edition): Volume 2, *Reproductive, Maternal, Newborn, and Child Health*, edited by R. Black, R. Laxminarayan, M. Temmerman, and N. Walker. Washington, DC: World Bank.
- Huda, S. N., S. M. Grantham-McGregor, and A. Tomkins. 2001. "Cognitive and Motor Functions of Iodine-Deficient but Euthyroid Children in Bangladesh Do Not Benefit from Iodized Poppy Seed Oil." *Journal of Nutrition* 131 (1): 72–77.
- Huda, T. M. N., L. Unicomb, R. B. Johnston, A. K. Halder, M. A. Y. Sharker, and others. 2012. "Interim Evaluation of a Large Scale Sanitation, Hygiene and Water Improvement Programme on Childhood Diarrhea and Respiratory Disease in Rural Bangladesh." *Social Science and Medicine* 75 (4): 604–11.
- Humphrey, J. H. 2009. "Child Undernutrition, Tropical Enteropathy, Toilets, and Handwashing." *The Lancet* 374: 1032–35.
- Hutton, G., and C. Chase. Forthcoming. "Water and Sanitation." In *Disease Control Priorities* (third edition): Volume 7, *Injury Prevention and Environmental Health*, edited by C. N. Mock, R. Nugent, and O. Kobusingye. Washington, DC: World Bank.
- Iannotti, L. L., C. K. Lutter, D. A. Bunn, and C. P. Stewart. 2014. "Eggs: The Uncracked Potential for Improving Maternal and Young Child Nutrition among the World's Poor." *Nutrition Reviews* 72 (6): 355–68.
- Imdad, A., M. Y. Yakoob, and Z. A. Bhutta. 2011. "Impact of Maternal Education about Complementary Feeding and Provision of Complementary Foods on Child Growth in Developing Countries." *BMC Public Health* 11 (Suppl. 3): S25.
- Isabella, R. A. 1993. "Origins of Attachment: Maternal Interactive Behavior across the First Year." *Child Development* 64 (2): 605–21.
- Jiang, N. M., F. Tofail, S. N. Moonah, R. J. Scharf, M. Taniuchi, and others. 2014. "Febrile Illness and Pro-Inflammatory Cytokines Are Associated with Lower Neurodevelopmental Scores in Bangladeshi Infants Living in Poverty." *BMC Pediatrics* 14: 50.
- Jin, X., Y. Su, F. Jiang, J. Ma, C. Morgan, and X. Shen. 2007. "'Care for Development' Intervention in Rural China: A Prospective Follow-Up Study." *Journal of Developmental and Behavioral Pediatrics* 28 (3): 213–18.
- John, C. C., P. Bangirana, J. Byarugaba, R. O. Opoka, R. Idro, and others. 2008. "Cerebral Malaria in Children Is Associated with Long-Term Cognitive Impairment." *Pediatrics* 122 (1): e92–99.
- Jones, A. D., B. I. Scott, L. E. Smith, M. M. N. Mbuya, B. Chasekwa, and others. 2014. "World Health Organization Infant and Young Child Feeding Indicators and their Associations with Child Anthropometry: A Synthesis of Recent Findings." *Maternal and Child Nutrition* 10 (1): 1–17.
- Kariger, P., E. A. Frongillo, P. Engle, P. M. Rebello Britto, S. M. Sywulka, and others. 2012. "Indicators of Family Care for Development for Use in Multicountry Surveys." *Journal of Health, Population and Nutrition* 30 (4): 472–86.
- Keusch, G. T., C. Fischer Walker, J. K. Das, S. Horton, and D. Habte. 2016. "Diarrheal Diseases." In *Disease Control Priorities* (third edition): Volume 2, *Reproductive, Maternal, Newborn, and Child Health*, edited by R. Black, R. Laxminarayan, M. Temmerman, and N. Walker. Washington, DC: World Bank.
- Khan, N. Z., H. Muslima, M. Parveen, M. Bhattcharya, N. Begun, and others. 2009. "Neurodevelopmental Outcomes of Preterm Infants in Bangladesh." *Pediatrics* 118 (1): 280–89.
- Kilburn, R. M., and L. A. Karoly. 2008. *The Economics of Early Childhood Policy: What the Dismal Science Has to Say about Investing in Children*. Santa Monica, CA: RAND Cooperation.
- Kooistra, L., S. Crawford, A. L. van Baar, E. O. Brouwers, and V. J. Pop. 2006. "Neonatal Effects of Maternal Hypothyroxinemia during Early Pregnancy." *Pediatrics* 117 (1): 161–67.
- Kosek, M., C. Bern, and R. L. Guerrant. 2003. "The Global Burden of Diarrhoeal Disease, as Estimated from Studies Published between 1992 and 2000." *Bulletin of the World Health Organization* 81 (3): 197–204.
- Kramer, M. S., F. E. Aboud, E. Mironova, I. Vanilovich, R. W. Platt, and others. 2008. "Breastfeeding and Child Cognitive Development: New Evidence from a Large Randomized Trial." *Archives of General Psychiatry* 65 (5): 578–84.
- Kramer, M. S., B. Chalmers, E. D. Hodnett, Z. Sevkovskaya, I. Dzikovich, and others. 2001. "Promotion of Breastfeeding Intervention Trial (PROBIT): A Randomized Trial in the

- Republic of Belarus.” *Journal of the American Medical Association* 285 (4): 413–20.
- Larson, L. M., and A. K. Yousafzai. 2014. “Meta-Analyses of Nutrition and Stimulation Interventions: Effects on Child Development.” Micronutrient Forum Conference, Addis Ababa, June 2.
- Larson, L. M., and A. K. Yousafzai. Forthcoming. “A Meta-analysis of Nutrition Interventions on Mental Development of Children Under-Two in Low- and Middle-Income Countries.” *Maternal & Child Nutrition*.
- Lawn, J. E., H. Blencowe, S. Oza, D. You, A. C. C. Lee, and others. 2014. “Every Newborn: Progress, Priorities, and Potential beyond Survival.” *The Lancet* 384 (9938): 189–205.
- Lee, A. C. C., J. Katz, H. Blencowe, S. Cousens, N. Kozuki, and others. 2013. “National and Regional Estimates of Term and Preterm Babies Born Small for Gestational Age in 138 Low-Income and Middle-Income Countries in 2010.” *The Lancet Global Health* 1: e26–36.
- Lenters, L., K. Wazny, and Z. A. Bhutta. 2016. “Management of Severe and Moderate Acute Malnutrition in Children.” In *Disease Control Priorities* (third edition): Volume 2, *Reproductive, Maternal, Newborn, and Child Health*, edited by R. Black, R. Laxminarayan, M. Temmerman, and N. Walker. Washington, DC: World Bank.
- Lobel, M., D. L. Cannella, J. E. Graham, C. DeVincent, J. Schneider, and others. 2008. “Pregnancy-Specific Stress, Prenatal Health Behaviors, and Birth Outcomes.” *Health Psychology* 27 (5): 604–15.
- Lozoff, B., J. Beard, J. Connor, B. Felt, M. Georgieff, and others. 2006. “Long-Lasting Neural and Behavioral Effects of Iron Deficiency in Infancy.” *Nutrition Reviews* 64 (5): S34–43.
- Lozoff, B., G. M. Brittenham, A. W. Wolf, D. K. McClish, P. M. Kuhnert, and others. 1987. “Iron Deficiency Anemia and Iron Therapy Effects on Infant Developmental Test Performance.” *Pediatrics* 79 (6): 981–95.
- Lozoff, B., J. B. Smith, K. M. Clark, C. G. Perales, F. Rivera, and others. 2010. “Home Intervention Improves Cognitive and Social-Emotional Scores in Iron-Deficient Anemic Infants.” *Pediatrics* 126 (4): e884–94.
- Luby, S. P., C. Mendoza, B. H. Keswick, T. M. Chiller, and R. M. Hoekstra. 2008. “Difficulties in Bringing Point-of-Use Water Treatment to Scale in Rural Guatemala.” *American Journal of Tropical Medicine and Hygiene* 78 (3): 382–87.
- Ludermir, A. B., L. B. Schraiber, A. F. P. L. D’Oliveira, I. França-Junior, and H. A. Jansen. 2008. “Violence against Women by their Intimate Partner and Common Mental Disorders.” *Social Science and Medicine* 66 (4): 1008–18.
- Macete, E., P. Aide, J. J. Aponte, S. Sanz, I. Mandomando, and others. 2006. “Intermittent Preventive Treatment for Malaria Control Administered at the Time of Routine Vaccinations in Mozambican Infants: A Randomized, Placebo-Controlled Trial.” *Journal of Infectious Diseases* 194 (3): 276–85.
- Macours, K., N. Schady, and R. Vakis. 2012. “Cash Transfers, Behavioral Changes, and Cognitive Development in Early Childhood: Evidence from a Randomized Experiment.” *American Economic Journal: Applied Economics* 4 (2): 247–73.
- Manno, D., P. K. Kowa, H. K. Bwalya, J. Siame, S. Grantham-McGregor, and others. 2012. “Rich Micronutrient Fortification of Locally Produced Infant Food Does Not Improve Mental and Motor Development of Zambian Infants: A Randomized Controlled Trial.” *British Journal of Nutrition* 107: 556–66.
- Mariotti, S. P., D. Pascolini, and J. Rose-Nussbaumer. 2009. “Trachoma: Global Magnitude of a Preventable Cause of Blindness.” *British Journal of Ophthalmology* 93: 563–68.
- McKay, S., E. Gaudier, D. I. Campbell, A. M. Prentice, and R. Albers. 2010. “Environmental Enteropathy: New Targets for Nutritional Interventions.” *International Health* 2 (3): 172–80.
- Mecaskey, J. W., C. A. Knirsch, J. A. Kumaresan, and J. A. Cook. 2003. “The Possibility of Eliminating Blinding Trachoma.” *The Lancet Infectious Diseases* 3 (11): 728–34.
- Morrongiello, B. A., S. L. Schell, and S. Schmidt. 2010. “‘Please Keep an Eye on Your Younger Sister’: Sibling Supervision and Young Children’s Risk of Unintentional Injury.” *Injury Prevention* 16 (6): 398–402.
- Nair, M. C. K., E. Philip, G. B. Jeyaseelan, S. Mathews, and K. Padma. 2009. “Effect of Child Development Centre Model Early Stimulation among At-Risk Babies: A Randomized Controlled Trial.” *Indian Pediatrics* 46: s20–26.
- Neumann, C. G., S. P. Murphy, C. Gewa, M. Grillenberger, and N. O. Bwibo. 2007. “Meat Supplementation Improves Growth, Cognitive, and Behavioural Outcomes in Kenyan Children.” *Journal of Nutrition* 137 (4): 1119–23.
- Ngondi, J., A. Onsarigo, L. Adamu, I. Matende, S. Baba, and others. 2005. “The Epidemiology of Trachoma in Eastern Equatoria and Upper Nile States, Southern Sudan.” *Bulletin of the World Health Organization* 83 (12): 904–12.
- Ngure, F. M., B. M. Reid, J. H. Humphrey, M. N. Mbuya, G. Pelto, and others. 2014. “Water, Sanitation, and Hygiene (WASH), Environmental Enteropathy, Nutrition, and Early Child Development: Making the Links.” *Annals of the New York Academy of Sciences* 1308: 118–28.
- Ogden, S., and P. Emerson. 2012. “How Communities Can Control Trachoma without a Big Budget.” *Community Eye Health Journal* 25 (79 & 80): 80–81.
- Olney, D., P. Kariger, R. Stoltzfus, S. Khalfan, N. Ali, and others. 2009. “Development of Nutritionally At-Risk Young Children Is Predicted by Malaria, Anemia, and Stunting in Pemba, Zanzibar.” *Journal of Nutrition* 139 (4): 763–72.
- Oweye, O., F. Aina, and O. Morakinyo. 2006. “Risk Factors of Postpartum Depression and EPDS Scores in a Group of Nigerian Women.” *Tropical Doctor* 36 (2): 100–3.
- Pasricha, S.-R., E. Hayes, K. Kalumba, and B.-A. Biggs. 2013. “Effect of Daily Iron Supplementation on Health in Children Aged 4–23 Months: A Systematic Review and Meta-Analysis of Randomised Controlled Trials.” *The Lancet Global Health* 1 (2): e77–86.
- Patel, A. B., M. R. Mamtani, T. P. Thakre, and H. Kulkarni. 2006. “Association of Umbilical Cord Blood Lead with Neonatal Behaviour at Varying Levels of Exposure.” *Behavioral and Brain Functions* 2: 22. doi:10.1186/1744-9081-2-22.
- Patel, V., A. Rahman, K. S. Jacob, and M. Hughes. 2004. “Effect of Maternal Mental Health on Infant Growth in Low

- Income Countries: New Evidence from South Asia." *British Medical Journal* 328 (7443): 820–23.
- Paxson, C., and N. Schady. 2010. "Does Money Matter? The Effects of Cash Transfers on Child Health and Development in Rural Ecuador." *Economic Development and Cultural Change* 59 (1): 187–229.
- Peairson, S., A. M. B. Austin, C. N. de Aquino, and E. U. de Burró. 2008. "Cognitive Development and Home Environment of Rural Paraguayan Infants and Toddlers Participating in Pastoral del Niño, an Early Child Development Program." *Journal of Research in Childhood Education* 22 (4): 343–62.
- Persson, L. A., S. El Arifeen, E.-C. Ekstrom, K. M. Rasmussen, E. A. Frongillo, and others. 2012. "Effects of Prenatal Micronutrient and Daily Food Supplementation on Maternal Hemoglobin, Birth Weight, and Infant Mortality among Children in Bangladesh." *Journal of the American Medical Association* 307 (19): 2050–59.
- Platt, M. J. 2014. "Outcomes in Preterm Infants." *Public Health* 128 (5): 399–403. doi:10.1016/j.puhe.2014.03.010.
- Pollitt, E., C. Saco-Pollitt, M. A. Husaini, and J. Huang. 2000. "Effects of an Energy and Micronutrient Supplement on Mental Development and Behavior under Natural Conditions in Undernourished Children in Indonesia." *European Journal of Clinical Nutrition* 54: S80–90.
- Potterton, J., A. Stewart, P. Cooper, and P. Becker. 2010. "The Effect of a Basic Home Stimulation Programme on the Development of Young Children Infected with HIV." *Developmental Medicine and Child Neurology* 52 (6): 547–51.
- Prado, E. L., A. A. Abubakar, S. Abbeddou, E. Y. Jimenez, J. W. Somé, and others. 2014. "Extending the Developmental Milestones Checklist for Use in a Different Context in Sub-Saharan Africa." *Acta Paediatrica* 103 (4): 447–54.
- Prado, E. L., and K. G. Dewey. 2014. "Nutrition and Brain Development in Early Life." *Nutrition Reviews* 72 (4): 267–84.
- Qawasmi, A., A. Landeros-Weisenberger, J. F. Leckman, and M. H. Bloch. 2012. "Meta-Analysis of Long-Chain Polyunsaturated Fatty Acid Supplementation of Formula and Infant Cognition." *Pediatrics* 129 (6): 1141–49.
- Rahman, A., J. Bunn, H. Lovel, and F. Creed. 2007. "Maternal Depression Increases Infant Risk of Diarrhoeal Illness: A Cohort Study." *Archives of Disease in Childhood* 92 (1): 24–28.
- Rahman, A., and F. Creed. 2007. "Outcome of Prenatal Depression and Risk Factors Associated with Persistence in the First Postnatal Year: Prospective Study from Rawalpindi, Pakistan." *Journal of Affective Disorders* 100 (1–3): 115–21.
- Rahman, A., Z. Iqbal, and R. Harrington. 2003. "Life Events, Social Support and Depression in Childbirth: Perspectives from a Rural Community in the Developing World." *Psychological Medicine* 33 (7): 1161–67.
- Rahman, A., A. Malik, S. Sikander, C. Roberts, and F. Creed. 2008. "Cognitive Behaviour Therapy-Based Intervention by Community Health Workers for Mothers with Depression and Their Infants in Rural Pakistan: A Cluster-Randomised Controlled Trial." *The Lancet* 372 (9642): 902–09.
- Rahman, A., M. Vahter, E.-C. Ekstrom, M. Rahman, A. H. Mustafa, and others. 2007. "Association of Arsenic Exposure during Pregnancy with Fetal Loss and Infant Death: A Cohort Study in Bangladesh." *American Journal of Epidemiology* 165 (12): 1389–96.
- Rosado, J. L., P. López, O. P. Garcia, J. Alatorre, and C. Alvarado. 2011. "Effectiveness of the Nutritional Supplement Used in the Mexican Oportunidades Programme on Growth, Anaemia, Morbidity and Cognitive Development in Children Aged 12–24 Months." *Public Health Nutrition* 14 (5): 931–37.
- Servili, C., G. Medhin, C. Hanlon, M. Tomlinson, B. Worku, and others. 2010. "Maternal Common Mental Disorders and Infant Development in Ethiopia: The P=MaMiE Birth Cohort." *BMC Public Health* 10: 693.
- Singla, D. R., E. Kumbakumba, and F. E. Aboud. 2015. "Effects of a Parenting Intervention to Address Both Maternal Psychological Wellbeing and Child Development and Growth in Rural Uganda: A Community-Based, Cluster-Randomised Trial." *The Lancet Global Health* 3 (8): e458–e469.
- Smithers, L. G., R. A. Gibson, A. McPhee, and M. Makrides. 2008. "Effect of Long-Chain Polyunsaturated Fatty Acid Supplementation of Preterm Infants on Disease Risk and Neurodevelopment: A Systematic Review of Randomized Controlled Trials." *American Journal of Clinical Nutrition* 87 (4): 912–20.
- Sroufe, L. A. 2005. "Attachment and Development: A Prospective, Longitudinal Study from Birth to Adulthood." *Attachment and Human Development* 7 (4): 349–67.
- Stevens, G., M. Finucane, and C. Paciorek. 2016. "Levels and Trends in Low Height-for-Age." In *Disease Control Priorities* (third edition): Volume 2, *Reproductive, Maternal, Newborn, and Child Health*, edited by R. Black, R. Laxminarayan, M. Temmerman, and N. Walker. Washington, DC: World Bank.
- Taylor-Robinson, D., A. Jones, and P. Garner. 2007. "Deworming Drugs for Treating Soil-Transmitted Intestinal Worms in Children: Effects on Growth and School Performance (Review)." *Cochrane Database of Systematic Reviews* 4: CD000371.
- Tofail, F., J. D. Hamadani, A. Z. T. Ahmed, F. Mehrin, M. Hakin, and others. 2012. "The Mental Development and Behavior of Low-Birth-Weight Bangladeshi Infants from an Urban Low-Income Community." *European Journal of Clinical Nutrition* 66 (2): 237–43.
- Tofail, F., J. D. Hamadani, F. Mehrin, D. A. Ridout, S. N. Huda, and others. 2013. "Psychosocial Stimulation Benefits Development in Nonanemic Children but Not in Anemic, Iron-Deficient Children." *Journal of Nutrition* 143 (6): 885–93.
- Tofail, F., I. Kabir, J. D. Hamadani, F. Chowdhury, S. Yesmin, and others. 2006. "Supplementation of Fish-Oil and Soy-Oil during Pregnancy and Psychomotor Development of Infants." *Journal of Health, Population and Nutrition* 24 (1): 48–56.
- Tofail, F., L. A. Persson, S. E. Arifeen, J. D. Hamadani, F. Mehrin, and others. 2008. "Effects of Prenatal Food and

- Micronutrient Supplementation on Infant Development: A Randomized Trial from the Maternal and Infant Nutrition Interventions, Matlab (MINIMat) Study." *American Journal of Clinical Nutrition* 87 (3): 704–11.
- Tomlinson, M., A. Rahman, D. Sanders, J. Maselko, and M. J. Rotheram-Borus. 2014. "Leveraging Paraprofessionals and Family Strengths to Improve Coverage and Penetration of Nutrition and Early Child Development Services." *Annals of the New York Academy of Sciences* 1308: 162–72.
- UNICEF (United Nations Children's Fund). 2013. *The State of the World's Children*. New York: UNICEF.
- and WHO (World Health Organization). 2009. *Care for Child Development*. New York: UNICEF and WHO.
- Valenzuela, M. 1990. "Attachment in Chronically Underweight Young Children." *Child Development* 61 (6): 1984–96.
- van den Briel, T., C. E. West, N. Bleichrodt, F. J. R. van de Vijver, E. A. Ategbo, and others. 2000. "Improved Iodine Status Is Associated with Improved Mental Performance of Schoolchildren in Benin." *American Journal of Clinical Nutrition* 72 (5): 1179–85.
- Vazir, S., P. Engle, N. Balakrishna, P. L. Griffiths, S. L. Johnson, and others. 2013. "Cluster-Randomized Trial on Complementary and Responsive Feeding Education to Caregivers Found Improved Dietary Intake, Growth and Development among Rural Indian Toddlers." *Maternal and Child Nutrition* 9 (1): 99–117.
- Victora, C. G., M. de Onis, and P. C. Hallal. 2010. "Worldwide Timing of Growth Faltering: Revisiting Implications for Interventions Using the World Health Organization Growth Standards." *Pediatrics* 125 (3): e473–80.
- Walker, S. P., S. Chang, C. Powell, and S. M. Grantham-McGregor. 2004. "Psychosocial Intervention Improves the Development of Term Low Birth Weight Infants." *Journal of Nutrition* 134 (6): 1417–23.
- Walker, S. P., T. D. Wachs, S. Grantham-McGregor, M. M. Black, C. A. Nelson, and others. 2011. "Inequality in Early Childhood: Risk and Protective Factors for Early Child Development." *The Lancet* 378 (9799): 1325–38.
- Weisz, A. J., M. J. Manary, K. Stephenson, S. Agapova, F. G. Manary, and others. 2012. "Abnormal Gut Integrity Is Associated with Reduced Linear Growth in Rural Malawian Children." *Journal of Pediatric Gastroenterology and Nutrition* 55 (6): 747–50.
- Weobong, B., B. Akpalu, V. Doku, S. Owusu-Agyei, L. Hurt, and others. 2009. "The Comparative Validity of Screening Scales for Postnatal Common Mental Disorder in Kintampo Ghana." *Journal of Affective Disorders* 113 (1–2): 109–17.
- Werker, J. F., and T. K. Hensch. 2015. "Critical Periods in Speech Perception: New Directions." *Annual Review of Psychology* 66: 173–96.
- Williams, P., U. Piamjariyakul, A. Williams, P. Hornboonherm, P. Meena, and others. 2003. "Thai Mothers and Children and the HOME Observation for Measurement of the Environment (Home Inventory): Pilot Study." *International Journal of Nursing Studies* 40 (3): 249–58.
- Yousafzai, A. K., P. Lynch, and M. Gladstone. 2014. "Moving beyond Prevalence Studies: Screening and Interventions for Children with Disabilities in Low- and Middle-Income Countries." *Archives of Disease in Childhood* 99 (9): 840–48. doi:10.1136/archdischild-2012-302066.
- Yousafzai, A. K., M. A. Rasheed, A. Rizvi, R. Armstrong, and Z. A. Bhutta. 2014. "Effect of Integrated Responsive Stimulation and Nutrition Interventions in the Lady Health Worker Programme in Pakistan on Child Development, Growth, and Health Outcomes: A Cluster Randomized Factorial Effectiveness Trial." *The Lancet* 384 (9950): 1282–93. doi:10.1016/S0140-6736(14)60455-4.
- Zimmermann, M. B. 2012. "The Effects of Iodine Deficiency in Pregnancy and Infancy." *Paediatric and Perinatal Epidemiology* 26 (Suppl. 1): 108–17.
- , P. L. Jooste, and C. S. Pandav. 2008. "Iodine-Deficiency Disorders." *The Lancet* 372 (9645): 1251–62.