

Chapter 13. Very Early Childhood Development

Frances E. Aboud and Aisha K. Yousafzai

Frances E. Aboud, McGill University, Department of Psychology, 1205 Dr. Penfield Avenue, Montreal, Canada. frances.aboud@mcgill.ca

Aisha K. Yousafzai, Aga Khan University, Department of Paediatrics and Child Health, Stadium Road PO Box 3500, Karachi, Pakistan.

Abstract

The review examines prenatal and postnatal conditions that contribute to the failure of 39 percent of children to reach their developmental potential, specifically, cognitive and language development. The evidence shows the negative effects of inadequate psychosocial stimulation, prenatal and postnatal nutrition, brain injuries caused by cerebral malaria and birth asphyxia, contaminated environments, and maternal depression. Because adverse conditions co-occur, integrated interventions are needed. We referred to systematic reviews and meta-analyses to highlight the effectiveness of *development-specific interventions*, such as psychosocial stimulation, child nutrition and disease reduction, as well as *development-sensitive interventions*, such as maternal nutrition and mental health.

Keywords: cognitive development, child health, nutrition, psychosocial stimulation, first 1000 days, parenting interventions

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I. 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 does not attain this potential (Grantham-McGregor and others 2007).

The main impetus to give prominent attention to mental development from conception through to 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. Re-generating 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 a secure emotional attachment to an adult will have difficulty coping with stresses and challenges throughout life.

A second impetus to attend 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; educated mothers 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).

This chapter discusses mental development from birth to 24 months of age in low- and middle-income countries (LMICs). Although we focus on cognitive and language domains, we touch on socio-emotional, 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.

II. Prevalence and Measurement: What Does Mental Development Entail at this Age?

In the absence of well-validated indicators, the Ten Questions Survey was used in 18 countries as part of the Multiple Indicator Cluster Survey 2005-06 (MICS3). It screens for disabilities by asking mothers of children ages two to nine 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 7.0 percent of children had a cognitive disability, and 21.0 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).

The mental competencies of children over 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 over 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 with standardized behavioral tests, such as the Bayley Scales of Infant and Toddler Development III (Bayley 2006) and the Griffith Developmental 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 and so is not addressed here (Hamadani and others 2013).

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 Scale includes items tapping personal-social skills, such as recognition of one's mother, enjoying playmates, and feeding and dressing oneself. The Bayley also includes 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. 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 appear to be less emotionally secure than well-nourished children (Valenzuela 1990). Social-environmental determinants of secure attachment during infancy have been identified as parental warmth and responsivity (Isabella 1993). Interventions to encourage warm and responsive mother-child interactions were successful in fostering secure attachments in children living in a deprived South African community (Cooper and others 2009).

III. Conditions that Impact Child Development

Many of the conditions that affect the health and growth of children in the first 1,000 days could impact mental development. These includes 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 incur.

A. 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 under 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. So the focus is on opportunities to play and converse in a way that stretches the child's thinking and understanding of speech. Scores on the HOME 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 they satisfied less than half to two-thirds of the items (see Figure 1.2). In all studies, there were very strong correlations between HOME scores and children's mental development, with low HOME scores associated with poor mental development.

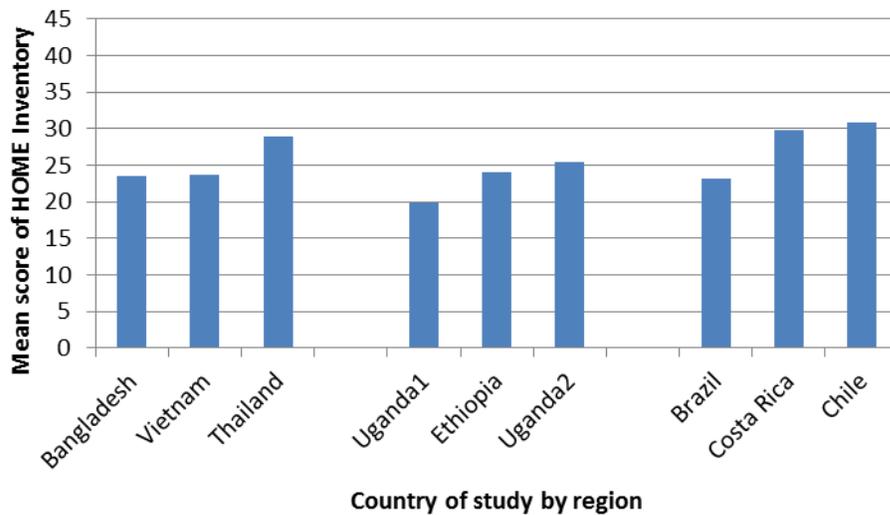


Figure x.1. Mean HOME Inventory Score and Study: *Bangladesh*- 23.5, Aboud & Akhter 2011 ; *Vietnam*- 23.6, Williams et al. 2003; *Thailand*- 28.9, Williams et al. 2003; *Uganda1*- 19.8, Boivin et al. 2013; *Ethiopia*- 24.0, Bougma 2014; *Uganda2*- 25.4, Singla et al. 2014; *Brazil*- 23.1, Eickmann et al. 2003; *Costa Rica*- 29.8, Lozoff et al. 1987; *Chile*- 30.8, Lozoff et al. 2010.

A brief version of the inventory called the Family Care Indicators is now available for use in national surveys. Consisting of 10 interview questions for the caregiver, it has been validated in South Asia and Africa (Hamadani, Tofail, and others 2010; Kariger and others 2012) and used to evaluate responsive and stimulating caregiving in 28 developing countries (Bornstein and Putnick 2012). Mothers (caregivers) were asked what they did with their children aged under 5 years in the past 3 days. Items largely focus on the variety of play materials available for the child (e.g. things for making music, things for pretending, things

for drawing) and play activities (e.g., read or look at pictures, tell stories, sing songs). Only 25% of mothers said they had read to their children in the past 3 days, 25% had sung songs, and 35% had told them stories. Scores did not vary by child's gender but were lower in families with more children. So, more children do 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 siblings are not able to deliver the sophisticated language of an adult or accurately perceive when a young child is in danger (Morrongiello, Schell, and Schmidt, 2010). Across all 28 developing countries surveyed, the average number of caregiving practices out of six performed in the past 3 days with a child under 5 years was 3.03. Many parents from countries in Africa and South Asia practiced only one or two. This is insufficient to support mental development.

Both the HOME Inventory and its briefer version are highly correlated with children's mental development, ranging from $r = 0.20$ to 0.46 (Aboud and others 2013; Boivin and others 2013; Hamadani and others 2010; Tofail and others 2012). Our framework (see Figure x.2) shows the theoretical pathways. One is that an adult's child-directed conversation directly 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 the child's current state, it is expected to expand the child's receptive language and grammar. This helps the child translate his/her 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 and weight, as well as problem solving. The material must be challenging so that the child has opportunities to construct the material in new ways.

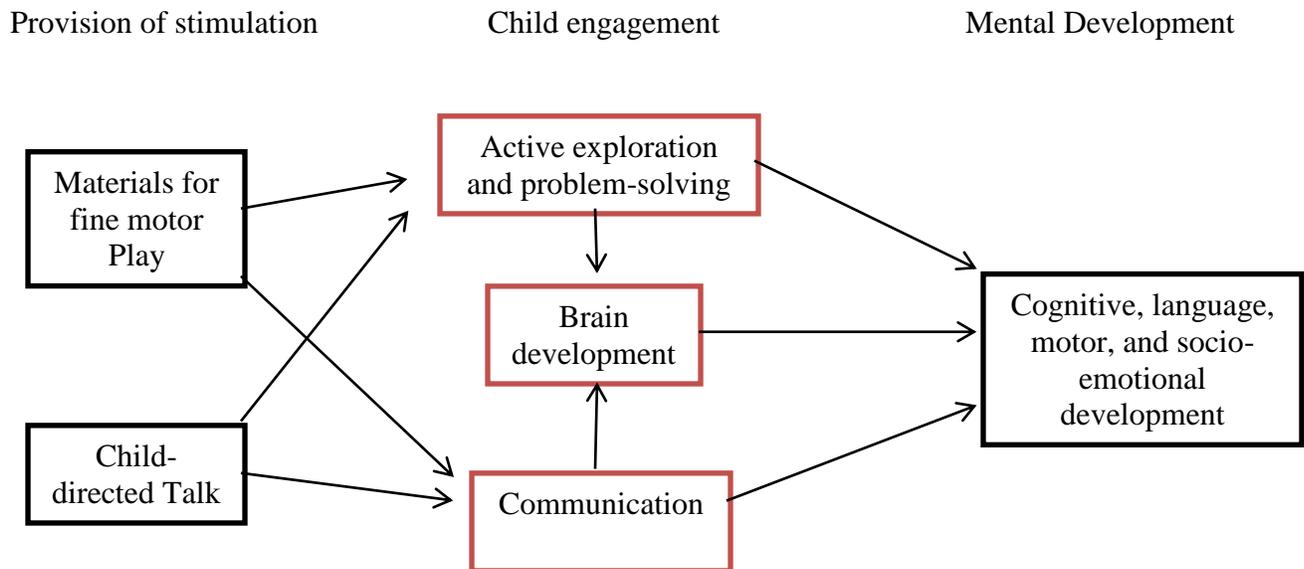


Figure x.2 Framework illustrating pathways from psychosocial stimulation to mental development (Larson and Yousafzai 2014).

B. 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, defined as more than 2.00 standard deviations below the age- and sex-specific norm, 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 x.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.

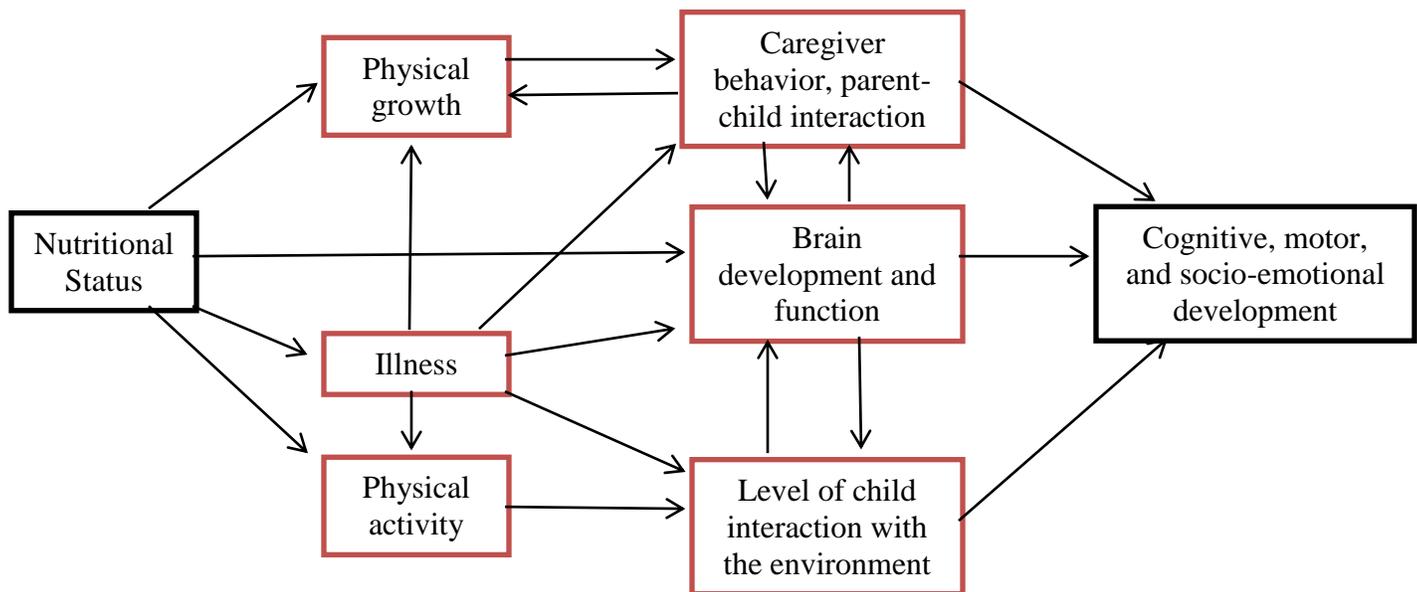


Figure __.3 Framework illustrating pathways from Nutritional Status to Mental Development

Source: Prado and Dewey 2014.

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). 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 where these data were analyzed (Jones and others 2014). Improving dietary diversity, especially with animal-source foods, is a critical message in nutrition education interventions. In eight studies, nutrition education alone for mothers of children ages six to 24 months, usually about foods to feed and number of meals, led to gains in length, with an effect size of $d = 0.21$ (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. Numerous studies have demonstrated high levels of anemia in young children, especially in South Asia and Sub-Saharan Africa, where 20 percent of children less 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 do not frequently improve their mental development scores. 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 under age 24 months (Zimmermann 2012; Zimmerman, Jooste, and Pandav 2008). Many countries lack naturally occurring iodine in the soil and water and so must fortify a product such as salt. Most of the data on prevalence has been collected from children ages six to 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 entire Asian population are iodine deficient (Black and others 2013). Four prospective studies found that mental development scores of children with inadequate iodine levels at birth were half a standard deviation below those with healthy levels (Bougma and others 2013); this translates into a development quotient difference of 8 points on a standard mental test—a meaningful difference.

Multiple Vitamin and Mineral Supplements

Multiple micronutrients now 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 where 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 will report 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 (~ 0.12), and better for energy alone (~0.25) and the provision of food with extra proteins and nutrients (~0.28) (Bhutta and others 2013; Dewey and Adu-Afarwuah 2008). The effect sizes for nutrition education were 0.20, especially those 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).

C. 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 (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 in the region of southern Sudan found that 64 percent of children ages one to nine years had active trachoma; 46.2 percent of infants had signs of active trachoma (Ngondi and others 2005). It 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 six and 24 months of age; children have on average four to five episodes a year (Kosek and others 2003). The most common source is the rotavirus, for which vaccines are being given to infants in many countries of Asia and Sub-Saharan Africa (Armah and others 2010). Other common sources are geohelminths and bacteria, such as cholera and *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).

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 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. One study found 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 (Jiang and others 2014). Although preliminary, it suggests a connection between inflammation and mental development. If enteropathy is as prevalent and severe as feared, it will require a serious reconsideration of how to eliminate sources of contamination in the environment, without restricting children's access to psychosocial stimulation around the home.

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. *Plasmodium falciparum*, in particular, is the parasite 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 to controls. For example, a prospective study with children ages five to nine

years in Kampala, Uganda, found 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 age six months and two-year follow-ups, compared to 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.

D. Maternal Nutrition

The optimum body mass index (BMI) for women at the start of pregnancy is 18.5 to 24 kg/m². In LMICs, over 10 percent of women are less than 18.5, with the highest rates 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 cm., 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 and/or short stature put their children at risk of being small-for-gestational-age (SGA). SGA, defined as having birthweight less than the 10th percentile for gestational age, includes newborns who are at term—37 to 40 weeks—but small—less than 2,500 gm at 37 weeks and less than 2,900 gm at 40 weeks, as well as those who are preterm and small. In 2010, an estimated 32.4 million newborns, 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 over the first month, the second hurdle is early neurodevelopmental disabilities (Blencowe and others 2013). These 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), indicated that approximately 7 percent showed mild or moderate-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-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 younger than 33 weeks found that 73 percent had mild or serious impairments

when tested under 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 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, 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 is linear growth restriction, an important determinant of mental development. SGA newborns have experienced fetal growth restriction and are unlikely to catch up due to 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, LBW children were almost three times more likely to be stunted (< -2.00 HAZ) than normal birth weight children, but this 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) found that at 10 months of age, LBW Bangladeshi infants, most of whom were term, had lower mental and motor Bayley scores than normal birthweight children, after controlling for a range of covariates, such as weight, length, and gestational age. Similarly, Walker and others (2004) found lower Griffiths scores at 15 and 24 months on cognitive and motor subscales for term-LBW Jamaican children compared to 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.

E. 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). A systematic review reported 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% and 13% respectively (Fisher and others 2012). Prevalence is higher in many South Asian countries, for example, in Pakistan, where one study reported 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 pre- and postpartum period, many researchers monitoring maternal depression for 24 months after birth and beyond found it to be high in South Asia and Sub-Saharan Africa, between 20 percent to 30 percent, using the 20-item Self-Reporting Questionnaire (Harpham and others 2005; Servili and others 2010; Weobong and others 2009).

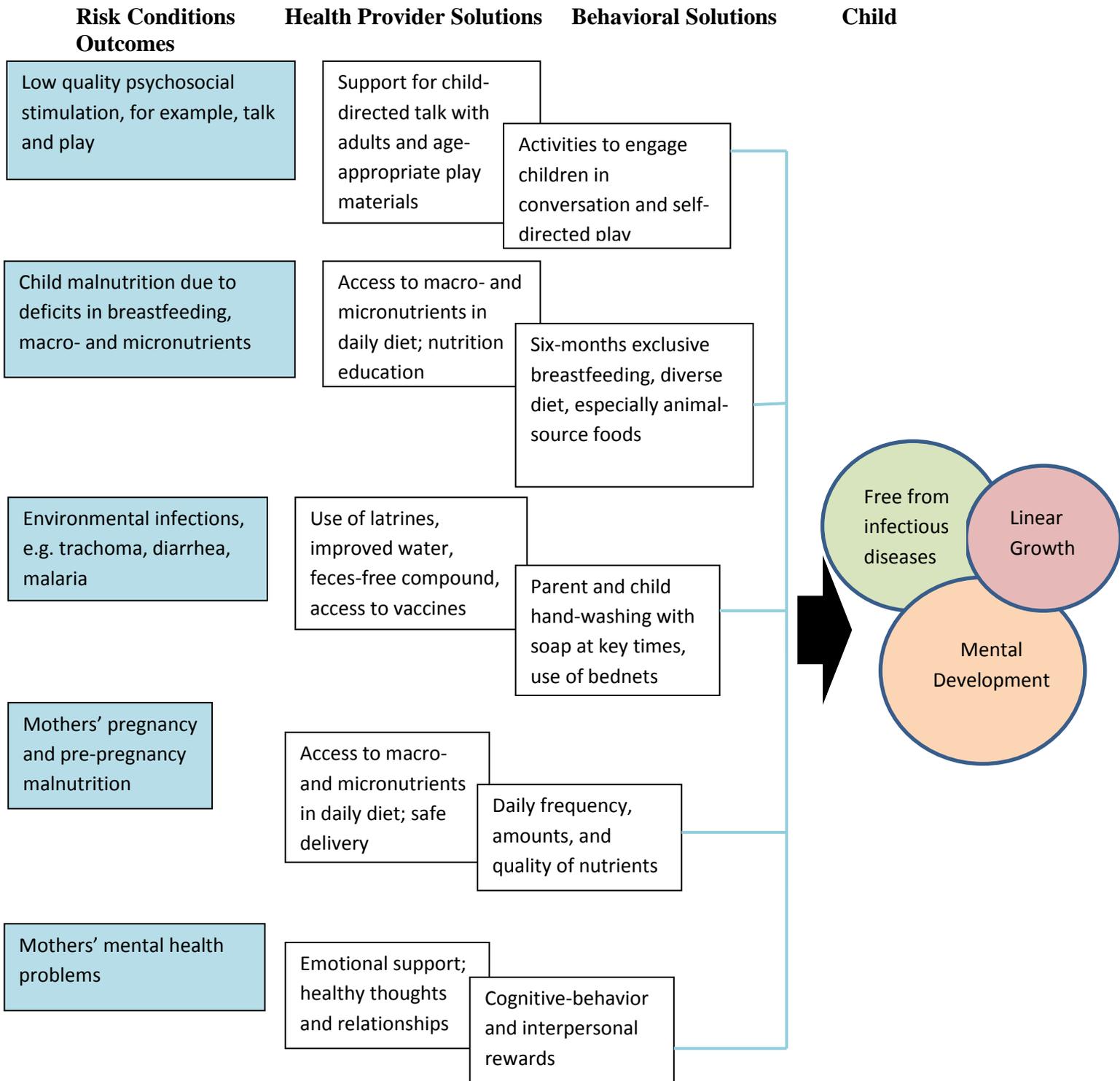
Important determinants of maternal mental health include intimate partner violence (Ludermir and others 2008), social support (Rahman and Creed 2007), the quality of her relationships with her husband (Oweye, Aina, and Morakinyo 2006) and other close relatives, such as in-laws (Chandran and others 2002), 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 non-depressed mothers (Rahman 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 (e.g. 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.

IV. Interventions to Enhance Mental Development

Despite questions about the outcome benefits of combining stimulation, nutrition, and hygiene components into one program, there appear to be cost, health system efficiency, and recipient-preference benefits. We consider each component's outcome (figure __.4), organizing them into development-specific interventions that focus on the child, and development-sensitive interventions that focus on the mother and might indirectly affect the child.

Figure x.4 Conditions That Put Children at Risk of Poor Mental Development, and Solutions Entailing Health Provider Support and Parental Behavior Changes



Source: Created for this chapter.

A. Development-Specific Interventions

1. 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 yielded 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. Three models of delivery have been implemented and evaluated (box __.1), but all require special training of professionals or para-professionals 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.

Box __.1 Three Models of Stimulation Program Delivery

Three delivery formats of home visits, group sessions, and clinic appointments are widely used. A fourth, combining group with home visits, has become increasingly common. Home visits entail weekly or fortnightly visits by a para-professional 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 had more than 24 visits over 12 months (Lozoff and others 2010; Tofail and others 2013; Vazir and others 2013).

Group sessions entailed meetings with eight to 20 mothers, and sometimes fathers, with their children at convenient locations in communities. Para-professionals from the community or local community health workers conducted the sessions. Group leaders demonstrated specific activities, coached mothers as they practiced with their children; groups could engage in discussions and general problem solving. Interventions based on group sessions usually were fewer in number (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 were addressed during group sessions, and family-specific problems were addressed during home visits. These combined interventions usually had more than 15 contacts over 12 or 24 months.

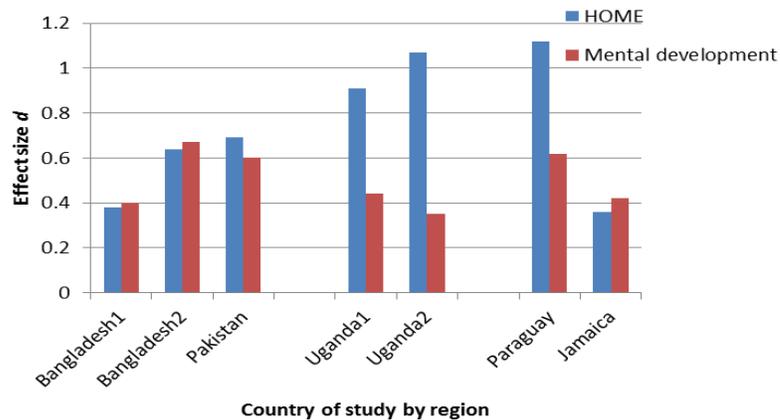
The final model uses well- or sick-baby clinic visits to inquire what mothers know about stimulating their children with toys and talk and counseling them on improved practices. This step is usually provided by professionals, sometimes with two to four contacts (Jin and others 2007; Potterton and others 2010) and sometimes with 12 monthly contacts (Nair and others 2009). All models of delivery require a curriculum manual for providers. Those employing para-professionals require more training and supervision. Group and clinic models explicitly aim to change parents' behavior, particularly the opportunities they provide for play and conversation.

<<end of box __.1>>

Changing behavior is difficult, and a recent review has identified 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 techniques of active learning, such as demonstrations; practicing with children and receiving coaching and feedback; identifying and solving problems to enacting the practice; providing visual reminders; and engaging social support from peers and family members. Actual changes to the 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 relation between changes to stimulation and mental development (figure x.5). Typically, changes are small though 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, have been successful in improving mental development. This success may be partly attributed to their effect on raising parental stimulation practices, which, in addition to linear growth, is one of the strongest correlates of mental development.

Figure x.5 HOME Effect Size, Mental Development Effect Size and Study



Sources: Prepared for the chapter

Bangladesh 1: HOME 0.38, Mental Development 0.40, Aboud and Akhter 2011;
Bangladesh 2: HOME 0.64, Mental Development 0.67, Aboud and others 2013;
Pakistan: Home 0.69, Mental Development 0.60, Yousafzai and others 2014;
Uganda 1: HOME 0.91, Mental Development 0.44, Boivin and others 2013;
Uganda 2: HOME 1.07, Mental Development 0.35, Singla and others 2014;
Paraguay: HOME 1.12, Mental Development 0.62, Peairson 2008;

Jamaica: HOME 0.36, Mental Development 0.42, Walker and others 2004.

2. 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 upheld by a trial in Belarus, where half of the hospitals were randomly assigned to start the World Health Organization (WHO)-supported Baby-Friendly activities early. 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 high-income countries (HICs). Long-chain polyunsaturated fatty acids, which are present in the brain and breast milk, were considered 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 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 polyunsaturated fatty acids in colostrum and who were breastfed with greater intensity or duration had higher mental development scores (Guxens and others 2011). Thus although there are clear cognitive benefits to breastfeeding, the explanation appears to include high levels of n-3 PUFA and cumulative amounts of ingested breastmilk.

Research is being conducted on multiple micronutrients with and without lipids. Some studies use vitamin A as the baseline and compare it to 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 $d = 0.088$ (Larson and Yousafzai 2014). 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.

Researchers and program implementers are paying closer attention to optimizing integrated packages of stimulation and nutrition care given the independent and potential additive benefits to promote mental development. This is illustrated in the recently completed stimulation and nutrition trial in Pakistan.

Box __.2 Pakistan Early Child Development Scale-up Trial: Case Study of a Successful Program

The Pakistan Early Child Development Scale-up Trial (PEDS) was successful in enhancing 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 had clear benefits for parenting practices that improved mother-child interactions and the quality of home stimulation. Lady Health Workers (LHWs), who monthly 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 WHO, 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 strengthen 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 (MNP) for young children ages six to 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 that they 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. 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*. doi: 10.1016/S0140-6736(14)60455-4.

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.

<<end of box __.2>>

3. Reducing Infection Transmitted by Ground Contamination, Mosquitoes, and Flies

The most commonly implemented solutions to environmental causes of infection are constructing and using latrines, improved 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 seen an immediate reduction in diarrheal diseases (Fewtrell and others 2005). However, a 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 of 94 percent and 76 percent, respectively, is narrower. Concern about the effects of very high levels of arsenic in drinking water is supported by evidence of fetal loss and infant mortality (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 the rotavirus vaccine as part of the national immunization schedule has begun in over 35 countries, with support from the GAVI. 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 treatments 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. Trachoma elimination strategies also include hygiene (facewashing) and environmental management as part of their SAFE strategy (surgery and antibiotics are the first two) as the more sustainable approaches (Mecaskey and others 2003).

Environmental management of stagnant water is only one of the means to control malaria. The use of 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 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 due to 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; Luby and others 2008).

B. Development-Sensitive Interventions

1. 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 antimalarial treatment (Gies and others 2009) and maternal nutrition, respectively.

Raising birthweights 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 and/or energy-protein supplements 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 to 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 benefitting only those with low BMI mothers who received early energy-protein supplements (Tofail and others 2008). The non-significant findings of this study are supported by a preliminary meta-analysis of 10 RCT studies 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 2014). Many scientists conclude that providing nutrition supplements during pregnancy is too late to benefit significantly 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 studying 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 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 or children, improves the mental development of children. Careful scrutiny of RCTs in which school-aged children were given an iodine capsule or a placebo reveal 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.

2. 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 handful of evaluated interventions available suggests that alleviating maternal depression may help mothers to better meet their children's needs. In Pakistan, the Thinking Healthy program was developed using principles of cognitive-behavior therapy, although it also includes elements of interpersonal therapy. Cognitive-behavior 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 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, psychosocial stimulation, and nutrition was effective in reducing depression and enhancing children's cognitive and language development (Singla, Aboud, and Kumbakumba 2014).

V. Costs of Interventions

Recognition of the beneficial societal returns of investing in early childhood is increasing (Kilburn and Karoly 2008). 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 about the costs of early stimulation interventions for children younger than age two years. A recent attempt at a cost and cost-effectiveness analysis points to the challenges that contribute to this lack of data from LMICs (Batura and others 2014). One challenge is that the follow-up is short, and second outcomes do not focus on productivity. An exception has become a centerpiece in demonstrating long-term benefits. An analysis of labor market returns of the Jamaica cohort (Grantham-McGregor and others 1991) found a significant increase in earnings of

25 percent in adults ages 22 years who received early psychosocial stimulation compared with control counterparts (Gertler and others 2014).

A short-term cost effectiveness analysis of the Pakistan PEDS trial compared the costs and benefits of a nutrition education-plus-supplement package with one that counseled psychosocial stimulation (Gowani and others 2014). Both used Lady Health Workers from the health system but gave them extra training and supervision beyond the basic health package. The former provided micronutrient fortification while the latter provided some play and book materials, costing approximately US\$4.10 per child per month using group and home visits. The sensitivity analysis showed that the stimulation program was slightly more cost-effective, although combining nutrition with stimulation did not substantially add costs but could have extra benefits. More psychosocial stimulation intervention studies need to conduct cost analyses, as well as programs that combine nutrition and hygiene with stimulation and maternal mental health.

VI. Conclusions

The risk factors of greatest importance concern low quality psychosocial stimulation at home, child nutrition, infection from environmental vectors, such as trachoma and malaria, 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 employ techniques of active learning to help parents and community para-professionals adopt the recommended practices. The programs allow for an integration of a limited number of critical messages encouraging stimulation, as well as better nutrition, hygiene, and maternal well-being. Such integrated interventions are likely to include improved access and commitment to vaccines and bednets, as well as behavior changes with respect to handwashing, optimal feeding, and provision of stimulation. The components of a successful program are known; efforts are needed to adapt the various delivery modes—group, home, and clinic visits—to existing health and community platforms so that providers and parents work together to create healthy environments.
- **Child nutrition:** The effects of macro- and micronutrients on development are increasingly clear as the pathways through health, behavior, and brain development have been elucidated.
- **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, impact child nutrition and development outcomes.
- **Maternal nutrition:** A number of promising nutrients available to the child from the pregnant and lactating mother are still being examined. These include iodine, iron and polyunsaturated fatty acids
- **Maternal mental health:** Given the high prevalence of many social determinants of maternal mental health in LMICs, mental health can no longer be neglected in maternal,

newborn, and child 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:

1. 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.
2. The adoption by program planners and implementers of a social-ecological approach that improves access to food, a clean environment, and play materials, as well as parent practices that support child development.
3. The communication via multiple delivery modes—including community groups, home visits, clinic visits, and mass media—of supportive practices so they are seen as normative and approved by respected authorities.
4. The implementation of cost-effectiveness analyses in LMICs
5. The development and provision of advocacy materials for effective programs and their dissemination among government officials, policy makers, health and education professionals, media, and civil society organizations.

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