Fetal and Early Childhood Undernutrition, Mortality, and Lifelong Health
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Never breast-fed versus...full

Breast-feeding...inferred. A person-year is the sum of the number of years that each study participant...in the United States alone were recently estimated at $13 billion annually (5).

Child undernutrition is a broad and complex phenomenon, encompassing fetal undernutrition; insufficient breast-feeding; and complementary feeding of diets low in energy-dense foods, essential fatty acids, and micronutrients. The effects of undernutrition include low birth weight and deficits in height and weight, as well as physiological outcomes later in life. The importance of these factors prompted U.S. Secretary of State Hillary Clinton to describe the benefits of improved nutrition in utero and during the first 24 months of life as providing a valuable “1,000 day window of opportunity” for lifelong health and development (6).

Table 1. Breast-feeding and selected maternal health outcomes. CI, confidence interval. A person-year is the sum of the number of years that each study participant’s health condition was observed.

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Measure of breast-feeding</th>
<th>Effect size</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ovarian cancer</td>
<td>Length of breast-feeding</td>
<td>Reduced risk of ovarian cancer by 28%</td>
<td>Meta-analysis of nine studies with 4387 cancer ovarian cancer cases and 10,574 controls (32)</td>
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<tr>
<td></td>
<td></td>
<td>(odds ratio: 0.72; 95% CI: 0.54 to 0.97)</td>
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<tr>
<td>Breast cancer</td>
<td>Length of breast-feeding</td>
<td>Reduced risk of breast cancer by 4.3%</td>
<td>First meta-analysis included 45 studies conducted through 2001; second meta-analysis included 23 studies published between 1980 and 1998 (32)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(odds ratio: 0.61; 95% CI: 0.45 to 0.84)</td>
<td></td>
</tr>
<tr>
<td>Type 2 diabetes</td>
<td>Length of breast-feeding</td>
<td>Reduced diabetes risk by 4%; 95% CI: 1 to 9%</td>
<td>Two cohorts from a high-quality longitudinal study of 150,000 parous women in the U.S. (32)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>per year of breast-feeding in first cohort and 12%; CI: 6 to 18% in second cohort</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>Never breast-fed versus</td>
<td>Increased risk of hypertension by 29%</td>
<td>55,636 parous women in the U.S., reported 8861 cases during 660,880 person-years of observations (30)</td>
</tr>
<tr>
<td></td>
<td>exclusively breast-fed</td>
<td>(hazard ratio: 1.29; 95% CI: 1.20 to 1.40)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>first child for ≥6 months</td>
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At the risk of oversimplifying the topic, we review the recent and growing evidence of benefits of early nutrition, particularly breast-feeding, on child mortality and maternal and child health outcomes. We endeavor to distinguish between effects reported in low- and high-income countries, as these effects and the success of interventions may differ with diet and general sanitary conditions. Our review covers research in low- and high-income countries, including observational, case control, prospective cohort, and randomized studies. Our survey indicates there is credible evidence that improved population coverage of child nutrition interventions, particularly related to breast-feeding and complementary feeding, could provide large benefits in absolute terms and that these measures could do so at exceptionally low cost. However, public health funding for child nutrition research and programs is still relatively low compared with that for other life-saving child health interventions (7).

Here, we present evidence for benefits, an economic rationale for government intervention in breast-feeding, and a review of breast-feeding practices and policies. The rest of this paper addresses the early nutritional origins of disease, effective nutrition interventions in the first 1000 days, breast-feeding and NCD risk, the economic rationale for breast-feeding promotion, data on current breast-feeding and complementary feeding practices, and, finally, conclusions.

Early Nutritional Origins of Disease

The past few decades have seen an explosion of research suggesting that nutrition insults during fetal life have surprising and long-lasting ramifications for health (8, 9). Analysis of such effects is complicated by the lack of accepted measures of in utero exposure, the difficulty separating in utero exposure from exposure during infancy or early childhood, and the possibility of effects sufficiently severe to increase perinatal mortality, thus masking later adverse effects (10). Researchers have addressed these complications by focusing on “natural experiments” such as the Dutch Hunger Winter (resulting from severe wartime food shortages during the winter of 1944–1945) and religious fasts—episodes for which earlier or later cohorts provide suitable controls.

Effects of prenatal exposure to the Dutch Hunger Winter include obesity among 19-year-old men, fat deposition for women, schizophrenia, and elevated blood pressure (10). Prenatal exposure to daytime fasting during Ramadan has been reported to increase the likelihood of adult disability by more than 20% among Iraqis and Uganda’s Muslims, with substantially larger effects for mental and learning disabilities (10). One study considered effects of dietary supplementation with iodine during pregnancy in Tanzania—iodine deficiencies can cause low IQ scores. Before the advent of iodized salt, maternal iodine deficiency was the leading preventable cause of mental retardation globally. After accounting for differences in uptake among families, girls who received iodine supplementation in utero were found to have had about an extra 6 months of schooling relative to siblings, even though their health was apparently unaffected (11).

All of these estimates should be seen as illustrative of how nutrition in utero affects long-term health and even schooling, rather than as concrete, quantitative estimates. One reason for this caution is that the biological effects of in utero and early childhood nutritional insults depend on their precise nature, severity, and timing during development. In addition, the effects also probably vary with later diet, physical activity, and genetic predisposition. Another reason for caution is that nonhealth outcomes, such as years of schooling, also depend on how families treat children who may be subtly different, and this probably varies with differences in culture or economic opportunities. Regardless, a growing amount of literature shows that fetal undernutrition, as reflected in size at birth, has been associated with a host of chronic diseases later in life, including coronary heart disease, diabetes, and hypertension (8). Such risks are exacerbated when infants grow up in environments where metabolic disorders are prevalent.

Ongoing prospective cohort studies in Brazil, Guatemala, India, the Philippines, and South Africa show that size at birth and accelerated weight gain after 48 months of life is related to insulin resistance (12), whereas greater weight gain during the first 5 years is associated with elevated blood pressure (13). These damaging effects are more pronounced if children become overweight during later childhood and adolescence. The damaging effects of undernutrition are associated with a wide range of lifetime prospects. For example, among Guatemalan boys living in villages where severe stunting was prevalent, random assignment of infants to high-quality dietary supplementation in the first 2 years of life led to a 46% increase in average wages in adulthood (14). Furthermore, women who were undernourished as children tend to have underweight babies, illustrating intergenerational effects of poor nutrition (15).

Interventions in the First 1000 Days

A wide variety of policy interventions affecting nutrition in the first 1000 days of life can have long-lasting effects on health. Interventions to prevent child mortality, as highlighted in a Lancet series on maternal and child undernutrition in low-income countries, include breast-feeding and complementary-feeding counseling, as well as food supplements (when necessary) in children 6 to 24 months of age (16). Providing vitamin A and zinc supplements, ensuring universal salt iodization, and timely treatment of severe acute malnutrition are all interventions known to be effective in reducing child mortality (16). Iron supplements are also recommended, but not where malaria is prevalent because of the risk that iron supplements may increase mortality by increasing vulnerability to infections (17).

An important attribute of breast-feeding is that it enhances a child’s IQ, according to numerous studies in high- and low-income countries. A randomized, though unblinded, trial showed that breast-feeding promotion raised IQ six points (18); other studies show gains more on the order of one to three points. Regardless of the exact number, these are large gains, comparable to the well-established effects of eliminating lead from gasoline (19). Analyses by the U.S. Environmental Protection Agency (EPA) suggest that an increase of one point in an individual’s IQ increases the present value of lifetime earnings by between 1.8 and 2.4%. Using data on median earnings of U.S. workers and assuming a discount rate of 3%, the EPA calculates the gain in net earnings from an increase of one IQ point to range from $8760 to $12,512 in 2006 U.S. dollars (20). To our knowledge, these estimates have not been included in economic studies of breast-feeding. Because IQ gains are expected in all breast-fed infants, IQ-related benefits appear sufficiently large to substantially improve the cost-effectiveness of breast-feeding interventions relative to other public health measures.

Maternal health matters too, not just intrinsically, but because mothers as the primary care givers for their children need to be physically and mentally healthy to provide adequate care. Indeed, maternal death is a risk factor for infant mortality. Anemia during pregnancy increases a woman’s risk of death from blood loss during delivery (1), and high-quality evidence supports the value of providing iron folate and multiple micronutrient supplements to reduce maternal anemia (16).

In addition, breast-feeding offers substantial benefits to mothers and their families because it...
delays the return of ovulation and menses, thereby extending the interval between pregnancies. Less frequent pregnancies reduce neonatal, infant, and child mortality (21) and undernutrition (22). Exclusive, on-demand breast-feeding during the first 6 months after giving birth is as effective at preventing pregnancy as condoms, diaphragms, and oral contraceptives (23). After 6 months, breast-feeding still has substantial contraceptive effects, which are particularly important as the use of active birth-control methods is still low in many countries, particularly in Africa. Nationally representative data on married women of reproductive age in 30 African countries between 2000 and 2012 show that, in more than half of these countries, less than one woman in five used contraceptives. Breast-feeding at current levels, compared with no breast-feeding, is estimated to avert 53 million births per year (24). Using the same data, we estimate that breast-feeding at global levels consistent with the World Health Organization (WHO)’s recommendations would further reduce births by another 12 million annually.

In addition to other benefits, improved basic sanitation (such as hand-washing and access to toilet facilities) can improve child nutrition in low-income countries by reducing intestinal diseases that reduce nutrient absorption and cause loss of appetite (25). A robust body of literature illustrates that the effects of acute illness, particularly diarrhea, in early childhood interact synergistically with poor diet to cause childhood stunting (26). Evidence is also accumulating to show that nutrition-sensitive agriculture and social protection interventions can positively affect child nutrition (27, 28).

Breast-Feeding and NCD Risk
Emerging data show that breast-feeding plays a role in reducing NCDs, which in 2010 were estimated to cost $863 billion globally in medical expenses and lost productivity (29); morbidity and mortality rates from NCDs surpass those from communicable diseases in every region but Africa. Furthermore, women who breast-feed reduce their risk of key NCDs, according to recent observational studies. These women experience lower rates of ovarian and premenopausal breast cancer and type 2 diabetes (Table 1). They also appear to have lower risk of some adverse cardiovascular outcomes (30).

Furthermore, data are beginning to reveal the effects of early childhood feeding patterns on NCD risk to children later in life (31). Systematic reviews of available evidence from low- and high-income countries suggest that children who were breast-fed had lower mean blood pressure and total cholesterol (3), as well as fewer cases of type 2 diabetes (3, 32). However, a more recent study from five prospective cohorts in low- and middle-income countries failed to substantiate these effects (33). Still, the role of different patterns of complementary feeding in relation to risk of NCDs is virtually unexplored (34). Unlike breast milk, which evidence has proven to be superior to other foods for infants, no set of complementary foods or feeding practices is shown to be of better quality, either for healthy growth in the short term or for lower NCD risk in the long term. However, exposure to high levels of salt early in life may damage developing kidneys, predisposing an individual to subsequent high blood pressure (35). A growing amount of literature suggests that gut microflora may develop differently in response to early introduction of different complementary foods, with potential long-term implications for the host’s overall health (36).

Breast-Feeding Promotion: The Economic Rationale
Among the causes of the global disease burden, communicable diseases have long been the targets of choice. The rationale for intervention is stronger with communicable diseases because of the risks of contagion. Often unrecognized, however, is a comparably strong economic rationale that exists for breast-feeding.

In a 1970 paper that later earned him a Nobel Prize, George Akerlof showed that lower-quality products can displace higher-quality products in instances where buyers cannot discern quality (37). Such instances of information asymmetry have long been recognized as market failures by the U.S. Office of Management and Budget (38). Breast milk is an example of a higher-quality good whose superiority relative to infant formula is very difficult for mothers to fully perceive. As a nonmarket good, breast milk defies conventional private solutions to information asymmetry problems, such as product warranties or investments in brand-name reputations. Breast-feeding requires successful initiation at birth, when mothers are vulnerable to influence from medical staff or family and ill-placed to make independent decisions. In addition, early use of infant formula hinders later breast-feeding. For mothers who study or work outside the home, breast-feeding requires a place and time for expression and storage of milk, which may be difficult arrangements to negotiate individually with schools or employers. Hence, there is a fundamental and legitimate need for coordinated action to protect breast-feeding, and history reflects recognition of this need.

In the late 1970s, compelling accounts emerged of infants who became acutely malnourished or died from contaminated or diluted formula after free samples were given to their mothers (39). To protect breast-feeding, the World Health Assembly (WHA) adopted the International Code of Marketing of Breast-milk Substitutes in 1981 (40). The code provides guidelines on marketing strategies associated with increased formula feeding, such as direct promotion to the public, free supplies to mothers and health care institutions, and the use of baby images on labels that idealize bottle-feeding. A total of 12 subsequent WHA resolutions—the most recent in 2010—have strengthened the original guidance; nonetheless, violations continue (41). The 1990 Innocenti Declaration endorsed by the WHA set operational targets that governments should achieve, and in 1991, WHO and United Nations Children’s Fund (UNICEF) launched the Baby Friendly Hospital Initiative to promote hospital environments conducive to breast-feeding. Elements of successful breast-feeding promotion strategies are well documented (42).

In 1996, breast-feeding promotion was estimated to be exceptionally cost-effective: $150 for each diarrheal death prevented in Latin America (43). This estimate placed breast-feeding promotion among the most cost-effective interventions for child survival, equal to other high-impact interventions such as immunizations. However, this assessment does not include the gains in IQ and reductions in NCDs, which would make estimates of cost-effectiveness substantially more attractive.

The revolution in information technology could further contribute to efficiencies in breast-feeding promotion. Timely delivery of information that is culturally sensitive, specific to the issue at hand, and authoritative is highly effective in getting mothers to breast-feed exclusively (44). Cell phones or smart phones have been effectively used to communicate...
health messages in HIV treatment (45) but have rarely been used in programs to promote breastfeeding or complementary feeding. Innovative use of these technologies could greatly improve the cost-effectiveness of child nutrition programs.

Of late, funding for breastfeeding promotion has declined (46). U.S. Agency for International Development (USAID) global spending on child nutrition, of which breastfeeding promotion was an important component, declined from $16.6 million in 1999 to $13.3 million in 2003. Between 1999 and 2005, investment in breastfeeding in USAID's flagship maternal and child nutrition project declined from $4.9 million to $2.3 million, while project expenditures for prevention of mother-to-child transmission of HIV increased, reflecting the seismic shift in global funding priorities related to the HIV/AIDS epidemic. Donors other than USAID also cut funding (46).

Data from African, Asian, and Latin American/Caribbean countries suggest that supportive policies and programs can markedly affect exclusive breastfeeding percentages (Fig. 1). In 1993, Ghana and nearby Mali had reasonably similar rates (~8%) of exclusive breastfeeding. Yet by 2005, the rates differed by 15 percentage points, despite improvement in both countries. Cambodia achieved a phenomenal gain in exclusive breastfeeding rates of nearly 50 percentage points in 5 years, whereas in Bangladesh, the rate slipped slightly from 46% over 15 years. In Brazil, exclusive breastfeeding increased 40 percentage points, from 3% to 43% between 1986 and 2006, but over roughly the same period in Mexico, the exclusive breastfeeding rate decreased by 5 percentage points. For Brazil, a 20-year chronology links key legislative, policy, and programmatic measures with improved breastfeeding practices (47). Thus, government policy and public health measures appear capable of effecting large gains in breastfeeding in some countries, even given concurrent increases in urbanization, female education, and employment that are traditionally associated with declines in breastfeeding rates.

Current Breast-Feeding and Complementary Feeding Practices in Selected Low- and Middle-Income Countries

A big gap still separates current practices from accepted breastfeeding recommendations in low- and middle-income countries (Fig. 2) (48). WHO recommends 6 months of exclusive breastfeeding, but current prevalence (36%) is much lower. Only about half of 20- to 23-month-old children are breastfed, despite the recommendation that all children be breast-fed for 2 years or beyond. Although early initiation prevented about one-fifth of neonatal deaths in Ghana and Nepal (49, 50), less than half of the infants in 46 low- and middle-income countries are put to the breast within 1 hour of birth.

Global practices in complementary feeding in low- and middle-income countries are poor (Fig. 2) (48). Only half of children 6 to 24 months of age met the recommended minimum daily numbers of meals, less than one-third met the minimum criteria for daily dietary diversity, and only one in five breast-fed children satisfied the criteria for minimum acceptable daily diet. Moreover, there are wide differences among countries with relatively similar income levels. In Ethiopia, which had a gross domestic product (GDP) of $1100 in 2011, only 3.9% of children 6 to 24 months of age met the minimum standard of daily dietary diversity. In contrast, in Uganda, with an estimated GDP of $1300 for same year, 23.6% of children in the same age group satisfied this criteria (51). Low national income, though important, is not the only impediment to improved complementary feeding.

Conclusions

The prenatal period and the first 24 months of life provide a 1000-day window in which sound nourishment, especially adherence to recommended breastfeeding and complementary feeding practices, can improve not only the health of vulnerable infants and young children, but also the trajectory of aspects of their well-being and the health of their mothers. However, a large gap between current and best practices exists. Research on how to cost-effectively improve the coverage of existing nutrition interventions is needed to help accelerate their health impacts (7).

Research is also needed to better understand the biological mechanisms through which the effects of improved breastfeeding occur, because randomization in breastfeeding studies is nearly impossible to achieve. Most evidence derives from observational studies whose interpretations are complicated by self-selection, measurement errors, and residual confounding (3). Knowledge of the underlying metabolic pathways through which breastfeeding or breast milk affects specific health outcomes, such as the role of human milk serum adiponectin exposure and early childhood weight gain (52) and how human milk and complementary foods affect the gut microbiome, will improve interpretation of epidemiological studies. Acquiring a deeper understanding of the most common breastfeeding and complementary feeding difficulties and identifying the most effective strategies to overcome these difficulties is essential. Surveys, randomized interventions, and systems analyses are needed to explore the functioning of health care systems and the behavior of health professionals in relation to the persistence of impediments to better feeding practices. Both basic and applied research are required to develop an evidence-based set of policies and programs to improve complementary feeding. Finally, research is needed to measure the population risk attributable to suboptimal feeding practices and child nutrition, as well as the costs in medical treatment and lost productivity.

The beneficial effects on child mortality and IQ and on maternal NCD risks of improved nutrition during the prenatal period and first 2 years of life appear large compared with other public health interventions. Because breastfeeding promotion provides the greatest short-term benefit for children living in poor environments, investments in breastfeeding protection and promotion will also improve global health equity. Nonetheless, funding for research and greater use of existing effective interventions is low compared with other life-saving child health interventions.

References and Notes

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Double Burden of Noncommunicable and Infectious Diseases in Developing Countries

I. C. Bygbjerg

On top of the unfinished agenda of infectious diseases in low- and middle-income countries, development, industrialization, urbanization, investment, and aging are drivers of an epidemic of noncommunicable diseases (NCDs). Malnutrition and infection in early life increase the risk of chronic NCDs in later life, and in adult life, combinations of major NCDs and infections, such as diabetes and tuberculosis, can interact adversely. Because intervention against either health problem will affect the other, intervening jointly against noncommunicable and infectious diseases, rather than competing for limited funds, is an important policy consideration requiring new thinking and approaches.

In 1971, Omran (1) described how health and disease patterns change over time in societies, depending, among other factors, on the degree of demographic transition and rate of economic development, to result in an epidemiological transition. Like individuals, societies have a “life cycle”: In a “young” society, infectious diseases and nutritional deficiencies dominate; hence in children, diarrhea and acute respiratory infections, including measles and malaria, predominate; in pregnant women, fetal loss, perinatal death from undernutrition, bleeding, and infection are major risks, and in the surviving adults, tuberculosis (TB) and other diseases related to poverty are important causes of morbidity. When societies “grow up,” accidents and violence-related disabilities and deaths increase, mostly among the young, and although infectious diseases such as TB still prevail, chronic noncommunicable diseases (NCDs) become more prevalent, particularly in urban populations. In aging societies, NCDs predominate: first, type 2 diabetes and cardiovascular diseases, followed by cancer and degenerative disorders. Simultaneously, in extreme cases the broad-based demographic pyramid inverts.

Demographic transition as the main explanation for the growing NCD burden has, however, been questioned. Stuckler (2), in a thorough analysis of causes that was published in the same journal as Omran’s historical paper, pointed out that particularly in low-income countries, economic growth, market integration, foreign direct investment, and urbanization together correlated threefold greater to epidemiological transition than did population aging. The projections of disease burden in Fig. 1 are made by considering the combined effect of demographical transition (population growth and increasing life expectancies) and expected impact of changing lifestyle, living conditions, and economic development (3).

Omran (1) has also been criticized for overlooking new epidemics of infectious diseases, but this author could not have predicted the HIV epidemic, which disturbed his model, set back the epidemiological and demographic transition, and, more importantly, reversed the reduction of deaths from infections in children and young adults, particularly in sub-Saharan Africa. As a consequence, combating HIV and other major infections and improving child and maternal health remained prominent among the Millennium Development Goals (MDGs) set in 2000. Similarly, the United Nations’ General Assembly (UNGASS) in 2001 committed all governments to combat the HIV epidemic (but not NCDs), and, consequently, WHO and UNAIDS updated their “Strategies for the Prevention and Control of Communicable Diseases” (4). In that document, NCDs—such as diabetes, as a potential risk factor for infections, or TB in particular—were not mentioned. None of the MDGs relate directly to NCDs, although Stuckler et al. (5) and others have indicated that MDGs may not be attained without addressing NCDs as risk or cofactors for communicable diseases.

Before the turn of the millennium, some researchers (6) and the World Health Organization (WHO) (7) had pointed at the danger of a “double burden of disease,” such as the emerging epidemic of chronic NCDs, in addition to the “unfinished agenda of infectious diseases” and problems of maternal and child health. Yach et al. (8) showed that even in the poorest countries, more deaths are caused by NCDs than from infections, and that the WHO Headquarters spent only US$0.50 on chronic diseases per death per person compared with US$7.50 for leading communicable diseases. Yet in 2005, the WHO in its report “Preventing chronic diseases—A vital investment” (9) underscored that NCDs do not only hit the old, the rich, and the fat, developing countries carry the heaviest burden of NCDs. In 2007, the World Bank (WB) issued a similar report on the conceptions, misconceptions, and challenges presented by chronic NCDs (10). In 2011, partly as a result of these reports and provoked by continuous lobbying by civil society and leading stakeholders in NCDs, including the International Union Against Cancer, the World Heart Federation, the Global Alliance against Chronic Respiratory Diseases, the International Diabetes Federation, and the International Union Against Tuberculosis and Lung Disease, UNGASS committed governments to fight the emerging epidemic of NCDs, acknowledging that NCDs hit developing countries hard (11). When reading and comparing the UNGASS declarations from 2001 and 2011, unfortunately, the known and potential links between infectious diseases and NCDs are barely visible. Similarly, in the 182-page 2005 WHO report (9) and the 188-page 2007 WB report (10) on NCDs, TB is mentioned once in each report, malaria once in the WHO report, and HIV six and three times, respectively.

A major barrier for integrated intervention against the double burden of infections and NCDs may be that their etiologies and pathologies at first glance appear to be diametrically opposed. As part of new public management, researchers, health professionals, donor agencies, and politicians are often forced to focus on a particular health problem to get visible results and fulfill result contracts. At a time of global financial crises and shrinking health budgets, there is a threat that the battle against common...