Chapter 17

Cost-Effectiveness of Interventions for Reproductive, Maternal, Neonatal, and Child Health

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INTRODUCTION

Substantial efforts and investment have been made in global reproductive, maternal, newborn, and child health (RMNCH) since 2000. The Millennium Development Goals (MDGs) have been one focus for efforts. The establishment of international funds—such as the Global Alliance for Vaccines and Immunization (Gavi, founded in 2000); and smaller foundations, such as the Clinton Health Access Initiative founded in 2007; the Children's Investment Fund Foundation, which made its first significant investments in 2009; and the Bill & Melinda Gates Foundation, founded in 1997—has brought new resources as well as an emphasis on value for money.

The amount of funding has been significant. In 1990, the members of the Development Assistance Committee of the Organisation for Economic Co-operation and Development provided an estimated US$5.6 billion for international health assistance (Ravishankar and others 2009). In 2011, this amount had grown to US$27.7 billion (Leach-Kemon and others 2012). Part of the increase was due to spending for human immunodeficiency virus/acquired immunodeficiency syndrome human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) (US$7.7 billion), but the increase in other areas was also substantial: RMNCH was the second largest component (US$6.1 billion) (IHME 2014).

The increase in resources and the growing interest in results combined to greatly increase the number of economic analyses of maternal and child health interventions. This chapter summarizes the findings of a systematic search of the cost-effectiveness literature on RMNCH, which builds on previous work, including several chapters in *Disease Control Priorities in Developing Countries*, second edition (Jamison and others 2006), as well as other systematic surveys and reviews on specific topics. The chapter's focus is on the cost-effectiveness of interventions; one section summarizes the findings on cost, building on a longer systematic search on unit cost (Levin and Brouwer 2014).

The studies identified in this chapter do not cover all of the interventions that affect maternal and child health. Some are covered in other volumes in this series (see table 17.1). The literature also has biases. Studies tend to concentrate on areas of current policy interest; for example, the literature on vaccines concentrates disproportionately on new vaccines—particularly those for pneumococcus and rotavirus, but also hepatitis B and *Haemophilus influenzae* B (HiB)—and not on older interventions known to be cost-effective, such as the original Expanded Program of Immunization (EPI) vaccines. Ideally, when resources are allocated across interventions, the full range would be considered. Funding could potentially be reallocated

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Table 17.1 Interventions Covered in This Chapter: Topics Covered in Other Volumes

Topics covered in this volume	Topics covered in other volumes
Reproductive health: Family planning, safe abortion, intimate partner violence	Adult male circumcision in volume 6 (*HIV/AIDS, STIs, Tuberculosis, and Malaria*)
Maternal and child mortality: Antenatal, intrapartum, and postpartum care; care of newborns	Intrapartum care also covered in volume 1 (*Essential Surgery*)
Febrile child: Diagnosis and treatment of malaria and pneumonia	Prevention of malaria covered in volume 6 (*HIV/AIDS, STIs, Tuberculosis, and Malaria*)
Diarrheal diseases: Treatment of diarrhea; brief review of interventions to prevent diarrhea, including water and sanitation	Water and sanitation also covered in volume 7 (*Injury Prevention and Environmental Health*)
Vaccines: 16 conditions (BCG, DPT, polio, measles, hepatitis B, *Haemophilus influenzae* B [HiB], Japanese encephalitis, meningitis A, yellow fever, pneumococcus, rubella, rotavirus, typhoid, and cholera)	HPV covered in volume 3 (*Cancer*)
Nutrition: Management of severe acute malnutrition, and infant and child growth	
Platforms for health care and public health interventions	

Note: BCG = Bacillus Calmette–Guérin; DPT = diphtheria, pertussis, and tetanus; HIV/AIDS = human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS); HPV = human papillomavirus; STIs = sexually transmitted infections.

from old but cost-ineffective interventions to promising new ones, or coverage of older and very cost-effective interventions could be completed before new ones that are less cost-effective are incorporated.

The next section discusses the methods used for the search and analysis of the literature. The findings are then organized according to the sequence of chapters in this volume:

- Reproductive health (chapter 6)
- Maternal and newborn child morbidity and mortality (chapter 7)
- Febrile conditions (chapter 8)
- Diarrheal disease (chapter 9)
- Vaccines (chapter 10)
- Treatment of severe acute malnutrition (chapter 11)
- Infant and young child growth (chapter 12)
- Platforms for the delivery of interventions (chapters 14 and 15).

Following a discussion of the literature on the cost and affordability of interventions, we provide conclusions. Throughout the chapter, unless otherwise specified, costs and cost-effectiveness are converted to 2012 U.S. dollars.

METHODS

We undertook a systematic survey of the literature beginning in 2000 on the cost-effectiveness of interventions for RMNCH, detailed in Horton and others (2015). The studies discussed here are primarily those measured as cost per discounted disability-adjusted life year (DALY) averted,[1] the most commonly considered outcome, but we also provide figures showing results for deaths averted. Studies using cost per quality-adjusted life year (QALY) saved and life-year saved (LYS) are included in the working paper (Horton and others 2015), as are studies using other outcomes, for example, per patient correctly treated. For studies that express outcomes in life-years or deaths, we have in some cases made an approximate conversion to DALYs, where one life-year is approximately 0.5 DALY for a newborn in low-income countries (LICs). Similarly the conversion from deaths to DALYs assumes that a newborn life is approximately 32 DALYs (a life expectancy of about 60 years, discounted at 3 percent). The flow charts for the searches on cost-effectiveness and cost are presented in Horton and others (2015).

In all, 222 articles were identified; of these, 21 covered reproductive care, 26 maternal and newborn morbidity, 10 febrile conditions, 10 diarrheal diseases, 131 vaccines, 3 community management of severe acute malnutrition (SAM), and 28 growth of infants and young children. Seven articles covered more than one category, and 104 included DALYs as one of the outcome measures. We benefited from several recent systematic reviews, including Gyles and others (2012); Mangham-Jefferies and others (2014); Ozawa and others (2012); and White and others (2011). All studies were read by two reviewers to extract the cost-effectiveness data; one reviewer graded the article quality using the Drummond Checklist (Drummond and others 2005); grades are presented in Horton and others (2015). In some cases we augmented systematic reviews with additional searches. For vaccines (Ozawa and others 2012), we added literature from 2010 onward for HiB, meningitis, pneumococcal, rotavirus, and syncytial virus. Small, focused searches in PubMed only were undertaken to find additional studies on meningitis, yellow fever, and rubella, which are not covered in Ozawa's review; however, no studies for these conditions report results in DALYs.

Cost-effectiveness data were converted to 2012 U.S. dollars using the original study country currency and consumer price index (World Bank 2013). Several studies provided multiple cost-effectiveness estimates for different interventions. This chapter discusses those that provided an incremental cost-effectiveness ratio compared with a clear alternative. Cost-effectiveness data from more complex interventions, for example, switching from fortification to supplementation combined

with another package of interventions, are not summarized here but are listed in Horton and others (2015).

The cost-effectiveness results measured in DALYs are summarized in figure 17.1; figure 17.2 provides similar results for deaths averted. The studies used to generate the figures are cited in tables 3 and 4, respectively, in Horton and others (2015). To interpret the results, a useful yardstick comes from the WHO (2001), which suggests that interventions costing less than per capita gross national income (GNI) per DALY averted can be termed "very cost-effective," and those costing less than three times per capita GNI can be termed "cost-effective." In 2012, according to the World Bank's World Development Indicators (World Bank 2013), only one country had a GNI per capita of less than US$320, and LICs' GNI per capita was up to and including US$1,035. Thus, all interventions costing less than US$320 per DALY averted are "very cost-effective" in all countries but one, and those costing less than about US$1,000 per DALY averted are cost-effective in LICs, and very cost-effective in middle-income countries.

REPRODUCTIVE HEALTH

Economic studies of family planning preceded those of health, just as international assistance and lending for family planning preceded that for health; the cost-effectiveness of modern contraceptives is well established. Only two surveys were identified on the cost-effectiveness of modern contraception using DALYs (Babigumira and others 2012; Seamans and Harner-Jay 2007); both indicate that contraceptives are very cost-effective in all countries as measured by the benefits to mothers' and children's health. Other studies were identified in which the outcome (couple-year of protection) is specific to contraception; these are discussed in chapter 6 of this volume (Stover and others 2016).

Safe abortion is cost saving compared with unsafe abortion, which leads to adverse health outcomes for mothers as demonstrated by Hu and others (2010) for Ghana and Nigeria; other studies with outcomes such as maternal lives saved are summarized in Horton and others (2015). Safe abortion remains an issue for policy; safe abortion methods are not available in all low- and middle-income countries (LMICs), and the availability of new methods, such as medical abortion, increases the options.

Only one economic study was found on intimate partner violence (Jan and others 2010); this study examines a microfinance initiative combined with gender training in South Africa. Although the cost-effectiveness was less than the per capita GNI for South Africa and thereby "very cost-effective" for that country, the cost of US$2,908 per DALY averted is at the higher end compared with other interventions in this chapter.

MATERNAL AND NEWBORN MORBIDITY AND MORTALITY

Expanding access to existing essential and cost-effective interventions for maternal and newborn care, while also focusing on impact, costs, and affordability, has been a priority for reaching MDG 4 (reduce child mortality) and MDG 5 (improve maternal health) (Bhutta and others 2014). Several new interventions have also become available, and efforts to deliver interventions more inexpensively and to encourage uptake have been undertaken. Goldie and others (2010) model an "expansion path" of interventions, suggesting that starting with family planning and safe abortion is the most cost-effective first step, followed by increasing the availability of skilled birth attendants, then improving antenatal and postpartum care. Shifting births to facilities comes next, and finally increasing referral for complicated cases and providing transport. The study by Goldie and others (2010) was restricted to India, but the findings are confirmed by the studies identified for this chapter.

A few innovations studied used new modest-cost health inputs and have costs per DALY averted in the range of US$20 to US$100, for example, skin emollients to help keep small newborns warm (Lefevre and others 2010), single-use injection devices for oxytocin delivery during labor (Tsu and others 2009), and clean delivery kits for in-home births (Sabin and others 2012). However, the total amount of DALYs averted by these methods are modest. Several studies (Borghi and others 2005; Fottrell and others 2013; Lewycka and others 2013; Tripathy and others 2010) look at the cost-effectiveness of participatory women's groups on health outcomes; cost per DALY averted ranges from US$150 to US$1,000. Training initiatives for village health workers and midwives have a similar range of costs per DALY averted (Lefevre and others 2013).

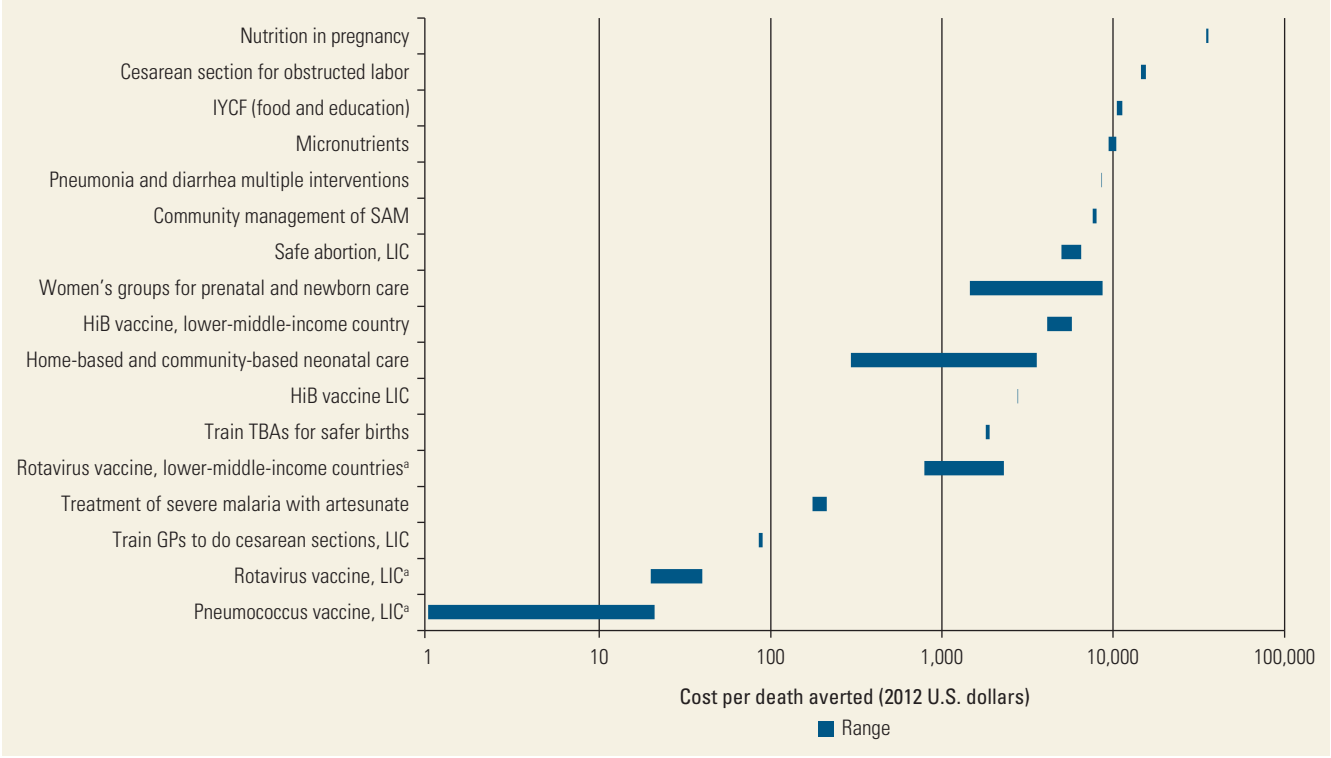
Safe motherhood initiatives (a package combining antenatal and postpartum care with trained birth attendants, potentially in a health facility) in various countries fall in the same range of US$150 to US$1,000 per DALY averted (Carvalho, Salehi, and Goldie 2013 for Afghanistan; Erim, Resch, and Goldie 2012 for Nigeria; Goldie and others 2010 for India; Hu and others 2007 for Mexico). Cesarean sections for obstructed labor have a wider range, from US$200 to US$4,000 per DALY averted, depending on the country, with a median of US$400 (Alkire and others 2012).

Figure 17.1 Cost-Effectiveness of Interventions for RMNCH, in 2012 U.S. Dollars per DALY Averted

Note: DALY = disability-adjusted life year; EPI = Expanded Program of Immunization; Gavi = Global Alliance for Vaccines and Immunization; HiB = *Haemophilus influenzae* B; LIC = low-income country; RMNCH = reproductive, maternal, newborn, and child health; WASH = water, sanitation, and hygiene.
a. Converted from life-years, assuming that a newborn life is equivalent to 32 DALYs or 60 life-years.

Bhutta and others (2014) undertake a more ambitious estimate of the cost-effectiveness of a package involving scaling up effective interventions in the 75 high-burden Countdown countries; the annual cost of the package would be US$5.65 billion. This investment would reduce maternal and neonatal deaths and prevent stillbirths at a cost of US$1,928 per life saved or US$60 per DALY averted. Bhutta and others (2014) estimate that 82 percent of the effect in lives saved would be from facility-based care.

Figure 17.2 Cost-Effectiveness of Interventions for RMNCH, 2012 U.S. Dollars per Death Averted



Note: If country group is not specified, results refer to low- and lower-middle-income countries combined. GP = general practitioner; HiB= *Haemophilus influenzae* B; IYCF = infant and young child feeding interventions (combine education with food distribution to poorest); LIC = low-income country; RMNCH = reproductive, maternal, newborn, and child health; SAM = severe acute malnutrition; TBA = traditional birth attendants.

a. Cost-effectiveness of vaccines is sensitive to vaccine price. Rotavirus and pneumococcus vaccine costs to LICs are a fraction (for example, 5 percent) of the price paid by Gavi, the Vaccine Alliance, to procure the vaccines; and Gavi in turn receives prices that are more favorable than in upper-middle income countries because of volume discounts and the like.

UNDER-FIVE ILLNESS

Febrile Conditions

The most recent cost-effectiveness estimates for the treatment of pneumonia are from the second edition of *Disease Control Priorities in Developing Countries* (Simoes and others 2006), and suggest that cost-effectiveness is US$516 per DALY averted in LMICs overall (US$342 per DALY averted in South Asia and US$282 per DALY averted in Sub-Saharan Africa). These costs are averaged across nonsevere cases treated in communities or local facilities along with severe and very severe cases treated in hospitals.

A significant amount of work has been done on malaria in the past decade, alongside policy efforts such as the Roll Back Malaria Partnership. Recent studies suggest that treatment of severe malaria with artesunate is very cost-effective, even in LICs. White and others (2011) identify four studies of treatment of severe malaria using artesunate. Lubell and others (2009) estimate the cost-effectiveness of artesunate compared with quinine as US$14 per DALY averted, pooling results for four countries in Sub-Saharan Africa; in pooled results for four countries in the WHO regions of South Asia and Southeast Asia, the cost-effectiveness is US$152 per DALY averted. Buchanan and others (2010) and Tozan and others (2010) examine the cost-effectiveness of presumptive treatment in the community with rectal artesunate for severe malaria in Sub-Saharan Africa. Cost-effectiveness is US$20 per DALY averted compared with no treatment (Buchanan and others 2010), and US$122 to US$1,855 per DALY averted compared with parenteral treatment (Tozan and others 2010). Nonvignon and others (2012) examine the cost-effectiveness of presumptive community-based treatment of malaria, using an artemisin combination therapy compared to standard care; standard care is a combination of treatment at health facilities, purchase of antimalarials at a pharmacy, and other types of treatment. They estimate the cost per DALY averted compared to standard care to be US$93.

In contrast, the literature suggests that rapid diagnostic tests (RDTs) for malaria are not generally very cost-effective in program settings. However, where

microscopy is poorly done, RDTs become more cost-effective. Microscopy has been considered the gold standard for the diagnosis of malaria, but it is not always feasible in low-resource environments. If not well done, it can lead to a relatively high rate of misdiagnosis, and can entail long waits for treatment, depending on the capacity for reading slides. In areas without microscopy, presumptive diagnosis has been used. Clinicians use their expert knowledge to determine whether a patient presenting with fever has malaria or another infection and treat accordingly. Thus, RDTs are potentially more cost-effective where *P. falciparum* predominates and the more effective but more costly artemisinin combination drugs are being used. RDTs are also cost-effective where transmission rates are low because presumptive treatment involves overuse of antimalarials and, possibly, delays antibiotic treatment if the underlying infection is bacterial rather than malarial (Ansah and others 2013; Babigumira and Gelband, forthcoming; Lemma and others 2011; Rolland and others 2006). RDTs and microscopy both perform more favorably if clinicians are more likely to use the results of the diagnosis in their prescription behavior, that is, if they only prescribe antimalarials if the test indicates malaria is the likely diagnosis, and only prescribe antibiotics if malaria is not the likely diagnosis (Yukich and others 2010). Two studies with outcomes measured in cost per deaths averted (Chanda, Castillo-Riquelme, and Masiye 2009; Uzochukwu and others 2009) suggest that RDTs do not rank as particularly cost-effective in program settings because clinicians apparently do not always prescribe according to test results. Chapter 8 in this volume (Hamer and others 2016) discusses some of these issues in more detail and cites other studies that did not fit the inclusion criteria here.

Diarrheal Disease

New developments for diarrheal disease since 2000 include the use of zinc as adjunct therapy in combination with oral rehydration solution (ORS), a substantial decrease in the cost of rotavirus vaccine, and additional research separating the cost-effectiveness of water supply from that of sanitation.

The most cost-effective interventions for diarrhea, based on cost per DALY averted, are prophylactic zinc supplementation as an adjunct to ORS (US$10 to US$50 per DALY averted), ORS (US$150 per DALY averted), rotavirus vaccine (US$100 per DALY averted at the Gavi price in LICs), and household-level water treatment in rural areas using chlorination or solar disinfection (US$180 to US$200 per DALY averted) (figure 17.1). The next most cost-effective group includes rural sanitation; piped water; and in selected countries, cholera vaccine (US$2,000 per DALY averted). Urban sanitation and cholera vaccine in lower mortality countries can cost US$3,000 or more per DALY averted.

The systematic search identified only one recent study of behavior change. Behavior change interventions tend to have heterogeneous results, and some are not effective (let alone cost-effective), but the one identified—a handwashing education intervention in Burkina Faso (Borghi and others 2002)—falls into the very cost-effective group (US$88 per DALY averted). It is quite possible that well-designed behavior change interventions to increase the use of clean water, of latrines where available, of ORS, of prophylactic zinc, and of vaccines could all be cost-effective.

Most studies estimate the cost-effectiveness of adding a single intervention to "usual care." If interventions are added in combination, the incremental cost-effectiveness of each additional individual intervention can decline. Fischer Walker and others (2011) estimate the combined effect of 10 interventions designed to reduce diarrhea in 68 countries with high child mortality, using the Lives Saved Tool (LiST). Two scenarios are modeled: an ambitious strategy designed to reach MDG 4 goals; and a universal strategy designed to bring coverage of many interventions to 90 percent or more, and water, sanitation, and handwashing interventions to 55 percent or more. Both strategies are scaled up from current coverage to the target over five years.

The ambitious strategy saves 3.8 million lives during a five-year period, at a cost of US$49.2 billion, which is US$12,847 per death averted or approximately US$405 per DALY averted in 2008 U.S. dollars. The universal strategy saves 5 million lives at a cost of US$19,460 per death averted, approximately US$608 per DALY averted in 2008 U.S. dollars. Although $608 per DALY averted certainly falls in the cost-effective or very cost-effective range for most countries, affordability remains problematic. The water and sanitation component is the main issue, accounting for 84 percent of the cost of the ambitious package and 87 percent of the universal one.

Vaccines

Vaccines rank among the most cost-effective health interventions because of their life-saving potential. The original EPI-6 vaccines (against tuberculosis, diphtheria, tetanus, pertussis, measles, and polio) are very cost-effective (less than $100 per DALY averted), although no studies on the basic six antigens that typically comprise a national EPI were identified by the systematic search.

One study published after our search examines Vietnam's national EPI, and estimates that 26,000 deaths were prevented by EPI since 1980, with a cost-effectiveness of about US$1,000 to US$27,000 (in 2010 U.S. dollars) per death averted (based on financial data for that same period) (Jit and others 2015). Since 2000, the focus has been on the introduction of new and underutilized vaccines and those in the pipeline. Of the 57 studies since 2000 using DALYs as an outcome, more than half focus on pneumococcus and rotavirus vaccines. Whether, and how, to adopt these vaccines has been the major LMIC childhood vaccine policy preoccupation of the past decade. Vaccine cost-effectiveness studies are frequently undertaken before governments or donors decide to fund the intervention.

The cost-effectiveness of new childhood vaccines is very much dependent on the price of the vaccine. For well-established vaccines with long-expired patent protection, a clear world market price may exist based on the cost of production. For new vaccines, the price is less clear. The companies that develop new vaccines retain patents but have increasingly been willing to offer differentiated prices to different markets. To take advantage of economies of scale, international organizations (particularly Gavi, but also the United Nations Children's Fund) have entered into agreements for bulk purchase or have made advance market commitments. Hence, cost-effectiveness studies are often undertaken at a variety of price points to gauge ability to develop a market for different groups of countries. Our summary is undertaken using current prices, which vary between Gavi-eligible countries, recent Gavi graduates, countries covered by the Pan-American Health Organization's revolving fund, and upper-middle-income countries facing the world market.

Table 10.1 (chapter 10 in this volume [Feikin and others 2016]) summarizes the cost-effectiveness findings in DALYs at current key price points and adds information for meningitis A (Miller and Shahab 2005), and yellow fever (Monath and Nasidi 1993).

Among the new and underutilized vaccines, cost-effectiveness ranges from about US$24 to US$2,500 per DALY averted in low-income settings, depending on the vaccine, geographic setting, income level, and associated price point. Rotavirus and Japanese encephalitis are the most cost-effective at less than US$50 per DALY averted in high-burden, LICs in Asia and Sub-Saharan Africa, followed by pneumococcal vaccines. Some vaccines in LICs have not yet been incorporated into EPI programs because their cost-effectiveness is less favorable, at more than US$1,000 per DALY averted. These vaccines include cholera and typhoid, which may meet the WHO's cost-effective criterion, but only in countries of high endemicity. However, these vaccines are planned for rollout by Gavi and its partners before 2020, assuming prices come down or effectiveness goes up (or both).

Cost-effectiveness ratios increase with country income per capita, but the general ranking of what is considered cost-effective stays the same. In lower-middle-income countries, hepatitis B, HiB, and rotavirus vaccines range between US$60 and US$350 per DALY averted and are among the most cost-effective. Rubella, pneumococcal, and polio vaccines are between US$1,000 and US$3,000 per DALY averted.

The estimates of cost per DALY averted for yellow fever and meningitis fall between US$100 and US$1,040 (converting from deaths prevented in children). For the rubella vaccine, the only study from LMICs (from the English-speaking Caribbean) reports that the vaccination is cost saving (Irons and others 2000). Other vaccines, such as meningitis A and yellow fever in selected countries that are being considered for EPI expansion, are typically between US$100 and US$200 per DALY averted or at least below US$500 in LICs (Miller and Shahab 2005). Cost-effectiveness of even newer vaccines, for example, malaria and respiratory syncytial virus, is more speculative, given that the effectiveness is still being investigated and price points are unknown.

Eradication through immunization—although costly in the short and medium terms—may be cost saving in the long term by eliminating the need for vaccination; smallpox is the best example. Polio eradication is potentially cost saving in the long term, but it requires a switch from oral polio vaccine (OPV) to the inactivated polio vaccine to prevent outbreaks from vaccine-derived polioviruses. However, the inactivated polio vaccine is 20 or more times more costly than OPV (Duintjer Tebbens and others 2010) and correspondingly less cost-effective and less affordable in the short term. Measles eradication is also potentially cost saving (Bishai and others 2010), but the second measles immunization needed to approach eradication has to be given outside of the traditional EPI schedule and hence incurs additional delivery cost. This delivery schedule also affects rubella because measles and rubella vaccines are typically delivered together.

A systematic review of studies of interventions to affect the demand side of vaccine uptake (Shea, Andersson, and Henry 2009) finds that the literature was of variable quality, with only two randomized controlled trials. Some of the interventions, such as mass media campaigns, do not lend themselves to randomized controlled trials. The review concludes that mass media campaigns might be effective, but their effectiveness depends on the context.

Incentives to households might help. Other interventions have been tried, such as conditional cash transfers and use of text message reminders, but no results on cost-effectiveness of these methods were found.

NUTRITION

Interventions for Severe Acute Malnutrition

Community management of SAM is attractive from a cost-effectiveness perspective, ranging from US$26 to US$39 per DALY averted across three studies. This finding is driven in part by the high probability, as high as 20 percent, that children will die if not treated. Initially, programs cost as much as US$200 per child for a four-month course of treatment; however, during the past decade or so the cost has declined by at least a third, with greater program efficiency. Experience suggests that substituting cheaper ready-to-use therapeutic food for proprietary ones does not lead to outcomes that are quite as good, although it may lower costs. All three studies examined in this section used Plumpy'Nut, a popular ready-to-use therapeutic food.

Interventions for Infant and Young Child Growth

The majority (14) of the studies of nutrition for the general population focus on micronutrient interventions, 1 on nutrition education, 1 on the effects of scaling up a comprehensive package of nutrition intervention, and 1 on outcomes other than nutrition. No new studies of cost-effectiveness were identified for breastfeeding.

Nutrition interventions are associated with impacts on multiple outcomes of importance. Some nutrition interventions reduce morbidity and save lives in the more malnourished populations. In these cases, the outcomes can be measured using cost-effectiveness methods, such as deaths averted, LYS, QALYs saved, or DALYs averted. In other cases, nutrition is associated with impacts on cognitive improvements, and these benefits are better measured using benefit-cost ratios because benefits can be measured in financial units (higher wages).

From the literature search, five studies for folic acid, iron, and iodine interventions all had very favorable benefit-cost ratios (Horton, Alderman, and Rivera 2008; Horton and Ross 2003, 2006; Sayed and others 2008; Sharieff, Horton, and Zlotkin 2006; Sharieff and others 2008). Hoddinott and others (2013) undertake a benefit-cost analysis for a comprehensive set of nutrition interventions. These studies cannot be compared with those using DALY outcomes without assigning a dollar value to DALYs, a task that involves judgments about the value of human life.

As in previous studies (Hoddinott, Rosegrant, and Torero 2012; Horton, Alderman, and Rivera 2008), micronutrient interventions remain very cost-effective (typically less than US$100 per DALY averted, and often less than US$50 per DALY averted), with some variation. Interventions are often more cost-effective in LICs with more widespread deficiencies; for example, the cost per DALY averted is lower in South Asia and Sub-Saharan Africa than in China. Fortification is more cost-effective than supplementation for micronutrients where deficiencies are widely spread throughout the population and the micronutrient is relatively cheap, for example, iron; the opposite is true for micronutrients that are relatively more expensive, and where the benefits are concentrated particularly in vulnerable groups, for example, vitamin A. Biofortification appears to be very cost-effective, with some estimates in the US$0 to US$20 range. However, the biofortification estimates for staple food crops, such as rice, were early stage projections, and it remains to be proven whether these optimistic projections can be realized. There has been more success to date for more minor crops (orange-flesh sweet potato, beans, and vitamin A–rich cassava), although iron-rich rice and wheat seeds are now beginning to be disseminated to farmers (Harvest Plus 2013).

The only intervention identified for nutrition education (Waters and others 2006) costs slightly more than US$100 per DALY averted; this was a modest-cost intervention (US$6 per child in 2001 U.S. dollars). Estimated costs per DALY averted for earlier, more elaborate interventions were at least two to three times higher than the single case here.

Another innovation since 2000 has been the evaluation of packages of nutritional interventions. When interventions are combined, the cost-effectiveness of each individual component tends to become less attractive. Either vitamin A supplements or measles immunization can save lives, but the combined effect of both vitamin A supplements and measles immunization saves fewer lives than the sum of the two individually. Bhutta, Das, Rivzi, and others (2013) estimate that the cost per DALY averted of three components of a comprehensive nutrition intervention—micronutrients, nutrition education with selected supplements regarding infant and young child feeding, and SAM management—ranges from US$240 to US$340 per DALY averted; this cost per DALY averted is three to five times higher than the cost per DALY averted of the components introduced individually. Hoddinott and others (2013) use the same intervention package and estimate that the median benefit-cost ratio is 35 to 1 for a group of 17 LMICs for interventions provided to children.

The cost per DALY averted for nutrition interventions provided to mothers is higher still—more than US$1,100, but still in the cost-effective range for middle-income countries (Bhutta, Das, Rivzi, and others 2013).

PLATFORMS FOR DELIVERY OF INTERVENTIONS

Maternal and child health services can be delivered from a variety of platforms, including the following:

- The household level or through mobile outreach
- The community level
- At health facilities, which range from health posts and community clinics to higher-level facilities such as first-level hospitals.

Service delivery can be combined on any of the platforms if doing so increases cost-effectiveness.

In part, the type of health activity determines the appropriate platform: surgical interventions related to delivery need to be provided at the facility level, whereas immunizations have achieved better coverage in some countries through mobile outreach or community-level delivery. Outreach and community-based strategies that deliver a package of child health interventions, including vitamin A (Fiedler and Chuko 2008); distribute insecticide-treated bednets (Ross and others 2011); provide home-based management of fevers (Nonvignon and others 2012); treat severely acute malnourished children (Puett and others 2013); and train traditional birth attendants to improve neonatal health (Sabin and others 2012) are cost-effective at less than US$100 per DALY averted (chapter 14 in this volume [Bhutta and Lassi 2016]).

Community health workers (CHWs) have become essential facilitators in delivering outreach and community-based services. They are also critical for linking beneficiaries to health facilities for preventive care and treatment, when essential. Depending on the country, condition, and setting, CHWs play different roles that change with the level of coverage of fixed health facilities and urbanization. For example, outreach workers, by going to households to provide family planning and maternal and child health services in Bangladesh, played an important role in reducing birth rates; but Routh and Khuda (2000) show that in urban Dhaka, the delivery of family planning and maternal and child health services at clinics now become more cost-effective. However, the delivery of vaccinations by community-based workers cost less and achieved greater coverage than outreach by health workers in communities reached by river in the Amazon (San Sebastian and others 2001).

Despite the growing evidence on effectiveness of CHW programs, data on the cost-effectiveness of such programs are still lacking. Cost-effectiveness analyses of CHW programs may pose methodological challenges because they do not capture the full benefits of enhanced equity, increased self-reliance by communities, and contributions to other social benefits and community norms (Lehmann and Sanders 2007).

Task-shifting through the use of lay workers sheds some light on the potential cost reductions and improved cost-effectiveness. Lewin and others (2010) undertake a Cochrane review on effectiveness of lay health workers for selected maternal and child health care interventions (not restricted to LMICs), and conclude that the use of lay health workers could increase vaccine uptake. A systematic review of the cost-effectiveness of vaccination programs delivered by lay health workers in LMICs (Corluka and others 2009) finds insufficient data to allow conclusions to be drawn. Sabin and others (2012) find that training traditional birth attendants in treating birth asphyxia, hypothermia, and sepsis was very cost-effective in situations in which access to facility care was not readily available; but this intervention would not be effective in addressing obstructed labor and deliveries requiring cesarean section. The cost-effectiveness of task-shifting is underresearched for LMICs, and additional studies are needed to strengthen policy guidance.

An emerging area of interest is the integration of services to improve impact and reduce costs. The cost-effectiveness of integrating services while maintaining the effectiveness of individual interventions is a high priority research area, given the investments in individual interventions. Some of the considerable interest in the cost-effectiveness of different delivery platforms has been driven by the literature on vertical services for HIV/AIDS, tuberculosis, and malaria that have been successful but where sustainability requires integration of services. Kahn and others (2012), for example, conclude that an integrated service in Kenya that provided HIV testing and early treatment, insecticide-treated nets for malaria prevention, and water filters for diarrhea prevention saved lives and was cost-effective. For some preventive services, there may be trade-offs between cost-effectiveness and coverage. However, campaigns and mobile delivery may be essential to achieve high and equitable levels of coverage in countries with poorer availability of facilities or greater population dispersion. Verguet and others (2013) find that child health campaigns that integrated supplementary immunization activity for measles with vitamin A supplements, deworming medications, and OPVs were more cost-effective than measles supplementary immunization activity alone.

Bartlett and others (2014) use the LiST to model the effect of scaling up an integrated midwifery, obstetrics, and family planning intervention in 58 LMICs. They conclude that scaling up any of the three individually is attractive in cost per death averted, but that scaling up midwifery combined with family planning costs half as much per death averted as scaling up obstetrics combined with family planning; the lowest cost per death averted occurs when all three are scaled up together. Midwifery saves lives across the continuum of prepregnancy, prenatal, delivery, and neonatal care; obstetrical care has a strong effect on mortality during delivery.

The only cost-effectiveness study undertaken for Integrated Management of Childhood Illness finds that mortality was lower in the intervention district than in the control, and the costs were no higher and possibly lower (Armstrong-Schellenberg and others 2004). However, experience was not uniformly positive in other effectiveness trials, and there have been some difficulties scaling up this intervention. No cost-effectiveness studies were identified on the Integrated Management of Neonatal and Child Illness (IMNCI) or integrated community case management. Prinja and others (2013) note that even though overall health expenditures per case did not increase as IMNCI was implemented, there was an increase from the perspective of the government, which they estimate to be 1 percent to 1.5 percent of the government's health budget (US$0.61 to US$2.60 per child covered), depending on which field workers implement the program. The additional costs arose because the program was effective, which led to increased utilization as households switched from using private health providers.

COSTS

The country setting, type and level of the facility, severity of the event, and specific treatment offered influence costs. Service delivery platforms that reach large numbers of beneficiaries close to their homes increase the coverage and lower the cost of services. Child health days in Ethiopia, Somalia, and Zambia offer a package of preventive services that cost US$1 to US$2 per child reached; facility-based integrated care offering similar services is closer to US$10 per child treated and may be as high as US$20, as in Brazil (Adam and others 2005; Adam and others 2009; Bryce and others 2005; Fiedler and Chuko 2008; Vijayaraghavan and others 2012). For many interventions, effective and cost-effective interventions exist but suffer from low uptake or coverage. Many of the studies that present specific costs of facility-based programs do not capture the shared health system costs or costs of demand creation to increase access to and use of services.

Information on RMNCH unit costs comes from a large selection of literature published primarily after 2007. The review assessed the quality of cost data found in 146 articles and chose to liberally include unit costs if the data sources and methods were clearly explained (Levin and Brouwer 2014). Unit costs vary substantially across country settings for similar interventions. In addition, a variety of methodological approaches confound the expected variation in costs due to country context and different choices of interventions evaluated. Identifying sources of heterogeneity is challenging because many studies lack detailed information on resource use and how costs were estimated (Crowell and others 2013; Pegurri, Fox-Rushby, and Walker 2004; Shearer, Walker, and Vlassoff 2010; Walker and others 2004).

In some areas in which cost or cost-effectiveness studies have been conducted and published dating back to the 1990s, representative and standardized data on long-running interventions, such as vitamin A or iron capsule supplementation or food-based strategies, is surprisingly lacking despite consistent calls for improved information on the costs and cost-effectiveness of nutrition interventions (Fiedler and Puett 2015; Gyles and others 2012; Morris, Gogill, and Uauy 2008; Ruel 2001; Ruel, Alderman, and the Maternal and Child Nutrition Study Group 2013). Similarly, in the area of family planning, for which effective coverage of modern contraceptive use still lags, little new information is available on country-level costs of scaling up interventions to increase the supply of and demand for services (Singh, Darroch, and Ashford 2014).

In general, average unit costs are relatively low for family planning interventions, antenatal care visits for pregnant women, and normal deliveries at home or at health centers with trained birth attendants. Unit costs tend to increase with the complexity of the service. For example, clinic-based breastfeeding support and prevention of micronutrient deficiencies are inexpensive, compared with home visits and peer counseling to support breastfeeding and optimal child feeding or community-based treatment of SAM. Treatment of febrile illness and diarrheal disease are less expensive per child (US$20 to US$100) than treatment of pneumonia and meningitis, which typically require inpatient admission (US$150 per visit, or US$800 per child treated for pneumonia; US$300 to US$500 for inpatient care). Although the treatment of diarrhea is typically between US$2 and US$20 per visit for outpatient visits, treatment costs can be much higher and more variable when inpatient hospital care is required.

Other interventions for which affordability is an issue, and has likely slowed the rate of scale up, include

community management of SAM (US$120 per child), and facility-based delivery. Safe motherhood interventions including facility-based delivery are estimated to cost US$1.15 per person in the population, not including the initial investment in new facilities (Bhutta and others 2014). The year for the costing is not specified, so these amounts are assumed to be in 2014 U.S. dollars. Although US$1.15 per person sounds modest, with a crude birth rate of 25–30 per 1,000 population, it amounts to an increased cost per birth of US$33 to US$40, not a small sum in resource-constrained settings.

Similarly, the relatively high cost for water and sanitation has likely hindered scale up. In 2007 the initial investment costs per household for standard urban requirements, namely, water piped to the house and a sewer connection, were estimated to be US$102 and US$120, respectively. For the lowest-cost interventions in a rural area, these costs were still substantial: the lowest-cost clean water supply was US$21 per household for a dug well and US$23 for a borehole. The lowest cost sanitation, a pit latrine, was US$39 per household (all costs from Haller, Hutton, and Bartram [2007] in 2000 U.S. dollars).

An enormous international effort has gone into universalizing coverage of children with the EPI. According to Brenzel (2015), the cost per fully immunized child was US$25 in LICs (higher in higher-income regions) in 2008–11. She estimates that HiB, pneumococcus, and rotavirus will increase this amount to US$45 or more per fully immunized child. This cost may lead to affordability issues, even though these immunizations are cost-effective.

CONCLUSIONS

The large literature surveyed in this chapter suggests that many very cost-effective interventions could be used to address maternal, neonatal, and child health conditions. Simple solutions for newborn health, treatment of febrile illness, immunization against preventable childhood diseases, and micronutrient interventions are among the most cost-effective interventions and are affordable in many settings. Other studies explore how to provide existing interventions using new platforms to increase outreach or decrease cost per person covered, or both. Interventions provided in the community—for example, community management of SAM—may achieve both purposes to differing extent. Task-shifting, such as training lay health workers to provide vaccines, may decrease costs. Training traditional birth attendants in skills for safer deliveries may increase coverage.

The main challenge is to increase coverage of interventions known to be effective and cost-effective. These include many old interventions for which no new cost-effectiveness findings were identified past 2000, as well as new innovations whose cost-effectiveness is assessed in this chapter, such as vaccines for rotavirus and pneumococcus; biofortification of staple crops; RDTs for malaria; new protocols for community management of nutrition and of malaria or severe malaria; and prophylactic zinc for diarrhea. A few studies have focused on how to increase demand for services in settings in which supply is less the issue. Changing people's behavior can be more difficult than identifying ways to supply effective interventions. Some promising findings emerge for women's groups surveyed in the section on maternal and neonatal conditions. No cost-effectiveness studies were found for mHealth (that is, utilizing mobile phones to improve health), a growth area. Studies on cost-effectiveness of conditional cash transfers designed to enhance uptake of health interventions were not covered in the survey, and few studies provide such information, even though some conditional cash transfer programs have been found to be effective.

Despite the very large number of studies, research gaps persist. More information on cost-effective approaches to integration, task-sharing, and the use of CHWs to deliver community-based services is needed, along with new studies on costs and impacts for demand creation to increase coverage. The volume of studies in this area is so large that a single repository for cost-effectiveness studies for health in LMICs would be useful, along the lines of similar registries for high-income countries, for example, the Tufts Cost-Effectiveness Analysis Registry (https://research.tufts--nemc.org/cear4/Default.aspx) or that maintained at the University of York. Although published systematic reviews and the rise of common standards for grading studies are extremely helpful, the reviews are undertaken in different years and costs are not standardized to a single year. There are plans for a single registry for unit costs for health for LMICs, and a parallel registry of cost-effectiveness studies for health interventions in LMICs would be valuable.

Methodological gaps exist as well. The method for standardizing costs is not uniform, whether done in the currency of the original study or in U.S. dollars. In vaccine studies, the vaccine prices are not adjusted for inflation when cost-effectiveness is adjusted to a different year. Studies done in international dollars for a region (as is the case for a number of WHO-CHOICE studies from the Choosing Interventions that are Cost-Effective project, http://www.who/int/choice/en) could not be updated to dollars of a common year, at the time of writing this chapter, because the WHO has not provided

a time series for this price index. The resulting limitation is that none of those studies could be included here because they could not be updated to 2012 U.S. dollars. For some interventions, particularly the nutrition ones, benefits include improved quality of life rather than lives saved, and a benefit-cost analysis is a more appropriate methodology than cost-effectiveness. These and other methodological issues are addressed at more length in volume 9 of this series.

A larger unresolved issue is that of the DALY measure itself. More studies surveyed here used the discounted DALY measure than the other main measures—QALY, life-years, or deaths. The recent suggestion by the Institute for Health Metrics and Evaluation (Murray and others 2012) not to discount DALYs is likely to lead to confusion in the literature, with practitioners unsure about whether a particular study uses discounted or undiscounted DALYs. It will also drive a wedge between studies of HICs, where QALYs are discounted on a standard basis, and those of LMICs. Already, the lack of a single outcome measure makes comparisons of interventions more difficult, and this recent methodological advice will exacerbate the difficulties.

An innovation in modeling the cost-effectiveness of integrated interventions has been the use of LiST to estimate the impact and costs of packages of RMNCH interventions (Bartlett and others 2014; Bhutta, Das, Rivzi, and others 2013; Bhutta, Das, Walker, and others 2013; Bhutta and others 2014). The LiST model accounts for the synergies in effects such that lives saved are not double counted. However, the extent to which services can remain effective when management of them becomes more complicated, and when demands increase on the time of community-level personnel, remains to be verified in practice.

Analysis of cost and cost-effectiveness data has been an important tool in progress toward the MDGs and seems likely to continue to be useful with the transition to the Sustainable Development Goals.

NOTES

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

- Low-income countries (LICs) = US$1,045 or less
- Middle-income countries (MICs) are subdivided:
  a) lower-middle-income (LMICs) = US$1,046 to US$4,125
  b) upper-middle-income (UMICs) = US$4,126 to US$12,745
- High-income countries (HICs) = US$12,746 or more.

1. Note that the WHO uses the term DALY to mean the loss of a healthy year of life; hence, deaths and DALYs are bad things that health interventions try to avert, whereas life-years and Quality-Adjusted Life Years are good things that health interventions try to save ("Health Statistics and Information Systems: Metrics: Disability-Adjusted Life Year [DALY])." http://www.who.int/healthinfo/global_burden_disease/metrics_daly/en/).

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