Part **3**

Economic Evaluation Results from *Disease Control Priorities,* Third Edition

Cost-Effectiveness Analysis in *Disease Control Priorities,* Third Edition

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INTRODUCTION

League tables, which rank the cost-effectiveness of health interventions, are a useful input for prioritizing health expenditures, especially for national health budgets. They have been used as policy tools for high-income countries (HICs), including a comprehensive analysis for Australia (Vos and others 2010) and a similar analysis for cancer across HICs (Greenberg and others 2010). Some low- and middle-income countries (LMICs), such as Mexico, have also used league tables in their policy-making process (Salomon and others 2012).

For LMICs as a group, two major reviews of cost-effectiveness have informed strategies to achieve the Millennium Development Goals (MDGs) (Evans and others 2005; Laxminarayan, Chow, and Shahid-Salles 2006). However, cost-effectiveness is not the only important criterion for policy choice; sustainability, equity, and affordability, among others, also matter. Nevertheless, cost-effectiveness provides a useful and comprehensible reference point.

As strategies and priorities are set for the Sustainable Development Goals and countries consider the transition to universal health coverage, updating the previous reviews for LMICs is appropriate. This chapter synthesizes the results from recent analyses in six different disease areas to provide a comprehensive, updated comparison across a broad range of conditions; to examine changes during the past 10–12 years; and to highlight research gaps.

METHODS

A database of cost and cost-effectiveness results was constructed for the first six volumes of the *Disease Control Priorities,* third edition (*DCP3*) (Black and others 2016; Debas and others 2015; Gelband and others 2015; Holmes and others 2017a; Patel and others 2015; Prabhakaran and others 2017). Systematic searches were conducted in six major health areas, supplemented by expert surveys and existing published systematic surveys and reviews (Gaziano and others 2017; Holmes and others 2017b; Horton and Gauvreau 2015; Horton and Levin 2016; Levin and Chisholm 2015; Prinja and others 2015). The surveys covered literature from 2000 to mid-2013 published in English, because the literature before 2000 had been reviewed previously (Laxminarayan, Chow, and Shahid-Salles 2006).

The searches undertaken employed keywords associated with economic outcomes, the names of all LMICs and regions, and the main disease conditions relevant for each major health area. In this chapter, we report the results per disability-adjusted life year (DALY) averted. In most *DCP3* volumes, studies were also graded according to the Drummond checklist to assess the quality of the economic analysis (Drummond and others 2005). Further details of the searches and summaries of the findings for the six major health areas are available (Gaziano and others 2017; Holmes and others 2017b; Horton and Gauvreau 2015; Horton and Levin 2016; Levin and Chisholm 2015; Prinja and others 2015).

Summary information about each of the 93 health interventions analyzed and full references for the 149 published studies are provided in annex 7A.

All costs were converted to 2012 U.S. dollars by adjusting prices to 2012 values in the original currency of the relevant country and then converting those amounts to U.S. dollars using the exchange rate for 2012. The costs for one group of studies were expressed in international dollars of a World Health Organization (WHO) region (Evans and others 2005) and could not be readily converted, because consumer price indices and exchange rates with the U.S. dollar are not publicly available for those regional aggregates. Although methods exist to make an approximate conversion, the additional information required is not always readily available from the original study, namely, the proportion of all costs (both of the intervention itself and, where relevant, of those costs averted by the intervention) accounted for by tradable and nontradable inputs.

We opted to use exchange rate conversions rather than purchasing power parity (PPP) conversions. Studies using the Choosing Interventions that are Cost-Effective (WHO-CHOICE) methodology (Evans and others 2005) have often used PPP conversions, which assume that health interventions have the same mix of tradable and nontradable inputs as the economy does overall. However, health interventions vary considerably, from those involving behavior change communication by community health workers (relying heavily on nontradable inputs) to vaccine delivery or use of rapid diagnostic tests (relying heavily on tradable inputs); no single conversion method is perfect. We opted for the exchange rate method because it is more readily understood by noneconomists, and it allows comparison with the earlier *Disease Control Priorities* work (Laxminarayan, Chow, and Shahid-Salles 2006). Using market exchange rates, however, can be problematic if they do not respond immediately to differential rates of inflation between countries.

The cost-effectiveness rankings from individual volumes were aggregated to provide two sets of league tables—one for adults and one for children. In a few cases where no study using DALYs was available for an important intervention—for example, human papillomavirus (HPV) vaccination—a study using quality-adjusted life years (QALYs) was used instead, and this substitution is indicated. A natural logarithmic scale was used for cost in the figures because small differences in cost per outcome are less important for the least cost-effective interventions, that is, those with the highest cost per outcome. For some interventions, a single study provided a point estimate for cost-effectiveness; for other interventions, multiple studies were available,

or the individual study provided a range of estimates. In the figures, the geometric mean of the endpoints of the range was the point estimate used. This approach works better for a natural log scale axis and is more appropriate when the ranges are very different.

The WHO has issued guidelines on thresholds for acceptable costs per DALY averted. The recommendation is that anything costing less than the per capita gross national income (GNI) per DALY averted is "very cost-effective" (WHO 2001); anything costing less than three times per capita GNI is "cost-effective." Recent research suggests that health budget constraints are too tight to be able to afford everything, even those items that are very cost-effective according to the WHO threshold. Accordingly, thresholds should be lower (Claxton and others 2015). Deriving a more appropriate threshold—for example, using the marginal health gain with the existing health budget—requires country-specific data. A recent analysis suggests that a threshold of approximately one-half of GNI per capita would be more appropriate for LMICs than the WHO-suggested threshold and better reflects funds that taxpayers in those countries are able and willing to spend from the public budget (Ochalek, Claxton, and Lomas 2016).

In our review, a lower threshold of US$200 per DALY is used to identify priority interventions for consideration in low-income countries (LICs); all but three countries in the World Bank database had per capita income above US$400 in 2014. A higher threshold of US$500 is used to identify priority interventions for consideration in lower-middle-income countries, all of which had per capita GNI above US$1,045 in 2014. Other considerations, such as equity, affordability, and feasibility will also be important in priority setting for individual countries, depending on the context.

RESULTS

We identified cost-effectiveness estimates for 93 interventions and contexts (figures 7.1–7.4), drawn from 149 studies. We excluded cost-effectiveness studies of tax and subsidy policies. Although broad national policy changes are very important, estimating their costs is more difficult, and their cost-effectiveness is not readily compared with that of individual health interventions.

In a few cases, the same intervention appears more than once in different contexts, with different costs per DALY averted. For example, the cost-effectiveness of HPV vaccination has been estimated at two different prices per vaccinated girl: the lower price from Gavi—the Vaccine Alliance (Gavi) is available to some lower-middle-income countries—and the usually higher price applies to countries ineligible for Gavi support.

Figure 7.1 Interventions Costing Less than US$100 per DALY Averted for Adults
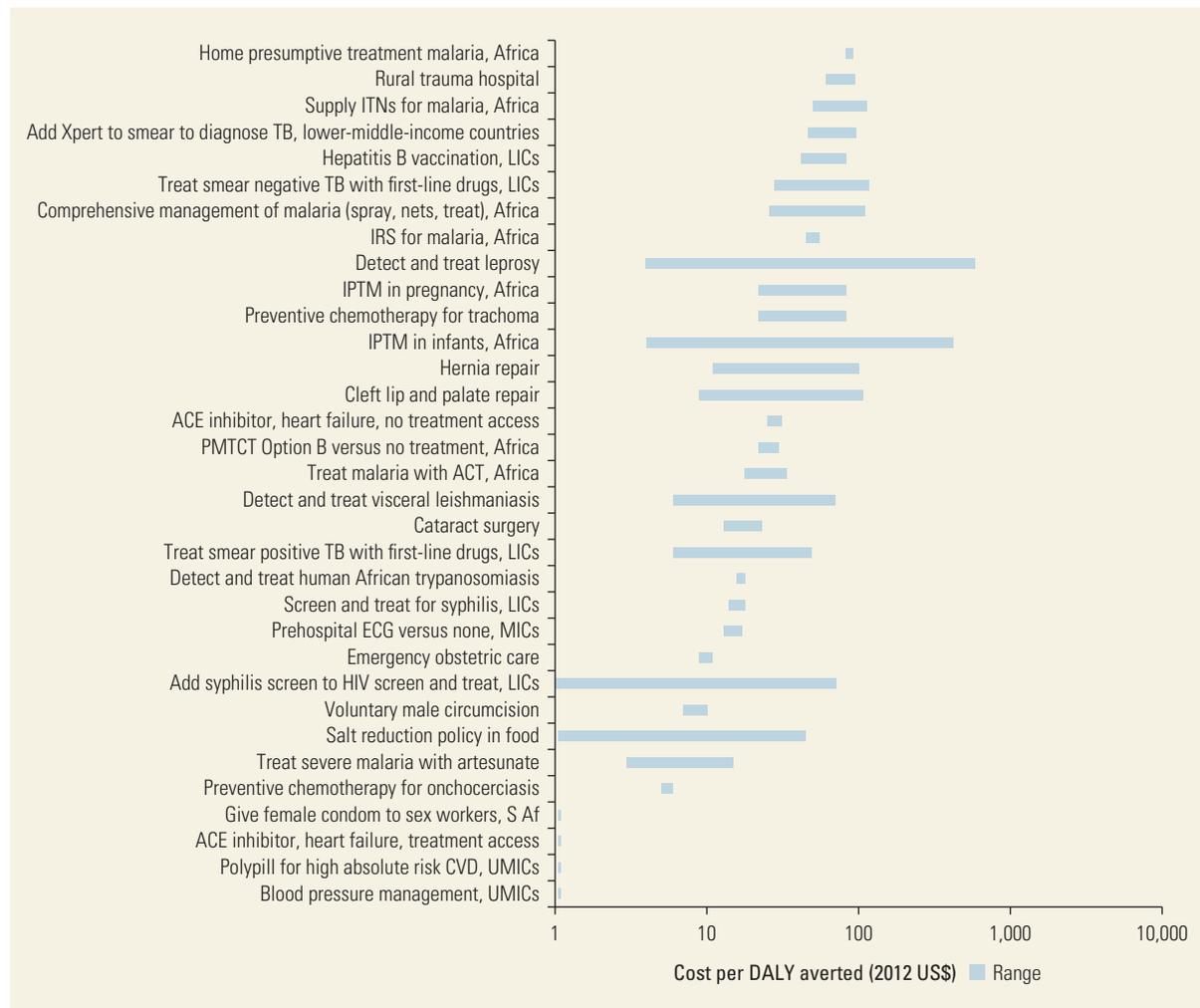
Note: ACE = angiotensin converting enzyme; ACT = artemisinin-based combination therapy; CVD = cardiovascular disease; ECG = electrocardiogram; IPTM = intermittent preventive treatment for malaria; IRS = indoor residual spraying; ITNs = insecticide-treated nets; LICs = low-income countries; mgt = management; MICs = middle-income countries; Option B = use of two-drug regime for pregnancy for PMTCT; PMTCT = Prevention of Mother-to-Child Transmission of HIV; S Af = South Africa; TB = tuberculosis; UMICs = upper-middle-income countries.

Gavi has used its ability to undertake bulk purchases and multiyear commitments for vaccines to obtain favorable prices. However, only those countries eligible for Gavi support have access to these prices; other countries must negotiate prices with manufacturers.

Where relevant, the economic level of the country where the study was conducted is identified (for example, LICs as compared to lower-middle-income countries and UMICs) because human resource costs vary significantly and disease patterns are different. In other cases, particularly for the human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS), the epidemiologic context is identified.

The results from southern Africa, which faces a generalized epidemic in a few countries, differ from those of other countries, where the epidemic is more concentrated in certain population groups. If no context is identified, the results are expected to be generally applicable in LMICs.

Of the 93 cost-effectiveness estimates, 37 percent relate to interventions for reproductive, maternal, newborn, and child health interventions and 24 percent relate to interventions for major infectious diseases—HIV/AIDS, tuberculosis, malaria, and neglected tropical diseases (NTDs). This finding is not surprising, given that the MDGs focused on these areas of health.

Figure 7.2 Interventions Costing between US$100 and US$999 per DALY Averted for Adults
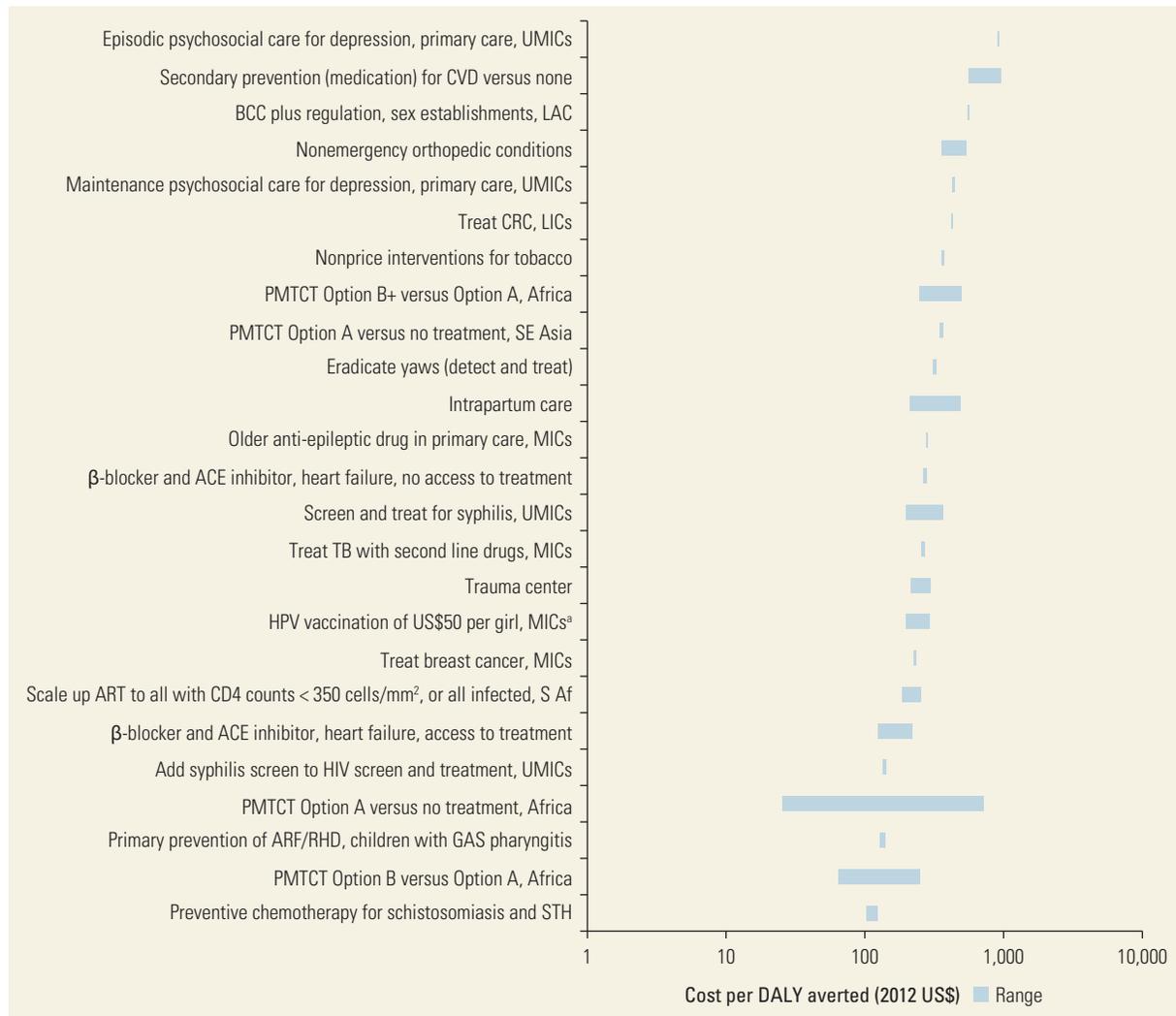
Note: ACE = angiotensin converting enzyme; ARF/RHD = acute respiratory failure/rheumatic heart disease; ART = antiretroviral therapy; BCC = behavior change communication; CRC = colorectal cancer; CVD = cardiovascular disease; HPV = human papillomavirus; LAC = Latin America and the Caribbean; LICs = low-income countries; MICs = middle-income countries; Option A = use of single-drug regime for pregnancy for PMTCT; Option B = use of two-drug regime for pregnancy for PMTCT; Option B+ = use of two-drug regime during pregnancy and then lifelong for PMTCT; PMTCT = Elimination of Mother-to-Child Transmission of HIV; STH = soil-transmitted helminths; TB = tuberculosis; UMICs = upper-middle-income countries.

a. Denotes outcome in QALYs (quality-adjusted life years).

International organizations, such as Gavi and the Global Fund to Fight AIDS, Tuberculosis, and Malaria, mobilized significant resources, leading to considerable interest in, and funding for, cost-effectiveness studies in these health areas. Far fewer economic studies are available for each of the other four areas considered: cancer, cardiovascular disease, mental health, and surgery.

Studies are typically conducted where new policy measures are being considered, such as new vaccines, new guidelines for treatment, and new diagnostic tools. Hence, no new studies were found for well-established interventions, such as the original Expanded Program of Immunization with six vaccines. Pre-2000 studies of some of these established interventions exist. In other cases, for example, emergency appendectomy, the importance of the intervention was established long before cost-effectiveness estimates became common for LMICs, and thus, no studies were found.

Figure 7.3 Interventions Costing US$1,000 or More per DALY Averted for Adults
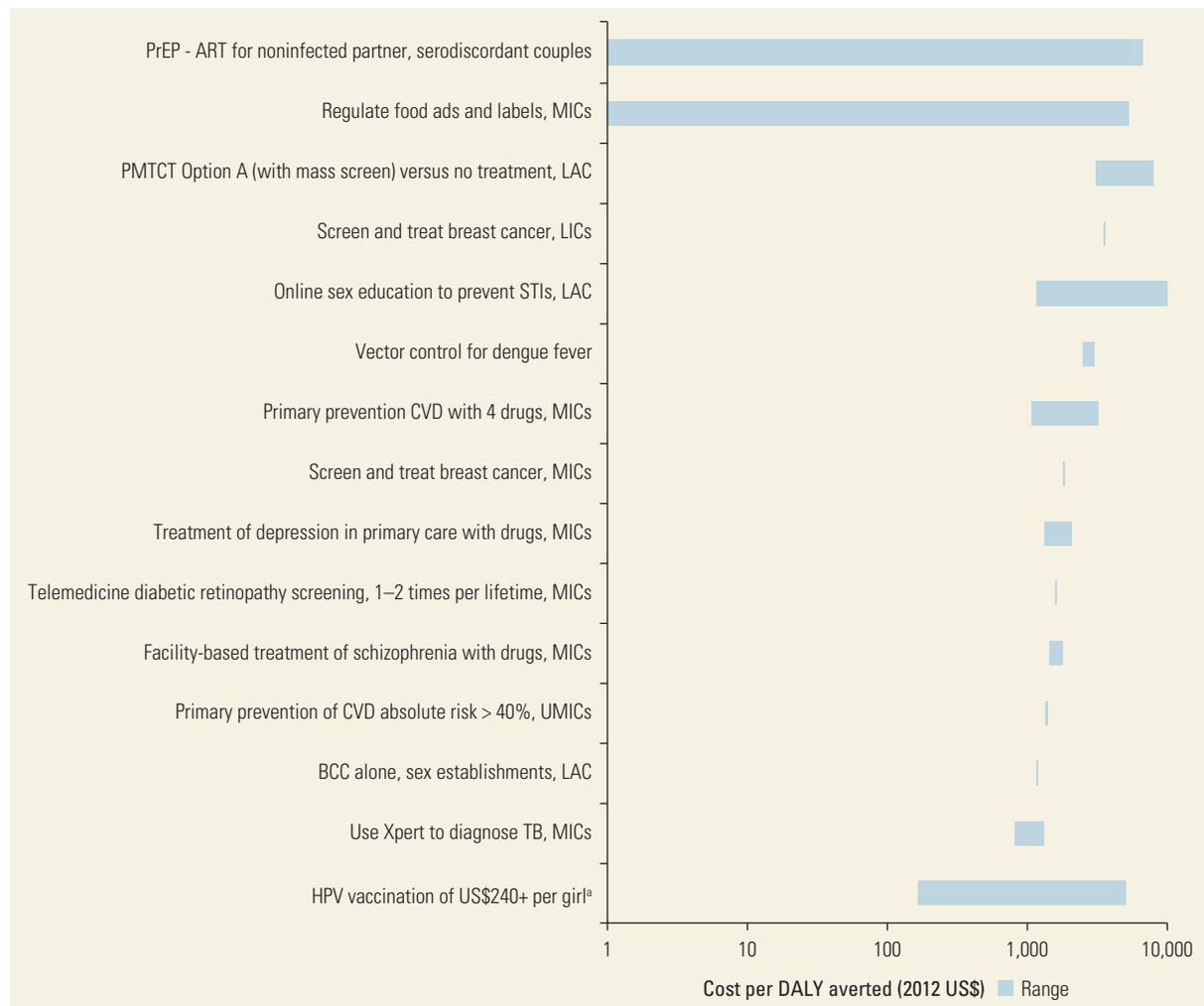
Note: ART = antiretroviral therapy; BCC = behavior change communication; CVD = cardiovascular disease; HPV = human papillomavirus; LAC = Latin America and the Caribbean; LICs = low-income countries; MICs = middle-income countries; Option A = use of single-drug regime for pregnancy for EMTCT; PrEP = pre-exposure prophylaxis; PMTCT = Prevention of Mother-to-Child Transmission of HIV; STIs = sexually transmitted infections; TB= tuberculosis; UMICs = upper-middle-income countries.
a. Denotes outcome in QALYs (quality-adjusted life years).

More than half of the interventions in figures 7.1–7.4 cost less than US$200 per DALY averted. These interventions could be considered for publicly funded health care in LICs and include the following:

- **Treatment of various, primarily infectious diseases**: Treatment for malaria, tuberculosis (including tuberculosis that is resistant to first-line drugs), HIV/AIDS, syphilis, and four of the NTDs; basic treatment using medication for heart failure
- **Prevention of various, primarily infectious diseases:** Male circumcision; intermittent preventive treatment in pregnant women and in infants against malaria, as well as insecticide-treated nets and indoor residual spraying; antiretroviral therapy for pregnant women; hepatitis B vaccinations; and HPV vaccination at US$50 per fully vaccinated girl
- **Pneumococcus, rotavirus, and Haemophilus influenza type b (Hib) vaccines in LICs**
- **Selected basic surgical interventions**: Basic trauma surgery and emergency obstetric care; surgery for cataracts, hernia, and cleft lip and palate
- **Other miscellaneous interventions:** Training traditional birth attendants and general practitioners for births; community-based neonatal care.

Figure 7.4 Interventions for Children
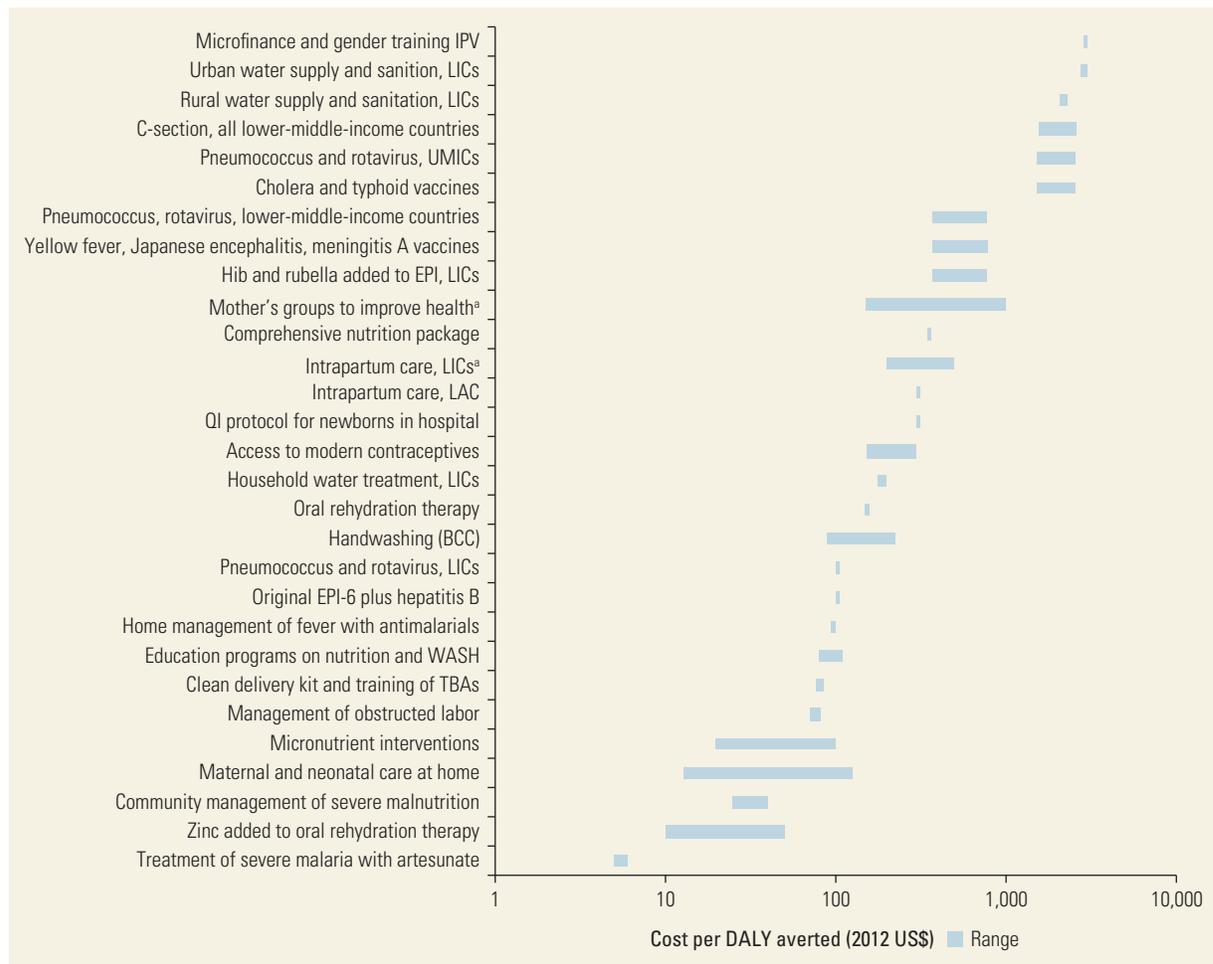
Note: BCC = behavior change communication; EPI = expanded program of immunization; Hib = *Haemophilus influenza* type b; IPV = intimate partner violence; LAC = Latin America and the Caribbean; LICs = low-income countries; QI = quality improvement; TBAs = traditional birth attendants; UMICs = upper-middle income countries; WASH = water, sanitation, and hygiene.

a. Denotes outcome in QALYs (quality-adjusted life years).

Those interventions costing US$200–US$500 per DALY averted could be considered for lower-middle-income countries in addition to the items listed. These include the following:

- Surgery for selected nonemergency orthopedic conditions
- Selected interventions for mental health in primary care settings
- Treatment of one additional NTD
- Various nutrition interventions.

Examples of interventions costing more than US$500 per DALY averted and potentially appropriate for consideration in upper-middle-income countries include the following:

- Secondary and primary prevention of cardiovascular disease with medication
- Additional mental health interventions
- Pre-exposure prophylaxis as antiretroviral treatment of uninfected partners of HIV-infected individuals
- Selected behavior-change interventions
- Provision of balanced protein–energy supplements in pregnancy.

DISCUSSION

A similar analysis to the one reported here was conducted for *Disease Control Priorities in Developing Countries* (second edition; Jamison and others 2006).

It covered studies through the year 2000 (Laxminarayan, Chow, and Shahid-Salles 2006) and provided an informative source of comparison for the current results that date from 2000 through part of 2013. The differences are not only in the results of cost-effectiveness studies but are also—tellingly—in the topics studied.

About half of the interventions appear in both the pre- and post-2000 compilations; the remainders represent some significant changes. Some new interventions that were not in widespread use before 2000—many of them related to substantial investments in new technologies and new methods to change behavior over the MDG period—have been evaluated. For some interventions, substantial reductions in prices have occurred that have made previously unaffordable interventions less costly and more cost-effective. This is particularly true for vaccines, in cases where efforts by Gavi and others have led to lower vaccine prices, and for malaria and AIDS treatments, in cases where efforts by the Global Fund to Fight AIDS, Tuberculosis, and Malaria and Médecins sans Frontières, among others, have similarly led to reduced drug prices. Some new areas of health care, particularly those not involving MDG targets, have been studied, making more detailed cost-effectiveness data available beyond the areas of maternal and child health and major infectious diseases. Some interventions have changed priorities, either as the disease context has changed or as experience has led to a revision of what was expected, based on pilot programs.

Finally, some interventions no longer appear on the list, despite being found to be cost-effective in the previous study. This may be because they have been mainstreamed and either no further need exists to estimate or update cost-effectiveness or they have been superseded by other more effective or more cost-effective interventions. Examples in each of these categories are given in the following sections.

New Technologies and Methods

New interventions for which cost-effectiveness data have become available for LMICs include treating severe malaria with rectal or injected artesunate, which can be done before hospital arrival; adding GeneXpert testing to sputum-smear testing to diagnose disease and determine antibiotic susceptibility; and HPV vaccination for girls to prevent cervical cancer. These all fall into the range of less than US$200 per DALY averted in the appropriate contexts. However, other new technologies, such as pre-exposure prophylaxis, have a relatively high cost per DALY averted in most cases.

Changes in Prices

Reduced prices of pneumococcal and rotavirus vaccines are examples of changes in costs that dramatically change the cost-effectiveness of the interventions. These interventions were high cost per DALY averted in the pre-2000 review, but at current Gavi prices for LICs, the cost is now less than US$100 per DALY averted. Another major example is the NTDs. Following the 2012 London Declaration (Uniting to Combat NTDs Coalition 2016), the key drugs to combat NTDs have been donated by the manufacturers, which has moved the elimination of NTDs by prevention and treatment substantially higher up the priority list in terms of cost-effectiveness in the past decade.

New Health Areas

Efforts by the surgical community (for example, the *Lancet* Commission on Global Surgery and the *DCP3* volume 1 on surgery [Debas and others 2015]) have increased the interest in and emphasis on cost-effectiveness of surgery. Several surgical interventions cost less than US$200 per DALY averted. In urgent cases, these same interventions can be implemented in a first-level hospital with a general surgeon (for example, emergency obstetric care and basic trauma care); in nonurgent cases, they can be implemented in a specialized facility with high volume and modest cost (for example, cataract surgery or repair of cleft lip and cleft palate). Similar efforts are underway in the global cancer community. One study suggests that treatment of early-stage breast cancer falls in the category of less than US$200 per DALY averted for middle-income countries (although not in LICs, where screen-and-treat approaches cost more than US$200 per DALY averted).

Interventions That Have Changed Priority

School-based adolescent health and nutrition programs appeared as a high priority because of their low cost per DALY averted in 2006. This was not the case in 2016, because more recent studies are much more cautious about whether these programs will have long-term positive effects.

Interventions That Are No Longer on the List

Changing technology also means that some previously cost-effective interventions have been superseded or have become usual care. This is particularly evident

for HIV/AIDS. In the pre-2000 compilation, eight interventions appeared in the highest-priority list. Peer and education programs for high-risk groups; condom promotion and distribution; voluntary counseling and testing without treatment; diagnosis and treatment of sexually transmitted infections; blood and needle safety; tuberculosis coinfection prevention and treatment; opportunistic infection treatment; and prevention of mother-to-child transmission were included among the most cost-effective interventions (using less than US$150 per DALY averted in 2001 U.S. dollars, roughly comparable to less than US$200 per DALY averted in 2012 U.S. dollars). A decade later, with treatment with antiretroviral agents on the highest priority list, all but two of the other interventions fell off the list; the remaining two are prevention of mother-to-child transmission and testing for and treatment of other sexually transmitted infections. Most of the interventions had become usual care, but voluntary counseling and testing without treatment had been superseded by test-and-treat approaches.

A major limitation of the cost-effectiveness literature, particularly acute in LMICs, is its bias toward the diseases of greatest interest during the period under study. In the current study, the literature overrepresents infectious conditions and childbirth, because these have been prioritized by international donors. Drugs and vaccines tend to be overrepresented relative to behavior change interventions, because manufacturers use cost-effectiveness data as part of the adoption process.

Measurement Issues

The ability to conduct a large comparative study such as this relies on use of common methodologies by individual study authors. For effectiveness studies, progress has been made applying standard guidelines for systematic reviews and using explicit criteria for evaluating evidence. For economics studies, the fairly recent adoption of a common set of reporting standards (Husereau and others 2013) and the development of a reference case for conducting economic evaluations in LMICs (NICE International 2014) are moves in the same direction.

A larger issue is the common metric for cost-effectiveness. The DALY has been the predominant health outcome metric used for studies of LMICs over the past decade or more. It has the advantage over the QALY for work in multiple countries in that a single set of disability weights is used across countries, whereas QALY weightings are, in theory, country specific, and generating QALY weights can be a costly process.

Recent concerns about the DALY relate to the issue of discounting costs and health benefits further in the future. Although this issue is very much accepted by economists, some health specialists find it more problematic. The Institute for Health Metrics and Evaluation has begun using undiscounted DALYs to measure global burden of disease (Murray and others 2012) but without using a new term to differentiate these undiscounted DALYs. This approach is already causing confusion.

The DALY measure itself has limitations. Using the DALY measure tends to underrepresent interventions where outcomes are not readily measured in this metric, such as family planning, and interventions in nutrition where the outcomes are improved cognition rather than improved health, more readily measured with benefit:cost analysis ratios.

On the cost side, studies predominantly use market exchange rates to compare across different currencies. However, an influential body of work from the WHO, the WHO-CHOICE study, used international dollars for WHO subregions rather than countries. International dollars make cross-country comparisons somewhat easier to understand by adjusting for salary differences as a component of costs. The downside is that international dollars make comparison more difficult with other studies not using international dollars. One does not simply use the US$/PPP exchange rate, because having information about cost structure is necessary. A further complication is the lack of published indices for PPP exchange rates of regions.

The advantage of WHO-CHOICE was the ability to compare many interventions at one time, when the MDG strategies were being evaluated, and to compare the outcome of combinations of interventions. The disadvantage is that funding to replicate such a large comprehensive evaluation is difficult to attain. The use of simpler methods, such as market exchange rates, allows the synthesis of many smaller, individually directed studies.

CONCLUSIONS

Cost-effectiveness is not the only criterion by which to choose health priorities, but it is useful for identifying what is given up when a less cost-effective intervention is prioritized. It is also a useful tool for advocacy for increased health budgets. This review has used cost-effectiveness measures from several hundred studies for LMICs to help identify candidates for priority health packages, which may assist policy makers considering how to move to universal health coverage.

This review has identified some of the gaps where future research on cost-effectiveness is needed:

- Given the ongoing decline in infectious disease burden and the growing burden of NCDs, more analyses for NCDs are needed for LMICs. Achieving the goal of health convergence within a generation will not be possible without initiating interventions to reduce NCDs, where the lag between intervention and outcomes is often much longer than for infectious diseases.
- The review highlights the lack of any study of cost-effectiveness for childhood cancer and the dearth of information on cost-effective interventions for mental health in LMICs.
- Another area for future work includes the cost-effectiveness of resource-appropriate treatment of early-stage cancers, such as breast and cervical cancers.
- Given the growth of obesity worldwide, cost-effectiveness studies of interventions to change patterns of diet and inactivity in urban areas are needed.

A publicly available online global database of cost-effectiveness studies using DALY outcomes will make future updates easier (Tufts University 2016).

The major changes in ranking of health priorities over the past decade underscore the need for periodic repetition of league table exercises such as this one.

ACKNOWLEDGMENTS

ANNEX

The annex to this chapter is as follows. It is available at http://www.dcp-3.org/DCP.
- Annex 7A. Details of Interventions Included in figures 7.1, 7.2, 7.3, and 7.4, by Increasing Cost per DALY Averted.

NOTE

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

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

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