Center for Global Development

HIV Modelling Consortium

THANZI LA ONSE

UNDERSTANDING THE OPPORTUNITY COST, SEIZING THE OPPORTUNITY

Report of the Working Group on Incorporating Economics and Modelling in Global Health Goals and Guidelines

Paul Revill and Amanda Glassman
Co-Chairs

Center for Global Development

HIV Modelling Consortium

THANZI LA ONSE

UNDERSTANDING THE OPPORTUNITY COST, SEIZING THE OPPORTUNITY

Report of the Working Group on Incorporating Economics and Modelling in Global Health Goals and Guidelines

Paul Revill and Amanda Glassman
Co-Chairs

Center for Global Development
2055 L Street, NW Fifth Floor
Washington, DC 20036
www.cgdev.org

Contents

Appendixes

Boxes

Figures

Tables

About the Working Group

The Center for Global Development (CGD) is a "think-and-do tank" that works to reduce global poverty and inequality through rigorous research and active engagement with the policy community. CGD's Global Health Policy program focuses primarily on the economics and financing of global health, with particular attention to how donor agencies and multilateral institutions allocate, distribute, and ensure accountability for global health funds to achieve the best possible value for money and meet key global health goals. CGD has amassed broad experience in the global health arena and in determining good practices for the efficient allocation and distribution of funds.

The Working Group on Incorporating Economics and Modelling in Global Health Goals and Guidelines, co-convened by the Center for Global Development, Thanzi la Onse, and the HIV Modelling Consortium, was launched to take stock of current approaches and methods to goal and guideline setting and to consider how approaches to informing resource prioritization can be enhanced and better implemented. Working group meetings were held between 2017 and 2019, and brought together economists, modelers, disease specialists, and policymakers from international organizations and national governments. The objective of the first meeting, held in November 2017 in Washington, DC, was to review the processes used by international organizations to generate global goals and guidelines and assess their impact at the national level. At the second meeting, held in October 2018 in London, participants reviewed the recommendations to be delivered from the working group. In addition to these two meetings, consultations were held with staff members from the World Health Organization (WHO) and the Joint United Nations Programme on HIV/AIDS (UNAIDS) in Geneva in February 2018 and April 2019.

Working Group Members

Ajay Rangaraj, World Health Organization

Andrea Ciaranello, CEPAC/Massachusetts General Hospital

Andrew Kambugu, Infectious Diseases Institute, Uganda

Andrew Phillips, University College London

Anthony McDonnell, University of Oxford

Carol Levin, University of Washington

Charlie Gilks, University of Queensland

Chutima Suraratdecha, Centers for Disease Control and Prevention

Daniel Klein, Institute for Disease Modelling

David Wilson, Bill & Melinda Gates Foundation

Edward Kataika, East Central Southern Africa (ECSA) Health Community

Eliana Barrenho, Imperial College London

Elizabeth Chizema, National Malaria Elimination Programme, Zambia

Elizabeth Stuart, Overseas Development Institute

Ellen McRobie, Imperial College London

Gesine Meyer-Rath, HE^{2}RO, University of Witwatersrand and Boston University

Ian Weller, University College London

John Stover, Avenir Health

Julie Jemutai, KEMRI-Wellcome Trust, Kenya

Kalipso Chalkidou, Center for Global Development

Katharina Hauck, Imperial College London

Kenneth Katumba, MRC/UVRI, Uganda

Krisantha Weerasuriya, Former World Health Organization

Marelize Gorgens, World Bank

Mark Sculpher, University of York

Martin Chalkley, University of York

Mead Over, Center for Global Development

Miqdad Asaria, London School of Economics and Political Science

Nishant Jain, GIZ, India

Ole Norheim, University of Bergen

Rachel Silverman, Center for Global Development

Ruanne Barnabas, University of Washington

Samantha Diamond, Clinton Health Access Initiative

Sibusiso Sibandze, East Central Southern Africa (ECSA) Health Community

Sergio Bautista, Public Health Institute of Mexico

Stefano Bertozzi, University of California-Berkeley

Tim Hallett, Imperial College London

Tommy Wilkinson, PRICELESS, South Africa

Yot Teerawattananon, HITAP, Thailand

Acknowledgements

This document is the final report of the Working Group on Incorporating Economics and Modelling in Global Health Goals and Guidelines, co-convened by the Center for Global Development, Thanzi la Onse, and the HIV Modelling Consortium between 2017 and 2019.

We are grateful to working group members as well as others who provided thoughtful comments, critiques, and suggestions. Although the report reflects the discussions and views of the working group, it is not a consensus document. All errors and omissions are those of the authors. The working group was chaired by Paul Revill (University of York and Center for Global Development) and Amanda Glassman (Center for Global Development), and the report was written by Paul Revill, Ajay Rangaraj, Martin Harker, and Amanda Glassman, with input from and special thanks to Ellen McRobie, Gesine Mayer-Rath, Rachel Silverman, Jessie Lu, Brin Datema, and Rebecca Forman. Emily Schabacker coordinated production of the report and Stephanie Brown designed the cover.

This work was supported by the International Decision Support Initiative (www.idsihealth.org), a global initiative to support countries to get the most from every dollar they spend on health. This work also received funding support from the Bill & Melinda Gates Foundation, UK Department for International Development, UK Research and Innovation as part of the Global Challenges Research Fund (Thanzi la Onse grant number MR/P028004/1), and individual CGD funders.

CGD is an independent and nonpartisan research institution. There are no conditions or limitations on CGD's independence in research, findings, conclusions, or resulting publications. Where appropriate, CGD may welcome and consider comments or views from donors, but CGD retains total discretion and final decision-making authority regarding program and project research topics, speakers, and participants in activities, and on the content of reports.

Abbreviations and Acronyms

AEM	Asian Epidemic Model
ART	Antiretroviral therapy
CDC	Centers for Disease Control and Prevention (United States)
CGD	Center for Global Development
CHAI	Clinton Health Access Initiative
CPR	Contraceptive prevalence rate
DALYs	Disability-adjusted life years
DOH	Department of Health
EGPAF	Elisabeth Glaser Pediatric AIDS Foundation
EHP	Essential Health Package (Malawi)
FP2020	Family Planning 2020
GDP	Gross domestic product
GPRM	Global Price Reporting Mechanism
GPW 13	13th General Program of Work
GRADE	Grading of Recommendations Assessment, Development and Evaluation
GRC	Guidelines Review Committee
HCV	Hepatitis C
HE^2RO	Health Economics and Epidemiology Research Office (South Africa)
HIV/AIDS	Human Immunodeficiency virus/ Acquired Immunodeficiency syndrome
HTA	Health technology assessment
ICER	Incremental cost-effectiveness ratio
iDSI	International Decision Support Initiative
LMICs	Low- and middle-income countries
MDGs	Millennium Development Goals
MOH	Ministry of Health
NAC	National ART Advisory Committee
NACM	National Antiretroviral Treatment Cost Model
NGOs	Nongovernmental organization
NHS	National Health Service (United Kingdom)
NICE	National Institute for Health and Care Excellence (United Kingdom)
NSP	National Strategic Plan
PEPFAR	President's Emergency Plan for AIDS Relief (United States)
PICO	Population, Interventions, Comparators, Outcomes
PLHIV	Person living with HIV
PMTCT	Prevention of mother-to-child transmission (of HIV)
QALYs	Quality-adjusted life years
RCT	Randomized clinical trial
SDGs	Sustainable development goals
UHC	Universal Health Coverage
UNAIDS	United Nations joint program for AIDS
UNMHCP	Uganda National Minimum Health Care Package
USAID	United States Agency for International Development
WHO	World Health Organization
WHO-CHOICE	Choosing Interventions that are Cost-Effective

Key Terms

Cost effectiveness: In its most general sense, the attainment of a given rate of output or outcome at the lowest possible opportunity cost. Whether the output or outcome in question is worth its cost is another matter, not addressed directly by cost effectiveness.

Cost-effectiveness analysis: A method for comparing the opportunity costs of various courses of action having the same benefit or in terms of a common unit of output, outcome, or some other form of measurement.

Economic evaluation/appraisal: Determining the value of a procedure, clinical intervention, or process through the systematic consideration of its advantages and disadvantages, their distributions, and probabilities attached to them.

Equity: Considerations related to the fairness of the distribution of such factors as health, opportunity, or accessibility.

GRADE approach (also referred to as "GRADE methodology"): A system for rating the quality of a body of evidence in systematic reviews, health technology assessment, and guidelines. This includes production of a GRADE evidence profile and/or a summary of findings table.

Grade process: Refers to the framework set out by the GRADE working group that encompasses the GRADE approach (see above) but also includes the process of specifying health care questions, prioritization of outcomes, and evaluation of all available evidence, accounting for patient values, preferences, and society. The process is typically initiated by the national/international body responsible for the production of normative guidelines.

Guidelines: Recommendations on the appropriate treatment and care of patients with specific diseases and conditions, usually drawn up by multidisciplinary groups of experts and, ideally, based on systematic reviews from literature.

Health economic analysis: Used here in relation to the economic evaluation or appraisal of health or health-related outcomes and costs.

Health economics: The application of economic theory to phenomena and problems associated with health.

Health opportunity cost: The value of a resource in its most highly valued alternative use, in this case pertaining to health care and health care decision making.

Modeling: Used here in reference to health economics, the term refers to empirical modeling, which is related to cost-effectiveness analysis and associated techniques. Modeling is generally constructed to project costs and consequences beyond the end points of clinical trials in order to estimate both clinical effectiveness and cost effectiveness.

Sources: Definitions for "grade approach" and "grade process" adapted from the GRADE Handbook, updated October 2013, https://gdt.gradepro.org/app/handbook/handbook.html); all others from A. J. Culyer, *The Dictionary of Health Economics*, 2nd ed. (Cheltenham: Edward Elgar, 2010).

Executive Summary

Internationally set goals and guidelines directly influence the setting of health care priorities at the national level, affecting how limited resources are generated and allocated across health care needs. The influence of global priority setting, such as through the formulation of overarching goals or normative guidelines for specific disease areas, is particularly significant in low- and middle-income countries that rely heavily on overseas development assistance. Because no systematic approach exists for dealing with resource constraints, however, which vary across countries, goals and guidance are often inappropriate for some country contexts; their implementation can, therefore, reduce the efficiency and equity of health care spending.

The Working Group on Incorporating Economics and Modelling in Global Health Goals and Guidelines, co-convened by the Center for Global Development, Thanzi la Onse, and the HIV Modelling Consortium, has brought together disease specialists, policymakers, economists, and modelers from national governments, international organizations, and academic institutions across the globe to address these issues, to take stock of current approaches, and make recommendations for better practice. The Working Group deliberated on the roles and purposes of goals and guidelines and considered how economic evidence might be formally incorporated into policy recommendations and health care decision making. The target audiences for this report are international health institutions, large stakeholders in disease programs across the world, and national governments.

The Working Group has established core principles and accompanying recommendations for policymakers seeking to support national governments in setting locally relevant priorities. The report also offers recommendations to international organizations—in particular, the World Health Organization (WHO)—on the appropriate use of economic analysis in the development of international guidelines.

The principles and recommendations emphasize the importance of recognizing local context and enabling and strengthening the capacity of national governments to set priorities locally. They also stress the strengths and limitations of international WHO guidelines; the value of epidemiological modeling and economic assessment to guiding policy under resource constraints; the importance of good-quality epidemiological and economic data to inform country decision making; and the benefits of increased interagency and intergovernmental cooperation, accountability, transparency, and information sharing.

The principles and recommendations are outlined below. If implemented in full, the recommendations would lead to a systemic shift, from a situation where priorities are largely set internationally and implemented locally to one where international priorities account for local contexts and constraints on delivery. These principles and recommendations are anticipated to lead to greater population health gains attained from within the limited resources available for health care by facilitating the use of resources where they have the largest beneficial impacts.

This approach has risks. When necessary evidence and capacity are lacking—a common scenario—priorities set using it may still be inappropriate, given local objectives and constraints. The final section of the report thus considers unanswered questions and outlines an agenda for additional research.

Recommendations

Our recommendations have two objectives: first, to empower countries to develop and analyze appropriate evidence to set health priorities for their populations; and, second, to strengthen the WHO guidelines program to increase its value and relevance for national decision makers. The working group understands and acknowledges the challenges that accompany a major shift in how goals and guidelines are developed and recognizes that changes of this magnitude take time to implement.

Empowering national governments to set evidence-based health priorities for their populations

Principles

- National health strategies and priorities should ideally be set by local decision makers who are accountable to their citizens, considering all available evidence.
- International health priorities and goals should primarily reflect and account for national priorities, whilst addressing common challenges that cross national borders.
- When deciding health priorities and goals, local decision makers should evaluate economic evidence using appropriate metrics that reflect local preferences and values.
    - Decision makers need measures of health benefit that facilitate comparisons across disease areas—for example, generic measures of health, such as quality-adjusted life years (QALYs) and disability-adjusted life years (DALYs). In line with local preferences and values, they may also consider benefit measures that reflect equity concerns and other dimensions of social value.
- Economic analysis and modeling, designed for or adapted to local context, is often required to inform prioritization within limited resources.
    - While the demand for such analyses should ideally be led by governments and local agencies, support in the form of funding and technical guidance from international bodies and experts will sometimes be required.
- Locally relevant clinical and economic evidence is required to inform such analyses.
    - Ideally, economic evidence (for example, on resource use and costs) will be generated locally. Where this is not feasible, evidence may be taken from other relevant jurisdictions.
    - Clinical studies will often be undertaken in different settings. The relevance of available clinical evidence to the local setting needs to be carefully assessed.

Recommendations for international agencies

- Reaffirm that decision-making responsibility for the adoption and funding of interventions lies at the country level or even lower, with decision makers who represent their citizens and are equipped with appropriate clinical and economic evidence.
- Support local production of economic and epidemiological analyses and enhance local capacity to produce such evidence.
    - Locally led research activities can be supported by providing funding and appropriate technical support.

- Support countries in establishing consistent resource allocation processes informed by appropriate local evaluations.
  - The establishment of health technology assessment (HTA) agencies is one approach that could receive greater support.
  - The International Decision Support Initiative (iDSI) reference case[1] for economic evaluation can inform locally led decision-making processes.
- Encourage cooperation among countries and support mandated regional bodies to facilitate the joint production and pooling of evidence, including economic and epidemiological analyses.

Increasing the value and local relevance of WHO guidelines

The working group supports ongoing reforms initiated from within the World Health Organization to incorporate modeling and economics into the development of guidelines. The following principles and recommendations are proposed to enhance these reforms.

Principles

- Evidence on clinical and public health efficacy and effectiveness is necessary but insufficient to inform policy decisions on resource allocation. Economic evidence is also required.
  - Resource allocation decisions made in the absence of economic evidence bear substantial risk of reducing population health and increasing health inequalities.
- WHO guidelines that make recommendations regarding the relative clinical and/or public health effectiveness of alternative interventions—when not informed by full economic evaluation—should not constitute or be interpreted as universal recommendations across all countries if their implementation implies commitment of limited resources.
  - WHO clinical and public health recommendations should offer clear caveats about the need for local economic evaluation to inform uptake.
- Local decision-making processes should take into consideration WHO recommendations regarding clinical effectiveness in the light of additional economic evidence and other considerations, as relevant to the local context.
  - At present, WHO does not routinely support any standardized process for the generation of such locally relevant economic evidence.

Recommendations for the World Health Organization

- Drawing upon expert advice, develop a standardized process to routinely consider economic factors either *within* or *alongside* WHO clinical and public health guidelines.
  - Where the goal of guidelines is to have recommendations directly inform resource allocation decisions, this process should be incorporated within the guideline process.
  - Where locally relevant economic factors are not considered within a guideline, WHO should suggest how the evidence in the guideline can be used as part of other local decision-making processes (such as nationally led health technology assessment).

1. See https://www.idsihealth.org/resource-items/idsi-reference-case-for-economic-evaluation/.

- Specify the principles and methods necessary for generating economic evidence, including modeling and economic evaluation studies, to reliably inform resource allocation decision making by mandated bodies at different levels (international, regional, national, subnational).
  - An expert panel should be convened to agree on the principles and features of such analyses.
- Where WHO guidelines are intended to inform policy affecting resource allocation directly, produce or commission modeling and economic analysis to inform guideline development.
  - As full economic evaluations likely cannot be produced for all guidelines, WHO should prioritize those most in need of economic analysis (recognizing that the availability of evidence will affect the recommendations the guideline can make). Analyses can be conducted at varying levels, from cost analyses to full economic evaluations.
- Seek support and funding from other international partners in global health—for example, bilateral and other multilateral donors—for the more frequent and routine production of modeling and economic analyses as part of a guideline's development processes.
  - Given that choice of intervention is central to health care delivery, increased funding for such analyses, if appropriately used to guide policymaking, is likely to produce substantial payoffs for improving the health of populations in different countries.
- Subject any modeling and economic analyses used in guideline development to independent expert peer review.
  - A suitable process is required for independent expert peer review of original research, with sufficient funding made available for its successful functioning. This process should reflect the principle of good research methods referred to above.

Chapter 1.
Guidelines and Goals: Why Should We Care?

Health care systems have many funding needs. They must be able to pay for appropriate diagnostic tools and treatments for acute and chronic medical conditions, as well as for preventative health care. They must also provide drugs, equipment, skilled personnel, suitable facilities, managerial capacity, and infrastructure, such as supply chains, to support the delivery of health care. Inevitably, needs exceed means. Important choices, therefore, must be made among investments in disease control priorities, delivery strategies, health systems strengthening activities, and other such areas.

In principle, health care spending should be efficiently allocated, both within and across countries, to generate the greatest possible gains in population health; the extent to which spending is equitable (for example, pro-poor) within countries can be included as an additional and important concern.

Yet the imperative of efficiency is challenging to implement in practice, and resource allocation is contested in most instances. The health consequences of inefficient spending in low- and middle-income countries (LMICs) are particularly high due to the severity of resource constraints and the consequences of lost opportunities to improve health.

In many countries, a large share of health care financing is sourced from external funders.[1] Health care allocation decisions depend on often complex interactions among various stakeholders, which can result in suboptimal outcomes for efficiency, and a large share of funding is ring-fenced for specific diseases or interventions. International funders have their own internal priorities (such as disease-specific priorities), as well as constraints on uses of their funding that do not always align with the preferences of national policymakers or their populations. Similarly, nongovernmental organizations (NGOs) and other advocacy groups may lobby for resources for their particular concerns rather than assessing needs across the entirety of LMIC health systems. The task facing policymakers—at various levels, from international to local—is far from straightforward.

The existence and influence of competing interests indicates a need for fair and transparent approaches to health care priority setting. The use of health and resource-use data to inform decision making has taken many forms over the years and demonstrates an evolutionary process, with the adoption of evidence-based medicine, the creation of the Cochrane Collaboration and WHO-CHOICE (Choosing Interventions that are Cost-Effective), and the global burden of disease analyses, all with varying degrees of success in implementation.[2] Despite being a prominent part of discussions, however, clinical departments, cognizant of the realities of resource constraints, have not generally adopted formal and systematic approaches to inform policymaking. This continues to be an issue of concern, despite the rise of cost-effectiveness analyses since the 1990s.[3]

1. El-Sadr et al. 2012.

2. Baltussen and Niessen 2006; Summerskill 2005; Claridge and Fabian 2005.
3. Drummond and McGuire 1997.

Until 2015, international development activities were guided by pursuit of the high-level Millennium Development Goals (MDGs)[4] and now they are guided by the Sustainable Development Goals (SDGs).[5] Under these, resource prioritization in health care relies primarily upon sectoral and subsectoral activities, often coordinated at the international level. Most recently, the 71st World Health Assembly has passed a resolution for the 13th General Programme of Work (GPW 13), 2019–2023.[6] The resolution emphasizes the importance of country-level action for affecting health, while its "Triple Billion" objectives include an ambition to cover a billion more people under universal health coverage (UHC) than are covered today. The combined focus at country level and on UHC highlights the role resource allocation will play in ensuring the success of these initiatives in the years to come.[7]

With the ambitious global commitments to universal health coverage as part of the SDGs, recognition has been growing of the need to understand better the consequences of alternative allocations of available health care resources to improve population health and promote equity in health care access and use, including financial protection. A window of opportunity exists to consider carefully approaches to resource prioritization adopted by international organizations and make improvements to the current system.

Three interlocked activities particularly affect the way priorities for health care activities in LMICs are set by international organizations and how these priorities influence local resource allocation:

- The production of clinical and public health guidelines, particularly by the World Health Organization, that recommend interventions in specific disease areas
- The setting of international disease-specific goals (also referred to as targets)
- Disease-specific investment cases that outline funding needs to meet targets and are used to advocate for international funding to be directed towards disease-specific interventions and activities

Guideline recommendations, goals, and investment cases can be very influential in terms of publicity and priority setting—and, hence, funding. Therefore, it is vital that goals and guideline recommendations lead to a net increase in health in LMICs—that is, that the health benefit of their adoption exceeds the potential health gain offered by competing uses of the same scarce funds. This means international goals and guideline recommendations must take into consideration the comparative impact of their adoption. Recommendations will inevitably be made for individual disease and intervention areas, but they should never be considered in isolation from a broader assessment of costs, benefits, and tradeoffs for other health priorities.

Economic analysis and modeling should inform resource allocation decisions by providing evidence about the comparative costs and health benefits of different interventions in local contexts. These costs and benefits could then inform priorities in the face of limited budgets and constraints on health care delivery. Use of these analytical methods can also identify key aspects of interventions (such as the sensitivity and specificity of diagnostic tests and their portability and ease of use) that are most likely to affect their successful implementation and, hence, population health. They can also make evident the consequences of activities that do not support efficient resource allocation—for example, when development partners' resources are committed only to specific disease areas.[8]

4. United Nations 2015a; United Nations 2000.
5. United Nations 2015b.
6. World Health Organization 2019a.
7. World Health Organization 2019b.
8. Culyer and Lomas 2006.

International processes to set disease-specific goals and build investment cases do not always reflect these ideals. Historically, efforts have focused on optimizing health benefits for individual patients or patient groups rather than overall populations, given limited health system resources and capacities.

Various methodologies have been adopted over the years to rationalize and streamline decision-making processes and guide priority setting. One such attempt at a comprehensive evaluative framework is the GRADE process, encased within the WHO guideline development process which is overseen by the Guidelines Review Committee (GRC).[9] WHO's guidelines are created within the GRC's recommended framework,[10] and are also subject to peer review, in an effort to make recommendations more evidence-based, credible, transparent, representative, and equitable. The GRADE approach also includes domains to account for costs, cost effectiveness, and feasibility but without formal guidance on how any of these should affect decision making by national health policymakers.

The guidelines process leads to interventions being "recommended," "conditionally recommended" on some other factors, or "not recommended."[11] In general, these processes place a relatively weak emphasis on an intervention's opportunity cost—and, if these knock-on effects are considered, the conclusions are usually based on expert judgement. Health needs, health system features, and resource constraints vary considerably, so a treatment that should rightly be a high priority in some countries may be a much lower priority for others. This can lead to countries' choosing to use some of their limited resources on an intervention because it is "recommended," when there may be other ways to allocate them that would generate a greater benefit to the health of the whole population.

While modeling and economic assessment could provide a necessary framework within which health policy decisions can be made, this is rarely the case; and important questions remain about how such analyses can best be employed. If modeling and economic assessment are considered at all, currently they are viewed as "add-ons" to the existing body of predominantly clinical evidence.

At the country level, appropriate epidemiological data and sufficiently detailed models still do not exist in many countries, while economic analysis using local data is rarely available for most LMICs.[12] A need exists, therefore, to prioritize the development of well-informed models and analyses.

9. Guyatt et al. 2008.
10. World Health Organisation 2014b.
11. Ibid.
12. Akhlaq et al. 2016.

Chapter 2.
A Fair and Equitable System for Allocating Resources

Limited resources

Before reviewing in the following chapters how current processes work, this chapter lays out a vision for health care that provides the greatest possible benefit to health.

The primary aim would be to improve as much as possible the health of the whole population, potentially including concern for equity, in each country. Decision makers would evaluate the health gain and distributional impacts offered by different available health interventions (including diagnostic tools, drugs, medical procedures, disease prevention, and lifestyle changes, as well as changes in how services are delivered), choosing the package of interventions that would lead to the greatest gains.

In almost all contexts, health needs exceed the resources available, meaning the capacity of people to benefit from interventions is constrained by available resources.[13] This is particularly the case in low- and middle-income settings. Available resources include annual health spending (from all sources of funding) but also infrastructure (buildings, equipment) and human resources for health. All these resources are finite and limited even if they are rising year to year.[14]

Decision makers must make challenging choices about what can be funded, amongst all available interventions, given the available resources. Allocating resources to one service will inevitably mean fewer or no resources available for other uses—in other words, for example, the decision to provide Treatment A for Condition A could mean no money is available to pay for Treatment B for Condition B. Alternatively, the same financial resources might be spent on training and employing more health care workers or building and maintaining more clinics.

The allocation process must also account for existing health system structures—for example, whether care is primarily delivered through vertical programs (including donor-funded programs) or through a horizontal approach (for instance, primary health care-led).[15]

Opportunity costs

The concept of "opportunity costs" is crucial for resource allocation. For health care, the opportunity cost measures the benefits the same amount of money could have generated if spent elsewhere in the health system. All spending on efficacious interventions is likely to benefit the health of some in the population; if resources were unlimited, policymakers should, therefore, be prepared to fund all clinically effective interventions. Funding is always limited, however—often extremely so—and some ways of spending the money will yield greater health benefits than others. Allocating funds to an intervention that would produce only a small health benefit at very high cost, for example (such as a single complex surgical procedure), would likely

13. Drummond et al. 2015.
14. Zhang et al. 2010.
15. Cairncross, Periès, and Cutts 1997.

produce an opportunity cost greater than the benefit gained—that is, the same amount of money could have produced much greater benefit to the population if spent elsewhere in the health system. Supplying bed nets for the prevention of malaria, for instance, which is a very inexpensive and effective intervention, would improve health for a great many people.

Available resources should, therefore, be allocated where they are expected to have the greatest impact on population health. Importantly, this does necessarily imply spending money on the diseases that impose the greatest burden of ill health.

When disease-specific global guidelines or goals lead to spending in a single disease area, not enough money may be left in the health budget to address all other health conditions adequately and to pay for health systems, infrastructure, and staffing. Although the large resources presently devoted to single-disease programs may be generating considerable health benefit in those areas, the opportunity cost of this spending may be even bigger; if not used for that specific disease, the money could have been allocated for other health priorities, potentially leading to a larger overall health impact.

Deciding how to allocate resources

The task of deciding how to allocate limited resources is challenging. Decision makers are understandably wary of saying "no"; they understand that a negative funding decision—for example, a decision not to purchase a given health product—will lead to real people's receiving less effective or even no treatment. But a "yes" decision cannot erase the reality of resource constraints. In some settings, this leads to a situation in which many treatments may theoretically be available in the health system but are distributed on an ad hoc basis or only to the privileged few; many patients are denied access when supplies or budgets simply run out. This is not a fair or humane system, and it will eventually be challenged in courts of law and in the public domain.[16] A consistent, explicit, and open process, based on social values and the ability of scarce money to best serve the entire population, would be more efficient, more fair, and more equitable.

For health care decision makers to prioritize fairly amongst the almost endless possible uses of resources, they must consider two aspects of each intervention in parallel: the health benefit given by the intervention and the resources used (that is, the costs incurred) as a result of its being implemented. Taken together, these considerations can be used to quantify the gains in population health that each unit of currency (such as a dollar) of spending would buy. Measures of total health benefit, such as those that combine the benefits of longer life and improved quality of life into a single measure of health, may represent a small benefit to many people or a large benefit to a few people.[17] A health system should, therefore, expend its resources on the interventions that give the greatest health benefit per dollar spent, prioritizing its spending until the whole budget is used up.

To adopt this system perfectly, full information would be required on the costs and effects of every possible intervention as well as its underlying epidemiological context—information that is unlikely to be available in any health system. One way to simplify the decision-making process is to agree upon a cost-effectiveness "threshold" as a benchmark against which costs and benefits can be compared.[18] The threshold reflects an empirical estimate of opportunity cost; put another way, it establishes how many dollars can be afforded per unit of health benefit (such as gaining one QALY or averting one DALY). Any intervention that offers health gains at an incremental cost-effectiveness ratio (i.e., cost per unit of health gain) below this threshold would be approved, and above this would not. How to estimate the threshold in each context is a very

16. Glassman and Chalkidou 2012.
17. Drummond et al. 2015.
18. Edejer 2003.

important problem, as the benefits of all conceivable interventions funded by a health system will never be fully known, although research has been conducted to estimate thresholds based on opportunity cost for all countries.[19]

Decision makers may choose to allocate resources based on social value judgments beyond just gains in population health. They may, for instance, value gains in health differently depending on how they are distributed. Gains in health for children, for example, may be given a greater value; or gains that reduce health inequality across the population may be prioritized; or interventions that affect labor productivity by increasing the health of the working-age population.

Challenges

Distance undoubtedly exists between an ideal allocation process and the complex reality of resource allocation in the health sector. In particular, the implementation of better systems for priority setting poses major challenges.

One of the greatest challenges is a lack of evidence on clinical safety and effectiveness. That evidence which is available from clinical trials, systematic reviews, and more recent methods, such as network meta-analysis, is by itself insufficient for decision making. Decision makers also need to know whether expenditure on an intervention will be cost effective compared to possible alternatives (that is, whether the health gains for the population from adopting the intervention are greater than the opportunity costs). Whether or not it is will always vary among local contexts because of differences in epidemiology, resource use and costs (for example, of drugs, equipment, infrastructure, overhead, and staffing), and opportunity costs; a determination on this question in a specific local context therefore requires tailored economic analysis. Greater domestic and international investment and focus are needed to support local generation of relevant evidence.[20]

Another set of challenges relates to how best to use existing but limited data to support the transferability of economic evaluations done in countries other than the country of interest. Since very few trials are conducted locally in LMICs, economic analysis can be informed by trials performed in neighboring countries. The performance of economic evaluations alongside randomized clinical trials (RCTs) is not uncommon; numerous examples are available in the medical literature,[21] and they are often a source of information on costs and health-related quality of life. An important component of trial design is ensuring good internal validity; however, individual trials sometimes provide for very limited external validity, which greatly compromises generalizability and transferability to other target populations. This is primarily because interventions, provision of health care, and protocols tend to differ from the prescribed standard of care in the country of the trial.[22]

This issue has been studied at length, and while a more complete discussion is beyond the scope of this report, it remains an important area of future work. One potential solution is the use of observational studies, combined with experimental studies (for example, RCTs), to help reflect local contexts and capture unobserved differences between trial patients and a target population. An expanding literature that explores statistical methods to combine RCTs with observational data enables researchers to address local policy questions and model specific characteristics in particular settings.[23] Investment by LMICs in large clinical trials for given interventions is neither expected nor necessarily recommended; pragmatic approaches are more likely to succeed in the short term.

19. Woods et al. 2016.

20. Boerma, Victora, and Abouzahr 2018.
21. Drummond and Davies 1991.
22. Allcott and Mullainathan 2012; Deaton 2009; Imbens 2010.
23. Hartman et al. 2015.

A key solution: Systematic economic analysis and modeling tailored to place

A solution to some of these challenges can be found in economic analysis and modeling tailored to local contexts. Based on local epidemiology and relevant effectiveness evidence, these methods can quantify the potential health benefits and expected costs of policy alternatives, including the longer-term costs of further treatment or later savings resulting from better health. Such modeling can, therefore, estimate the benefits and costs of alternative health spending options and provide a clearer guide for disinvestment or reallocation decisions.

Economic and epidemiological analyses can also provide the organizing framework to guide evidence generation and policy priorities. They can, for instance, highlight the types of studies and evidence that would be most useful in generating new knowledge and reducing uncertainties for decision making, and so best able to help direct future research.

Health technology assessment (HTA) that incorporates economic analysis is increasingly common in high-income and some middle-income countries as a means of informing prioritization decisions (see appendix 2 for an example of how this works in the United Kingdom). The need for HTA is even greater in LMICs, with their more constrained health budgets and greater health care needs. Without even increasing the total amount of spending on health, much greater benefit could be produced by reallocating resources to where they would make the biggest difference. But estimates of opportunity cost could also be used to inform decisions on the total resources made available to a health system (both from governments and external sources). Evidence of the additional health benefit that could derive from a given increase in the total funding would provide an informed basis on which to advocate for increased health funding in future. In other words, modeling and economic analysis can clarify what more could be done with increased resources, whilst ensuring the limited resources already available are being used to best effect. The processes for developing international guidelines and goals therefore need to incorporate economic evidence relating to local contexts.

A notable example of tailoring evidence and analysis to local needs whilst guided by international policies relates to how South Africa has prioritized spending on HIV (human immunodeficiency virus). HE^{2}RO, or the Health Economics and Epidemiology Research Office, based at the University of Witwatersrand in Johannesburg, designed its own National ART Cost Model (NACM) to answer specific HIV policy questions in the context of the country. It allowed the South African Department of Health (DOH) to plan for four new sets of ART (antiretroviral therapy) guidelines in a seven-year period and the National Treasury to allocate resources more efficiently in the light of an expanding HIV program. Unfortunately, not all of HE^{2}RO's work is taken on by the government; a case of how ignoring the evidence can lead to suboptimal outcomes is described in Box 1.

Conclusions

In principle, decisions are best made at a local level, by local decision makers, informed by local evidence and accounting for local values, and using the best available methods. The ability of local policymakers to make their own decisions, however, is constrained by several features of the global health policy and funding environment, as will be seen in the next chapter.

Box 1. Using budget modeling to influence HIV policy in South Africa: HE²RO's experience

South Africa is famous for having the world's largest antiretroviral treatment (ART) program; since the early 2000s, the country has been home to between a quarter and a fifth of the world's people on ART.

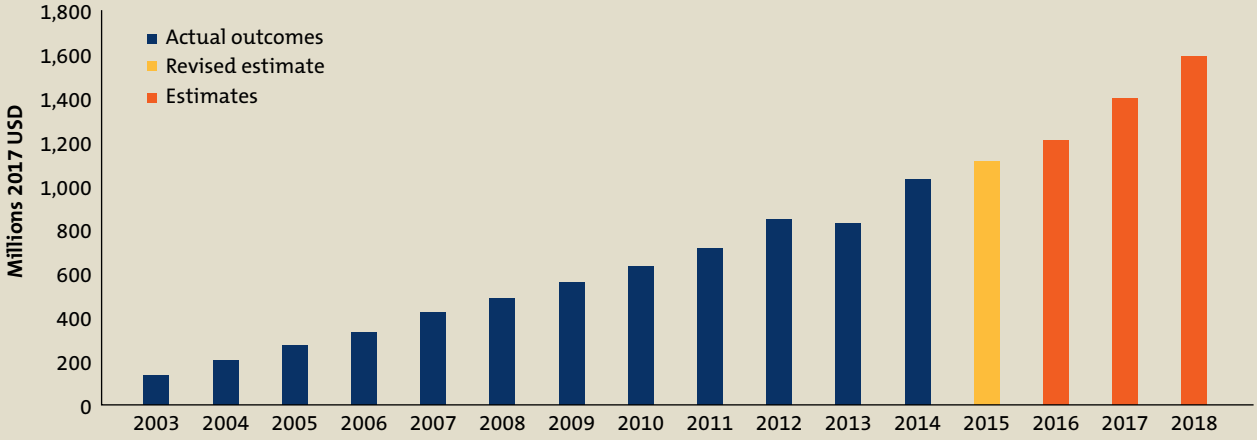
But four years into the public sector ART rollout, this success came under threat. In late 2008, several South African provinces stopped ART initiation because of the strain placed on financial and human resources by the program's rapid growth.

To deal with the bottleneck, researchers from HE²RO built the National ART Cost Model (NACM), a health-state transition model that could be modified to answer the Department of Health's key questions. The model incorporated several data sources, including Thembisa (formerly the ASSA AIDS Model), a local model that estimated the number of people infected with HIV and in need of ART, and analyses of the cost of providing ART to adults and children.

Over the years, the team used the NACM to analyze the expected costs of increasing the ART-eligible population and introducing new and better drugs for both adults and children. The model also suggested improvements in technical efficiency that could, at each turn, help offset the expected budget increases.

NACM findings enabled DOH to commit to four sets of new ART guidelines between 2010 and 2016, which increased the number of people on ART from under one million at the end of 2009 to more than four million by mid-2018. This analysis made it easier for the National Treasury to commit to the necessary expansion of the national ART budget, which almost tripled in real terms over the same period of time (Figure 1).

Figure 1. The South African HIV budget 2003–18



Source: https://doi.org/10.1371/journal.pone.018655.

(continued)

Box 1. Continued

In 2013, HE²RO researchers were tasked to take their modeling beyond ART to calculate the most cost-effective mixture of treatment and prevention interventions for the South African HIV Investment Case. Again, HE²RO combined Thembisa and its own cost analyses, as well as large evidence review exercises involving researchers and implementers.

During this work, it became evident that allocative efficiency was only one consideration in policy-making; compliance with international guidelines and targets was another.

HE²RO calculated that universal treatment was likely to be cost effective, but less so than access to treatment for those meeting the ART eligibility requirement of white blood cell count below 500 CD4 cells/microl (the standard in 2014 when work on the investment case started) Both were affordable under the current budget (Figure 2).

The team also demonstrated that the current number of new infections per year could be reduced—to around 200,000 by 2020—with the optimal package of services.

Despite this, the first draft of the current National Strategic Plan for South African included a target of 100,000 new infections by 2020; this was further decreased to 88,000 by the UNAIDS-led Global Prevention Coalition. The modeling had estimated only a 10 percent chance that the 100,000 target would be achievable, and the 88,000 target was deemed virtually impossible.

Figure 2. Results of the South African HIV Investment Case

Results of the South African HIV Investment Case	ICER (USD/LYS)
Condom availability	Cost saving
Male medical circumcision	Cost saving
ART at 500 CD4 cells/microl	**84**
PMTC	103
Universal treatment	**187**
Infant testing at 6 weeks	193
SBCC campaign 1 (HCT, reduction in MSP)	547
SBCC campaign 2 (condoms)	872
General population HCT	932
SBCC campaign 3 (condoms, HCT, MMC)	1,374
HCT for sex workers	2,004
Infant testing at birth	2,207
PrEP for sex workers	7,476
HCT for adolescents	15,307
PrEP for young women	19,993
Early infant male circumcision	68,969,435

Source: https://doi.org/10.1371/journal.pone.0186496.
Note: Yellow box in table represents the optimal package under the current budget.

Aspirational targets might serve a function in increasing pressure and focus on what *should* be done. But these kinds of targets do not improve the allocative efficiency of current budgets, as the modeling illustrates, and the experience makes clear that policymakers need to put evidence-based modeling ahead of advocacy targets when making resource allocation decisions if the goal is to make a dent in disease burdens in the real world.

Source: Gesine Meyer-Rath, working group member, based on HE²RO's experience; see http://www.heroza.org/.

Chapter 3.
How Global Guidelines and Goals Influence National Decision Making

In this chapter, we review current approaches to developing global guidelines and goals, including the use of economics and modeling to inform these processes in recent years. We reflect upon the challenges to decision makers resulting from current systems.

Development of WHO guidelines

Current processes

Guidelines on how best to prevent, diagnose, and treat particular medical conditions are developed and issued by a variety of governmental, intergovernmental, private, and specialist medical organizations. We concentrate in this report on the guidelines produced by the World Health Organization (WHO) because they are designed to be used across the whole world and are often seen as providing the most influential advice on managing relevant conditions in LMICs. WHO guidelines provide normative guidance for countries on best practice in various disease areas of global health importance, generally retaining the perspective of a public health approach, to inform choices amongst different interventions.[24]

The content of WHO guidelines is often guided by PICO (population, interventions, comparators, outcomes) questions and assessment of the evidence identified using the GRADE approach (Grading of Recommendations Assessment, Development, and Evaluation),[25] in line with the procedures established by the WHO Guidelines Review Committee (see appendix 1 for details on all elements of the WHO guideline development process). The PICO questions are subjected to the GRADE process, in which the intervention or strategy under consideration is compared to alternative strategies, interventions, or policies, and the certainty of the available evidence for these interventions is assessed. The process cannot produce answers to questions on risk or prognosis, but these may be indirectly accounted for. The "risks and benefits" are assessed in light of the GRADE evidence tables,[26] keeping in mind a clinical context, which ultimately leads to a "strong recommendation" or a "conditional recommendation" concerning the effectiveness or ineffectiveness of one or more interventions. This recommendation is taken into consideration and reflected in a normative guidelines document, which countries are encouraged to adopt into their own policies.

The developers and users of GRADE readily acknowledge the limitations associated with what is an otherwise fairly comprehensive assessment process for clinical, evidence-based decision making. GRADE has been optimized to answer specific clinical questions rather than address large-scale public health, resource allocation, or health system–related questions. It therefore has shortcomings in accounting for downstream effects of a change in policy, such as implications over the life course; dynamic health effects, such as the

24. World Health Organization 2014b; Gilks et al. 2006.
25. Guyatt et al. 2008.
26. Guyatt, Oxman, Akl, et al. 2011.

spread of resistance; or financial implications and the knock-on consequences of resource reallocations.[27]

The 2018 guideline on the "recommendation of calcium supplementation during pregnancy for the prevention of preeclampsia and its complications," for example, incorporates evidence from clinical trials in the form of a systematic review. The guideline acknowledges it is context specific and based on evidence of only moderate certainty; nevertheless, this large-scale public health intervention was recommended to countries for adoption with no formal assessment of the cost implications and only a cost-per-dose provided from the WHO OneHealth toolkit. No studies were included on resource use, cost effectiveness, equity, and feasibility—all of which can be incorporated in some manner with economic analysis and modeling. The opportunity costs of this recommendation were not considered.[28]

Another guideline from 2018 included the WHO recommendation on the duration of bladder catheterization after surgical repair of simple obstetric urinary fistula. Although no formal assessment was made of resource use, costs, or cost effectiveness, the recommendation was still reported in the guideline, seemingly based solely on the subjective opinion—and without any consideration of contexts or available budgets—that this would "probably be cost-effective."[29]

Assessment of resource use, costs, and opportunity costs has, to date, not been formally or systematically included in guidelines and, in some instances, this evidence not been recognized at all. No guidance currently exists on how best to utilize it or assess the types of scenarios where it would be particularly beneficial. At present, countries are expected to set up processes for considering if and how to adopt WHO guidelines, but advice on how to do this is limited. Furthermore, a widespread perception prevails in many quarters that close-to-direct adoption of international recommendations is wise or necessary—not least for the receipt of development assistance, upon which the health systems in many countries largely depend.[30]

Another important addition to the process of setting WHO guidelines in recent years are planned meetings amongst international organizations, stakeholders, ministries of health, and pharmaceutical companies (both branded and generic manufacturers). These have contributed in several ways to achieving lower acquisition costs of pharmaceuticals, as well as helping to set priorities for future drug development in the short, medium, and long terms, in light of existing evidence, to facilitate planning for a potential shift in policy, primarily in HIV.[31]

WHO has been considering the best role for economic evidence in its guideline development process and looking at the inclusion of modeling analyses in some guidelines on a case-by-case basis. Evidence from cost-effectiveness modeling analyses was considered in the development of the 2013 consolidated guidelines for HIV antiretroviral treatment (see Box 2);[32] and, subsequently, WHO and the GRADE working group reviewed the role of modeling analyses in developing guidelines.

Ideally, a combination of grading of available clinical and public health evidence, modeling, and economic assessment, as well as multilateral cooperation among stakeholders, international organizations, manufacturers, and countries, will produce clear and comprehensive guidelines more translatable at the country level. WHO should continue to play a leading role in shaping global health goals and guidelines, but it needs to be further informed and better supported to facilitate the formal inclusion of modeling and economic assessment in or alongside the guidelines produced, consistent with WHO policy of promoting UHC.

27. Guyatt et al. 2008; Guyatt, Oxman, Akl, et al. 2011; Guyatt, Oxman, Schünemann, et al. 2011.
28. World Health Organization 2018b.
29. World Health Organization 2018c.
30. McRobie 2017.
31. Vitoria et al. 2019; United Nations Programme on HIV/AIDS and World Health Organization 2018.
32. World Health Organization 2013; Easterbrook et al. 2014.

Box 2. Cost-effectiveness modeling to inform 2013 WHO HIV treatment guidelines

Economic modeling analyses that were commissioned to support the WHO chapter for program managers in the 2013 HIV treatment guidelines were also submitted alongside data from trials and observational studies in support of the development of clinical recommendations and were reviewed through GRADE. To reduce the uncertainty of relying on findings from a single model, a number of modeling analyses were compared for questions 1 and 2 below. The evidence from these analyses was noted, but the recommendations of the guidance did not emerge from them directly.

Questions:

1. *Is expanding the criteria for ART eligibility to be CD4 < 500 cost effective?*

   Twelve mathematical models with analyses for India, South Africa, Vietnam, and Zambia were utilized. Earlier ART initiation was found to be "very cost effective" across settings.

2. *What is the best way to monitor patients on ART?*

   Three models of generalized African regions were utilized. The opportunity costs of spending on monitoring were explored, and it was recommended countries with limited resources prioritize expanding ART coverage, first at CD4 < 350 cells and then at CD4 < 500, using lower-cost clinical or CD4 monitoring prior to viral load monitoring unless substantial drops occurred in the cost of viral load testing.

3. *What are the costs and benefits of Option B+ for prevention of mother-to-child transmission (PMTCT) of HIV?*

   One model was utilized to consider outcomes across four countries. Option B+ was found to be cost effective compared with other options for preventing mother-to-child transmission. It was advised, however, that greater health gains might be realized by providing treatment first to individuals who need this for their own health needs if substantial treatment gaps exist.

Modeling analyses were reviewed using GRADE; however, as GRADE is not designed to assess the quality of economic modeling studies, the Guidelines Review Committee faced challenges in attempting to apply the GRADE framework.

Source: Eaton et al. 2014; Gopalappa et al. 2014; Keebler et al. 2014.

A detailed description of the WHO guidelines process is available in appendix 1 of this report, while Figure 3 summarizes some key elements of guidelines development alongside the GRADE process.

As indicated above, information on resource use has not been routinely considered in the development of guideline recommendations. The inclusion of resource use in the GRADE process is not systematic, and limited guidance exists for how to evaluate the evidence when it is included. WHO advises national-level decision makers to conduct their own local analyses to assess whether the guidelines should be adopted or adapted.[33]

For vaccines, malaria control, tuberculosis, hepatitis C (HCV), and HIV, resource use has been considered in some cases within the decision-making process. The

33. World Health Organization 2016a.

Figure 3. Inclusion of economics or resource use and modeling in WHO guidelines

Source: Adapted from the WHO Guideline Development Handbook, 2nd ed., and the GRADE Handbook, updated October 2013, https://gdt.gradepro.org/app/handbook/handbook.html.

various attempts to consider cost and cost-effectiveness analyses for HIV are discussed in this report.

Recognition by WHO of the need to change current processes

In recent years, WHO has undertaken consultations on incorporating mathematical modeling and resource use into guidelines. In 2015, it conducted a consultation to explore when and how modeling analyses should be included in the guideline development process.[34] The consultants considered the following questions and generated the following findings.

Questions:

- When is it appropriate to consider modeling studies as part of the evidence that supports a guideline?
- How should the quality of and risk of bias in mathematical modeling studies be assessed?
- How can the GRADE approach be adapted to assess the certainty of a body of evidence that includes the results of modeling and to formulate recommendations?

Findings:

- WHO found that, between 2007 and 2015, it had utilized 42 modeling analyses to help inform the development of 185 guidelines it reviewed. Modeling analyses influenced the recommendations in 17 guidelines; however, the quality of the models was rarely assessed, and information on why certain models had been used was lacking.[35]
- Further to the consultation it was agreed that modeling analyses could provide significant added value to guideline development and should be considered in cases in which empirical evidence for the direct question of interest is not available, such as the comparative effectiveness or long-term effectiveness of interventions and where immediate action is needed for unprecedented health emergencies (such as the Ebola outbreak).
- The consultants came to agree that no "one size fits all" approach exists for including modeling analyses in the GRADE framework. Henceforth, modeling is to be included as a subcategory, and adapted criteria are needed for considering indirectness, inconsistency, imprecision, and publication bias specific to modeling.
- In 2017, WHO began a review of the incorporation of evidence on resource use into the WHO guidelines development process. It found that information on resource use was not routinely or systematically applied, and that it might have been beneficial in some instances in guiding the recommendations made by WHO.

Challenges posed by the current approach to WHO guidelines

The current approach for formulating WHO guidelines poses a number of challenges, outlined below.

1. Developers tend to focus on specific questions in disease areas, with a limited view of the broader context. The current approach to guidelines can lead developers to focus on questions for which clinical evidence is available and in which clinical and academic interest has been high (for example, the most effective drug to use for a particular condition). Little consideration is given to each question in the broader context of the causes of morbidity and mortality in the population and the cost-effective delivery of interventions to prevent or treat them, including the downstream consequences of these strategies.

2. Consideration of resource use in countries is inadequate. Historically, most guidelines have not included systematic evaluation of resource use or resource constraints,

34. Easterbrook et al. 2014.
35. Burda, Chambers, and Johnson 2014.

although such evaluation is consistently discussed (albeit ad hoc) in guideline development processes.

3. Risks and benefits of costs and resource use are judged intuitively. Experts now agree that economic factors need to be considered in the guideline development process, but this cannot be done merely by adding resource use as an outcome and then asking panel members to weigh the risks and benefits intuitively. The current process also does not ensure routine guideline updates will include a formalized process to evaluate costs and economic evidence. Whilst health outcomes can often be compared directly among alternative interventions and interpreted quite straightforwardly (for example, a lower all-cause mortality rate with Treatment A than with Treatment B), resource use and costs cannot be interpreted on their own. A more expensive intervention may be preferable to a less expensive one if it gives rise to health benefits that exceed the opportunity costs of the additional expenditure. No properly informed judgment can be made without relevant information on health benefits, costs, and opportunity costs all being considered together in a defined decision-making framework.

4. GRADE is not designed to assess economic data, which has presented problems in the past. The adoption of the GRADE process to synthesize and assess the quality of clinical evidence has been a step forward, systematically bringing together the known evidence on safety and effectiveness and judging the certainty of that evidence. The GRADE process is not well suited, however, to the task of evaluating the quality or reliability of economic studies, which depend on context much more than clinical evidence does. Any attempt to adjust the current GRADE process minimally to accommodate economic studies, treating the results in the same way as other outcomes without additional interpretation, is not likely to succeed, given its well-ascribed limitations.[36]

5. Current advice does not cater to differences in resources or the local epidemiological contexts of countries. In particular, if WHO guidelines are to provide useful advice to member nations regarding decision making on resource allocation, then methods are needed to reflect countries' different resource and epidemiological contexts, and any blanket recommendations that imply one particular intervention ought to be adopted in all countries must be avoided. As guidelines deal with a single disease, or sometimes a single clinical question with public health ramifications, the process should also avoid situations where the "best" treatment for any particular disease is recommended without consideration of whether countries can afford that treatment when all the other demands upon their health systems are also considered.

The working group also agrees no attempt should be made to fit modeling analyses into the GRADE framework. Instead, GRADE assessments (or an adaptation of the current process, which preferably would also include an assessment of the magnitude of uncertainty) should be used to provide the evidence necessary for a modeling study.

Conclusions for current WHO guidelines processes

Based on the working group's assessment of existing WHO guidelines processes, we conclude the following:

- The GRADE process on its own is ill suited to the task of informing guideline recommendations on the use of limited resources.
- Current use of economics and modeling in WHO guidelines is inconsistent, and in some instances they are not considered at all.
- Standardized methods are needed for integrating economics and modeling into guideline processes. A GRADE-like process should inform the modeling, not the other way around.

36. World Health Organization 2019b; Culyer and Lomas 2006.

- More needs to be done to ensure guidelines are mindful of competing priorities of health budgets.
- The guideline development process promotes greater transparency, considers the preferences and values of the wider community in some regards, and provides a framework for the synthesis of evidence to inform the development of a guideline, but it falls short in essential ways, as discussed.

Development of global health goals

Current processes

Global goals are aspirational targets formulated to focus the attention of funders, implementers, and national-level policymakers on mobilizing resources for a particular purpose, leading to policy change and improvement in health. Goals generally focus on the treatment of one specific disease or condition, and the outcomes of interest may relate to the resources expended (for example, the number of bed nets distributed or the number of people on antiretroviral therapy) instead of, or as well as, health outcomes (in terms of morbidity and mortality).

In past years, the process by which targets have been set has often not been transparent or inclusive, and the targets themselves have sometimes appeared arbitrary. As a result, they have been criticized for not being grounded in reality or for the developers' lacking sufficient engagement with national-level decision makers.

Some attempts have been made to estimate resource requirements in accordance with the Sustainable Development Goals (SDG 3). One such study in 2017 estimated an additional US$274 billion was required to meet the SDG targets.[37] Another WHO initiative—the Global Price Reporting Mechanism (GPRM)—helps collect price data for health commodities in selected therapeutic areas,[38] but, again, this does not estimate population health gain, resource requirements, or the opportunity costs associated with alternative resource allocations.

Goals are generally not, therefore, subjected to a comprehensive economic or modeling assessment. Many targets have not been set with a view toward competing demands on resources at the national level, and so may encourage distortion of priority setting by policymakers inside the countries. Instead, policymakers are sometimes keen to demonstrate a response to globally endorsed targets (the development of HIV policies in South Africa is one such example; see Box 1), as this may be required to obtain further grants or future overseas development assistance, even though it may not be the best allocation of limited resources for their particular contexts.

Example of global health goal setting

Many global health goals have been produced and disseminated without any modeling having been used to develop or support them.

Two recent examples of goal setting supported by the use of mathematical modeling and economic analysis are Family Planning 2020 and the HIV fast-track targets. These approaches have been used in a number of ways:

- To inform the setting of ambitious but feasible global goals for Family Planning 2020
- To assess if the preselected HIV fast-track targets would result in attainment of a policy goal (to end the AIDS epidemic by 2030, as advocated in the Sustainable Development Goals)
- To estimate the cost and impact of meeting the targets—often for advocacy purposes

More details on these two examples can be found in Appendix 3. The HIV response in particular has had

37. Stenberg et al. 2017.

38. World Health Organization 2011.

Box 3. HIV fast-track targets: "90-90-90" and "95-95-95"

In 2014, the Joint United Nations Programme on HIV/AIDS (UNAIDS) set the "fast-track" targets that operationalize what countries need to do and what program coverage targets they need to attain at certain time points to achieve the policy goal of ending the AIDS epidemic by 2030, as advocated in the SDGs.[a] By 2020, all countries are to have attained the following:

- 90 percent of people living with HIV (PLHIV) diagnosed and aware of their status
- 90 percent of those diagnosed with HIV receiving treatment
- 90 percent of those on treatment achieving viral suppression

For 2020 to 2030, these coverage targets all shift to 95 percent.

The fast-track targets were intended for adoption by all countries without translation to local contexts. Several countries have already succeeded in achieving the 90-90-90 target relatively quickly and have set their sights on the 95-95-95 target for 2030. Whilst exerting sustained pressure on countries to improve treatment and screening coverage rates, these kinds of targets may require resource allocation towards this use that comes at the expense of other vital health programs.

Modeling was not used in setting the fast-track targets to ensure they were feasible; instead, coverage targets were set first and modeling was conducted afterwards to explore whether they would achieve the policy goal of "ending the AIDS epidemic" by 2030. The modeling analysis demonstrated these coverage levels could enable the attainment of this goal if some assumptions underlying the modeling were accepted. The modeling also calculated the expected cost of this approach, but it was not used to assess whether pursuing the goals could actually be afforded within available budgets or was a cost-effective use of resources.

a. United Nations Programme on HIV/AIDS 2016; 2017.

numerous targets, often very ambitious (see Table 3, Appendix 4). Box 3 describes the HIV fast-track targets in brief.

Challenges posed by the current approach to setting global health goals

The fundamental danger of globally set goals is that they usually focus on a single or a few diseases and advocate for increased or continued funding of those causes without any consideration of the opportunity costs of allocating those resources for that purpose. This will almost inevitably lead to an inefficient allocation of resources, as areas of health care not covered by a goal will lose out on funds that could have made a greater impact on human health if used elsewhere.

Most goals are not informed by economic analysis, and few, if any, appear to take into consideration the full opportunity costs of concentrating funding on particular diseases. They may also, however, arise from a significant modeling exercise that demonstrates improved outcomes from a given intervention. A single goal is unlikely ever to be suitable for all countries, as epidemiology, available resources, opportunity costs, and, hence, priorities differ hugely among them. Many goals have been produced without any modeling,

either as part of their development or retrospectively to support them.

Goals are often political in origin or intended to bring attention to a specific medical condition or disease area. Whilst the purpose of highlighting a need for disease prevention or treatment is generally well-intentioned, goals tied to funding decisions can easily distort resource allocation.

Often, these goals are assumed to be relevant worldwide. In reality, intervention costs and impact are extremely variable, both over time and among jurisdictions. The analyses that produce these targets may, therefore, be misleading regarding the potential costs of responding to them. Country- and local-level decision makers need sufficient flexibility to prioritize health spending in response to their populations' greatest needs and where it can most benefit their health, which may or may not involve meeting a global target at a local level.

The practical challenges of implementing both global goals and global guidelines in specific, resource-constrained, contexts are further explored in Appendix 4, with reference to the experiences of Malawi and Uganda in seeking to implement HIV and family planning goals within the context of their health systems and the consequences for health care delivery in those countries.

One of the principal benefits often cited for goals, however, is that they have successfully led to additional resources being pledged by donors to global health, which would not have been made available without the motivation of the specific goal. Any changes that move the focus towards whole health systems and away from single diseases will need to consider that this approach may make it harder to attract funds. This is an important question for which further research is required.

Conclusions

Advocacy-based goals can potentially distort efficient resource allocation, particularly when they are specified with respect to particular diseases or interventions, as is usually the case. They can, however, be specified in ways less likely to have this effect and more likely to generate donor funding into health care that may not have otherwise been devoted to development. The working group concluded the following:

- Goals inherently encourage investment into specific areas of health care, which may not be the areas where that investment could produce the greatest health benefit in any given country.
- Current use of economics and modeling in goal setting is inconsistent or lacking.
- Goal setters need to be mindful of competing priorities for countries and the differences in their ability to meet the goals.
- A process of supporting goal setting at the national level is less likely to distort priority setting than imposing a uniform goal on all countries.
- It is important that modeling analyses are transparent, particularly with regard to the assumptions underlying target-setting processes, and they should be independently validated.
- Goals may generate additional resources for health care spending in low- and middle-income countries. Whether the benefits of these additional resources outweigh the adverse consequences for resource allocation is currently uncertain.

In sum, more evidence is required, and this should be focus for future research. We focus the recommendations of this working group report on how countries can be supported in making resource allocation decisions and how WHO guidelines can used, together with modeling and economic analysis, to better inform resource allocation.

Chapter 4. Recommendations to Help Governments Set Better Health Priorities

Our recommendations address two objectives: first, to empower countries to develop and analyze appropriate evidence to set health priorities for their populations; and, second, to strengthen the WHO guidelines program to increase its value and relevance for national decision makers.

Taken together, these measures can help change health priority setting from a situation in which priorities are primarily set internationally and implemented locally to one in which international priorities are built upon the foundations of local evidence and local prioritization.

The working group understands and acknowledges the magnitude of the challenge that accompanies a major shift in how goals and guidelines are developed and recognizes that changes of this magnitude take time to implement.

Empowering national governments to set evidence-based health priorities for their populations

Principles

A starting point to address the mismatch between global goals and guidelines and country-level budgets and contexts lies with the articulation of principles that support national governments in setting evidence-based health priorities for their populations. The working group suggests the following principles to country governments and the international partners who support their work:

- National health strategies and priorities should ideally be set by local decision makers, accountable to their citizens, considering all available evidence.
- International health priorities and goals should primarily reflect and account for national priorities, whilst addressing common challenges that cross national borders.
- When deciding health priorities and goals, local decision makers should evaluate economic evidence using appropriate metrics reflective of local preferences and values.
    - Decision makers need measures of health benefit that facilitate comparisons across disease areas (for example, generic measures of health, such as QALYs and DALYs). In line with local preferences and values, decision makers may also consider benefit measures that reflect equity concerns and other dimensions of social value.
- Economic analysis and modeling, designed for or adapted to local context, is often required to prioritize the use of limited resources.

- While the demand for such analyses should ideally be led by governments and local agencies, support in the form of funding and technical guidance will sometimes be required from international bodies.

- Locally relevant clinical and economic evidence is required to inform such analyses.
  - Ideally, economic evidence (for example, on resource use and costs) will be generated locally. Where this is not feasible, evidence may be taken from other, relevant jurisdictions.
  - Clinical studies will often be undertaken in different settings. The relevance of available clinical evidence to the local setting needs to be carefully assessed.

Recommendations for international agencies

In terms of specific actions, the working group proposes that international agencies do the following:

- Reaffirm that decision-making responsibility for the adoption and funding of interventions lies at the country level or even lower, with decision makers who represent their citizens and are equipped with appropriate clinical and economic evidence.
- Support local production of economic and epidemiological analyses, and enhance local capacity to produce such evidence.
  - This support can be provided through funding of locally led research activities and provision of appropriate technical support.
- Support countries in establishing consistent resource allocation processes, informed by appropriate local evaluations.
  - The establishment of health technology assessment (HTA) agencies is one approach that could be given greater support.
  - The International Decision Support Initiative (iDSI) reference case for economic evaluation can serve as a guide for the establishment of locally led decision-making processes.
- Encourage cooperation among countries and support mandated regional bodies to facilitate the joint production and pooling of evidence, including through economic and epidemiological analyses.

Increasing the value and local relevance of WHO guidelines

The working group supports ongoing reforms initiated from within the World Health Organization to incorporate modeling and economics into the development of guidelines. The following principles and recommendations are proposed to enhance these reforms.

Principles

- Evidence on clinical and public health efficacy and effectiveness is necessary but insufficient to inform policy decisions on resource allocation. Economic evidence is also required.
  - Resource allocation decisions made in the absence of economic evidence pose a substantial risk of reducing population health and increasing health inequalities.
- WHO guidelines that make recommendations regarding the relative clinical and/or public health effectiveness of alternative interventions should not, when not informed by full economic evaluation, constitute or be interpreted as universal recommendations across all countries if their implementation implies commitment of limited resources.
  - WHO clinical and public health recommendations should offer clear caveats about the need for local economic evaluation to inform uptake.

- Local decision-making processes should take into consideration WHO recommendations regarding clinical effectiveness in the light of additional economic evidence and other information relevant to the local context.
  - At present, WHO does not routinely support any standardized process for the generation of such locally relevant economic evidence.

Recommendations

Building on the principles, the working group recommends that WHO do the following:

- Drawing upon expert advice, develop a standardized process to consider economic factors routinely, either within or alongside WHO clinical and public health guidelines.
  - Where the goal of guidelines is that recommendations directly inform resource allocation decisions, this process should be incorporated within the guideline process.
  - Where locally relevant economic factors are not considered within a guideline itself, WHO should suggest how the evidence in the guideline can be used as part of other local decision-making processes (such as nationally led health technology assessment) alongside it.
- Specify the principles and methods necessary for economic evidence, including from modeling and economic evaluation studies, to reliably inform resource allocation by mandated bodies at different levels (international, regional, national, subnational).
  - An expert panel should be convened to agree to the principles and features of such analyses.
- Where WHO guidelines are intended to directly inform policy affecting resource allocation, produce or commission modeling and economic analysis to inform guideline development.
  - The production of full economic evaluations for all guidelines is unlikely, so WHO should prioritize those most in need of economic analysis (recognizing that the availability of evidence will affect the recommendations the guideline can make). Analyses can be at varying levels and depths, from cost analyses to full economic evaluations.
- Seek support and funding from other international partners in global health (for example, bilateral and other multilateral donors) for the more frequent and routine production of modeling and economic analyses as part of a guideline's development processes.
  - Given the centrality of intervention choice to health care delivery, increased funding for such analyses, if appropriately used to guide policymaking, is likely to produce substantial payoffs for the improvement of population health in countries.
- Subject any modeling and economic analyses used in guideline development to independent expert peer review.
  - A suitable process is required for independent expert peer review of original research, with sufficient funding made available for its successful functioning. This process should reflect the principle of good research methods referred to above.

Risks: Reaching for the stars but falling backwards

We acknowledge that attempting to make wholesale changes to current global processes around health care resource allocation can be dangerous. If incompletely implemented, this approach can lead to worse outcomes in the short-term, and perhaps in the long-term as well, if problems go unresolved.

One problematic scenario would involve removing current informal and ad hoc economic considerations from WHO guidelines, leaving only clinical and public health effectiveness data but no recommendations for or against implementing interventions. This could leave decision makers less informed than under the status quo. The problem would be compounded in countries that are unwilling or unable to implement new local processes to develop context-specific economic evidence.

Another risk would stem from continued failure to build technical capacity within LMICs, perpetuating a vacuum of locally appropriate economic evidence. Alternatively, LMICs may expend their limited resources on buying economic capacity from external parties. In the long run, all countries should be able to take ownership of their own analyses, but most are currently a long way from having this capability. This also means that progress, in terms of gains in population health, will be much harder to measure.

Incomplete reform could also subject health decision makers to competing and incompatible pressures. WHO could, for example, adopt in its guidelines process newer methods for including economic evidence that account for population-level measures of health and preferences, but the outputs may conflict with disease-specific global goals and advocacy.

Finally, there is a danger that international funders will be inclined to contribute less funding to development if it is not tied to disease-specific goals and programs, with the result that countries that try to implement systemwide prioritization will lose funding and so see their total resources decrease.

We have, however, already set out above the considerable dangers of maintaining the status quo. International commitments to the Sustainable Development Goals and universal health coverage open a window of opportunity to move towards more transparent and evidence-based systems of resource allocation, in which international organizations and other stakeholders can be appropriately held to account.[39]

39. Norheim 1999.

Chapter 5.
Next Steps for the Global Health Community

Summary and conclusions

Great effort goes into developing and implementing WHO guidelines and into designing and advocating for global health goals. Until now, however, less attention has been paid to coordinating the many competing demands imposed by guidelines and goals on health care systems in situations where available resources do not allow all guidelines to be followed or all goals to be met. Country-level decision makers need additional support to prioritize health needs through a process that reflects local context, preferences, and resource constraints.

Greater use of economic analysis and modeling would be invaluable in allowing decision makers to compare the relative merits of different health programs and to determine the most cost-effective use of resources for achieving the greatest possible health improvement for their populations. The recommendations in this report offer a path to realizing this vision.

Implications of the working group's recommendations

The recommendations proposed by this working group have been formulated recognizing the following:

- Resource prioritization informed by better economic assessment and economic modeling can improve the efficiency (that is, the potential for health improvement) of health expenditure while accounting for other social values, such as equity.
- A more efficient resource allocation process requires appropriate evidence and better information, giving stakeholders (for example, national budget holders and donors) increased confidence in their investments and the expected short- and long-term outcomes.
- Such a process will also allow countries to measure their progress in terms of overall population health (in terms, for example, of net QALYs gained or DALYs averted) and costs. Decisions made by governments, ministries of health, and international funders can be more transparent, enhancing accountability.
- Clarity on resource availability as well as knowledge of overall health gains can link to better-informed procurement agreements (for the procurement, for instance, of drugs, devices, diagnostic tools, or preventatives) between countries and commercial manufacturers. These negotiating processes can then be supported by international organizations, such as WHO and other major stakeholders, through normative guidelines and country-level support.
- Priorities for future research can be identified based on assessment of the extent to which further research and better information can contribute to improvements in population health.

Unanswered questions and priorities for further research

The working group has also identified research priorities related to how international and mandated national institutions interact to influence prioritization. Key questions include the following:

- To what extent is goal setting relating to specific diseases or interventions necessary and effective in generating resources for the purposes of global health and development, and to what extent is the use of such goals deleterious to efficient resource allocation? How can any positive effects of goal setting for resource generation be realized in the context of the processes and methods proposed by this working group?
- How can uncertainty be handled in the decision-making process, and how can questions that may not necessarily be captured through economic assessment or economic modeling be answered?
- What are the best ways for countries and development partners to invest in information and priority-setting capacity? How can countries better understand the importance of generating their own epidemiological and economic data?
- What would be the best way to consolidate existing information, strengthen existing data repositories, and expand these existing resources to accommodate new information?
- To what extent are economic models and analyses generalizable to or transferable amongst countries with similar health systems or epidemiology? How can models help determine when and where country-specific data collection would be valuable?
- What would be the best way to ensure the quality and representativeness of local data collection?

Appendix 1. Processes for developing WHO guidelines

The World Health Organization (WHO) produces normative guidance for countries on best practice approaches for the control of various diseases of global health importance to inform choices among different interventions that have an impact on health.

WHO guideline development process

The WHO Guideline Development Handbook (the latest version of which was published in 2014) was developed by WHO to inform the process of developing guidelines and ensure the approaches are standardized[40] and that the extent to which these processes are adhered to has been reviewed.[41] Guideline development is overseen by the WHO Guideline Review Committee.

The process begins by developing a planning proposal document. Three guideline groups are then established with differing responsibilities:

1. The Steering Group comprises WHO staff members responsible for overseeing the activities.
2. The Guidelines Development Group develops the PICO questions (on population, interventions, comparators, outcomes), collates and interprets evidence, and formulates the final recommendations.
3. The External Review Group comprises relevant stakeholders or experts who provide input and/or contribute evidence.

The expertise of the Guidelines Development Group is flexible and can include health economists and statisticians, if desired. A methodology expert to advise on the application of the GRADE process is generally necessary for ensuring evidence is assessed appropriately. If an economist is included in the group, he or she is expected to advise on how best to search for appropriate evidence on resource use and associated costs of the interventions considered within GRADE.

Eight domains are provided for considering equity, human rights, and gender issues throughout the process, with opportunities for these concerns to influence planning, decisions on guideline group membership, the formulation of questions, evidence retrieval, and the development of implementation plans and monitoring and evaluation. In regard to information on resource allocation, the guideline handbook acknowledges that fulfillment of a right to health is influenced by how resources are prioritized and advises guideline developers to reflect on the distribution of attention and resources.

Once the guideline groups have been established, a series of PICO questions is created. The handbook provides guidance on how best to create them and what sorts of outcomes should be considered, such

40. World Health Organization 2014b.
41. Burda, Chambers, and Johnson 2014; Sinclair et al. 2013.

as efficacy, cost effectiveness, and equity. A full list of the outcomes that might be considered is detailed and reviewed by the Guideline Steering Group, the Guideline Development Group, and the External Review Group and ranked using a formal rating scale so those that will have the most influence on decision making are put forward for evidence collation and synthesis.

The choice of outcomes, therefore, vitally influences what can be learnt from the PICO questions. Resource use may be included as an outcome for some questions (see Table 1 for an example), but this may also largely be omitted. Whilst it is clear that some questions may not require a full exploration of the impact on resources, the inclusion of resource considerations as an outcome has not, to date, been done consistently or systematically. Once outcomes are agreed on, PICO questions are finalized and prioritized. The choice of questions and outcomes considered heavily influences the recommendations that can be made in the final guideline.

Evidence is collated for each PICO question, either by utilizing previous relevant systematic reviews, or, where appropriate reviews are currently not available, by commissioning new systematic reviews. Originally, PICO questions were most often focused on clinical effectiveness, and, thus, systematic reviews were the most useful kind of evidence to input; but WHO now encourages a range of types of question, and so other types of evidence may be needed.

Once evidence has been synthesized, it is assessed for certainty using GRADE (grading of recommendations, assessment, development, and evaluation). These are internationally agreed standards for making recommendations in a transparent manner. The GRADE working group was established in 2000, and WHO has been using these methods since 2007.

Using GRADE, certainty of evidence is rated as high, moderate, low, or very low. The typical hierarchy of research evidence is followed—that is, randomized controlled trials receive the highest quality classification, with observational studies falling at the lower end of the spectrum (qualitative studies are often not included).

Initial ratings then may be up- or downgraded. Recommendations can be downgraded based on any of the following five criteria: (1) study limitations (no limitations, minor limitations, serious limitations, or very serious limitations), (2) consistency, (3) directness, (4) imprecision, or (5) reporting bias. Recommendations can be upgraded based on any of three criteria: (1) dose response gradient, (2) direction of plausible bias, or (3) magnitude of effect.

As certainty of evidence is assessed for each individual outcome, quality may vary widely. Once certainty has been assessed, recommendations are made utilizing the GRADE Evidence to Decision framework. Here

Table 1. An example of a PICO question with resource use as an outcome

Type of question	Syntax	Population	Intervention	Comparator	Outcome	Example
Resource considerations	What is the cost of intervention X in setting Y? What is the cost effectiveness of intervention X in setting Y, for outcome Z?	What is the population of interest? What is the subpopulation?	What intervention, treatment, or approach is being considered?	What is the cost of the original intervention/ standard of care? Or what is the expected resource use in the absence of any intervention?	What is the cost of intervention X? Which outcome matters most to individuals affected by the disease or condition, and would it provide a metric for cost effectiveness?	What is the cost (O) of a latex-free glove in West Africa (I) for use in managing persons in Ebola treatment units (P)?

Note: P = population; I = intervention; C = comparator; O = outcome.

consideration is given not just to the quality of the evidence from the GRADE process but also to values and preferences related to the outcomes of an intervention or exposure; the balance of benefits and harms; and resource implications.

The guideline group's consideration of resource implications at this point can be informed either by a full formal economic evaluation or by estimates collected during evidence retrieval. The more resources the intervention consumes, the less likely a strong recommendation is warranted. Uncertainty about resource use—questions of whether the net benefits are worth the costs, lack of information about the cost, or questions about whether the resource expenditure is justified by the anticipated benefit—make a conditional recommendation more likely.

Recommendations based on all these considerations may be either strong or conditional. Recommendations may also not be made, or research recommendations may be given. Strong recommendations come with the advice to policymakers that "these could be adopted as policy in most situations."

At this point in the process, draft recommendations are developed and reviewed by everyone who was involved. Draft evidence profiles are also shared so the path from evidence to decision is clear, and an external review is conducted. The guidelines thus produced are then subject to deliberation by the Guidelines Review Committee. Once approved, they are published, disseminated, and translated into different languages. A manual and toolkit developed by the Guidelines International Network has been recommended by WHO to help national decision makers consider whether to accept or reject particular guidelines in their contexts or to modify specific recommendations (see below on adaptation to local context).

Variations on this overall approach exist for rapid review guidelines.

Development of WHO HIV treatment guidelines

WHO has made some attempts in the past to reflect upon the consequences of restrictions on resource availability and, consequentially, to alter its policy recommendations, mainly by taking a "public health approach" to developing HIV guidelines. Considered in the first HIV guideline developed in 2002, this was later built upon, notably in the 2006 guidelines,[42] in response to the rising magnitude of the epidemic and the extremely high costs of antiretroviral treatment (ART) that were constraining coverage of treatment in low- and middle-income settings.[43]

In the 2006 guidelines, the public health approach adopted by WHO resulted in support for simplified treatment protocols and decentralized service delivery with the objective of enabling more HIV-positive patients to be enrolled into care in these settings, where the burden of HIV was greatest. Although some of the interventions recommended were supported despite a lack of high-quality evidence, the promotion of a simplified approach is considered to have driven the huge rise in treatment coverage that stood at 19.5 million individuals by 2016.[44]

By implication, therefore, economic concerns had been considered since the early stages in the roll-out of ART. The first formal use of evidence from cost-effectiveness modeling analyses, however, was in the development of the 2013 WHO HIV treatment guidelines.

This evidence was submitted to support the development of clinical recommendations alongside data from trials and observational studies and reviewed through GRADE. Although the cost-effectiveness modeling analyses were reviewed by the Guidelines Development Group, however, guidance on how to evaluate evidence for population-level effect estimates was not available, nor was there agreement on the appropriate

42. Gilks 2006.
43. Gilks et al. 2006.
44. Ford et al. 2018.

Table 2. Summary of challenges using cost-effectiveness modeling in WHO guideline development

Challenges: WHO Point of View	Challenges: Modelers' Point of View
■ Insufficient guidance on the types of questions that might be addressed with models ■ The question of when models add value to existing primary studies and data ■ The limitations of modeling ■ How to evaluate the quality of a model ■ How to apply the GRADE approach for evaluating the quality of a body of evidence ■ How to integrate the outcomes of models with primary data ■ How to present the results of modeling to a guideline development group tasked with formulating recommendations based on evidence	■ Informal manner in which modeling was incorporated into guidance ■ Modeling done for a small selection of scenarios in a few countries and extrapolated ■ Modeling not conducted in close collaboration with those countries, and therefore without the benefit of all the data that could have been helpful (in particular on costs, resource constraints, and cost-effectiveness thresholds) ■ Modelling done at the level of the "outcome" rather than the "strategy," leaving a gap between recommendations and the next steps of the "program planners"

Source: Easterbrook et al. 2014; Hallett et al. 2014.

place and contribution of modeling in WHO guidelines development processes. Some held the opinion that these analyses should not have a role in informing clinical guidance, which, some thought, should only be informed by primary empirical and observational evidence. Consequently, the Guidelines Review Committee faced a number of challenges in trying to determine the implications of the modeling analyses and report on the quality of the studies (Table 2).[45]

WHO recommended the following for future modeling:[46]

- Transparent reporting of model inputs and results
- Agreement on a set of standards for evaluating the quality of modeling for application in health care policymaking
- Acceptance of cost-effectiveness modeling as one of many pieces of information that can be considered in the development of WHO guideline recommendations
- Improved dialogue between model developers and model users or decision makers
- Giving WHO a role in convening and reviewing multi-model analyses for health care policy
- Facilitation of data collection that can usefully inform modeling analyses

Furthermore, for continued consideration of modeling analyses in subsequent guidelines, it was agreed that a consultation on the optimal inclusion of findings from modeling analyses was necessary.

The 2016 consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection did also consider modeling analyses contributed by members of the HIV Modelling Consortium; however, the analyses delivered were based on what the modelers felt they could most readily show, as opposed to being derived from PICO questions. A number of modeling analyses are presented in the appendices of this guidelines document.

Further challenges of the guideline development process

The use of the GRADE methodology for developing recommendations can lead to a focus on questions on which evidence on clinical and public health effectiveness and/or safety is available and academic interest is high (for

45. Easterbrook et al. 2014.
46. Ibid.

example, the most effective drug to use for a condition). Little consideration is given, however, to each question in the broader context of the causes of morbidity and mortality in the population and the effective delivery of interventions to prevent or treat them.

Whilst acceptance of resource constraints into guideline development represents progress, the GRADE process is ill-suited to the task of informing programs, particularly if the intention is to tailor these recommendations to very different contexts.

Incorporating resource use as an "outcome" mischaracterizes the nature of the policy issue. Resources or costs are not usually important in their own right but instead are of concern because total resources (budgets) are constrained, and making claims against them for one intervention has consequences for the delivery of others—that is, the issue is one of opportunity costs.

In a recent letter to The Lancet, members of WHO voiced the following challenges:

- WHO guidelines are generally disease-specific, which might not reflect the way national ministries of health are organized or care is delivered.
- Funding constraints might influence both priority setting (with guidelines developed according to financial opportunities) and the quality of guidelines.[47]

Adaptation of WHO guidelines at the country level

Once WHO guidelines have been developed, the recommendations are intended to be adopted or adapted at the country level, as appropriate. No standard guidance is provided by WHO on how to adapt guidelines for implementation at the local level.

A number of reviews have been conducted of WHO guidelines and the advice provided on how they can be adapted and implemented. These have largely concluded that this advice is limited. One study has described the guidance as "brief" and "passive," with WHO focused on the dissemination of guideline information but not on how to adapt it.[48] Passive approaches do not challenge the appropriateness of each recommendation for any given context based on local epidemiology and resource availability.

One study that reviewed a range of WHO guidelines found no standard set of guidance and called for a model to detail the steps for contextualization, adaptation, and implementation.[49] Another, reviewing the WHO nutrition guideline, found guideline adaptability in need of improvement.[50]

Examples do exist of additional information being provided to program managers that is specific to them—for HIV in 2013, for instance, and tuberculosis in 2014, as well as the 2014 and 2016 hepatitis C guidelines—providing a framework for policymakers to help them prioritize who receives treatment. This, however, is not routinely done.[51] For HIV, the chapter for program managers published to accompany the 2013 consolidated guidelines stated it was developed to help guide decision making in settings with a high burden of HIV, acknowledging that complex decisions regarding cost and cost-effectiveness would need to be made, as implementing all recommendations would not be possible given resource constraints.

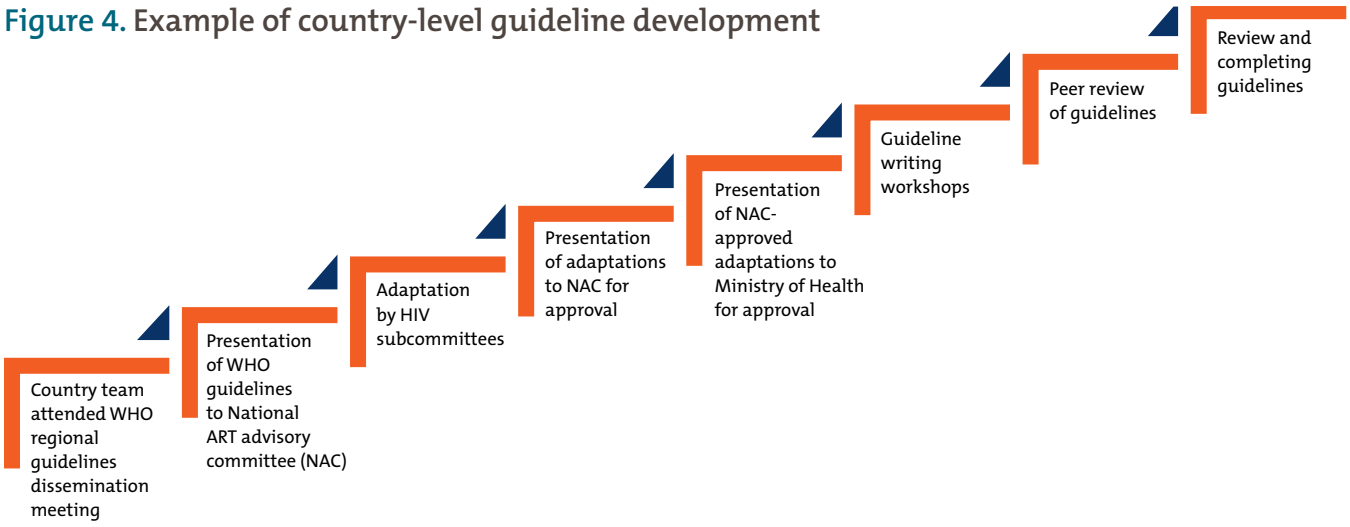
This document recommended the use of the Modes of Transmission model or "know your epidemic, know your response" analyses and use of service design and program performance analyses to help consider whether recommendations should be adopted or adapted. It advised consideration of opportunity costs associated with implementation of certain interventions.

In the more recent 2016 consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection, the chapter for program managers was not included; however, similar guidance was provided

47. Norris and Ford 2017.

48. Wang, Norris, and Bero 2015.
49. Ibid.
50. Dedios et al. 2017.
51. World Health Organization 2016b.

Figure 4. Example of country-level guideline development



within the final chapter on dissemination of the guidelines to countries and their adaptation and evaluation by them. This chapter highlighted the need to estimate costs of implementing the recommendations and assessing them in line with delivering a national health benefits package. In particular, it noted, "The package needs to be adapted for different populations, locations and settings and regularly reviewed and updated as necessary." WHO recommended the use of several program planning tools to help guide decision-making: Spectrum, One Health, Goals, Optima, and the Asian Epidemic Model (AEM, for concentrated epidemics).

A number of recommendations for improving adaptation of WHO guidelines have been put forward:[52]

- WHO guidelines should systematically include a widely accepted and standardized adaptation methodology.
- Evidence-to-decision frameworks should be shared to assist local decision makers or inform them on what influenced the recommendations. This has been done a few times—for example, with the HCV guidelines in 2014. The HCV guidelines present details on the evidence on resource use for each recommendation, alongside consideration about harms and benefits and implementation.[53]
- Reporting of previously used processes should be improved.
- Consolidated guidelines for prevention and treatment of HIV in Uganda (2016)

The case of Uganda illustrates the process for developing a national HIV treatment guideline, which begins with attendance at the WHO regional dissemination meeting and ends with adoption and approval of the guideline by local guidelines groups, including those from the community of people living with HIV and external experts. In Uganda, local adaptation included a review of evidence cited in the WHO guidelines, presentation and review of any local evidence, and discussion of and agreement on the adaptation.[54] Technical support and peer review of the guidelines was provided by representatives from WHO, the Centers for Disease Control and Prevention (CDC), the United States Agency for International Development (USAID), the Clinton Health Action Initiative (CHAI), and the Elisabeth Glaser Pediatric AIDS Foundation (EGPAF).

The process of guideline development is detailed in Figure 4.

52. Godah et al. 2016.
53. World Health Organization 2014a.
54. Republic of Uganda, Ministry of Health 2016.

Appendix 2.
Processes for developing national guidelines: A case study

A growing number of countries have health technology appraisal (HTA) agencies that conduct or oversee the process of developing recommendations on which health care interventions should be approved and funded within their health systems. As each has adopted its own locally approved procedures, processes differ among countries. Here we present as a case study one of the longer-established agencies.

England's HTA agency, NICE (the National Institute for Health and Care Excellence), first published clinical guidelines in 2002, but it has continually refined its processes and methods of guideline development.

NICE clinical guidelines have used GRADE to assess the quality of the evidence for outcomes since 2009. The use of GRADE is now being expanded to public health and social care guidelines. Unlike WHO, however, NICE does not use GRADE to formulate recommendations or grade their strength. Instead, NICE uses decision-making criteria based on cost effectiveness.[55]

Each NICE guideline is developed by a committee composed of experts in the relevant disease area, including doctors, nurses, other health professionals, and at least two lay people with experience of the condition (as patients or family members, or through involvement with patient organizations). They are supported by staff with technical expertise. The guideline committee decides the research questions to be included in each guideline in consultation with NICE. For each question, it conducts two complementary reviews of the published literature, one clinical and one economic.

The committee first constructs a clinical review protocol for each question based on the PICO format. The protocol includes up to seven outcomes, among which health-related quality of life is usually included. This means that if published studies have measured the effect on quality of life of the intervention being studied, these data should be identified and made available for any potential economic work, as well as being included in the clinical review.

Where relevant, the outcomes may also include other outcomes of interest in connection with resource use, such as length of hospital stay or number of repeat admissions or procedures. The remaining outcomes are measures of morbidity and mortality relevant to the intervention. Publications from all countries are considered for the clinical review if written in English.

When the literature has been reviewed and relevant papers identified, a meta-analysis is, where technically appropriate, conducted of data for each outcome. Each is assessed for quality using the GRADE approach, and a level of high-, moderate-, low- or very low–quality evidence assigned. The results of the meta-analysis and the GRADE quality rating are presented to the committee, with an explanation of the factors that have caused the quality to be reduced or increased in each case.

NICE's economic evidence review for each question is based on the same population, intervention, and comparators as the clinical review but includes full or partial economic evaluations or cost analyses rather than clinical trials or observational studies. The economic

55. National Institute for Health and Care Excellence 2014.

studies identified may be conducted alongside clinical studies that have also recorded and analyzed resource and cost data, or they may be based on economic modeling, or both.

For the economic review, both the applicability and the methodological quality of each study are assessed to determine whether they should be included. This is done with checklists developed by NICE, which are used to grade both applicability and quality at three levels. The applicability questions prioritize as "directly applicable" analyses conducted in the UK in recent years and with methods close to the NICE reference case, while old analyses conducted in health systems very dissimilar to the UK's or missing substantial relevant data may be rated as "not applicable." For quality, the checklist takes into consideration whether the data used are from the best possible sources, such as clinical effect sizes from a meta-analysis and cost data from up-to-date sources. If a model was used, it should include all relevant factors. Studies rated as "not applicable" or with "very serious limitations" as to their quality are not included in the review. Remaining studies will be included in the guideline, with their degree of applicability and quality stated alongside a summary of their results.

For certain particularly important questions, where no or insufficient published evidence has been identified, an original economic analysis may be developed for the guideline to provide additional evidence for the committee.

The decision-making process requires the committee to consider all the identified clinical and economic evidence, and the quality of each, whilst also discussing committee members' clinical experience and any relevant factors that may have been omitted from the published evidence. In light of all this information, the committee agrees on recommendations.

For an intervention to be recommended, it must first be clinically effective—that is, considering all the outcomes of the clinical review, it is expected to produce benefits for patients compared to at least some of the alternative options.

Second, the committee must be confident that adopting the intervention is a cost-effective use of National Health Service (NHS) resources. This is assessed with reference to a cost-effectiveness threshold of between £20,000 and £30,000 per QALY gained. If an intervention has an incremental cost-effectiveness ratio (ICER) of below £20,000 per QALY gained compared to an alternative, such as current practice—that is, it would cost less than an extra £20,000 spent on this intervention to improve the health of patients by one quality-adjusted life year compared to using the alternative intervention—then the intervention is usually recommended. An intervention with an ICER above £30,000 per QALY is usually not recommended, whilst between these figures various factors are considered, including the degree of certainty the committee has in the evidence. An exception is made to this threshold for end-of-life conditions, where a higher threshold may be used. Box 4 provides an example of the use of economic evidence in a NICE guideline.

Recommendations can either be strong (the intervention should normally be provided), or weaker (clinicians should consider providing the intervention). The quality of the clinical and economic evidence helps inform the committee regarding the level of certainty in the results found, and so may influence the strength of the recommendations made; but a recommendation may be made even with low-quality evidence—for example, if the magnitude of effect is large and consistent. If the evidence is clear that an intervention is not clinically effective, not safe, or not cost effective, the committee may make a strong negative recommendation, stating that the intervention should not be used.

If no published clinical evidence or no economic evidence was identified, then the committee must use its expert opinion to formulate recommendations. Guidelines may not, however, strongly recommend an intervention expected to lead to a significant increase

Box 4. The use of economic evidence in the NICE hearing loss guideline

The NICE guideline NG98 on hearing loss in adults (2018)[a] assessed the clinical and economic evidence on the effectiveness of hearing aid use. Because no published evidence relevant to the UK was found, NICE developed an original health economic model comparing early or late adoption of hearing aids with non-use. This quantified effectiveness as the increase in health-related quality of life caused by wearing hearing aids (which had previously been measured in the UK), used UK equipment and appointment costs, and modeled this over a lifetime horizon.

The model found hearing aid use to be cost effective compared to non-use, with the ICER below £5,000 per QALY gained, and explored the certainty of this result with a number of sensitivity analyses in which data inputs were varied. As a result, the committee recommended that hearing aids should be provided for all adults with relevant types of hearing loss.

a. National Institute for Health and Care Excellence 2018.

over current NHS costs (over £1 million per year) unless published or original economic evidence is available to support the recommendation. Where evidence is insufficient for the committee to be sure of the best course of action, it may alternatively make a recommendation for further research to be conducted.

All NICE guidelines are subject to public consultation with stakeholders, both at the scoping stage, when the areas to be researched are being proposed, and when draft recommendations have been made. Stakeholders include professional medical societies, patient groups, pharmaceutical companies, health care providers, such as hospitals, and local budget holders responsible for commissioning care. It is usual for some recommendations in each guideline to be revised following input from stakeholders.

While guidelines are not legally binding on the NHS, local service commissioners or providers need to demonstrate a reasoned decision-making process for not following NICE guidance.

Appendix 3.
Processes for developing global goals: Family planning 2020 and the HIV fast-track targets

Family Planning 2020: "120 by 20" target

Family Planning 2020 (FP2020) is a global partnership that supports the right of women and girls to decide, freely and for themselves, whether, when, and how many children they want to have. FP2020 works with governments, civil society, multilateral organizations, donors, the private sector, and the research and development community. The FP2020 target is to provide access to family planning to an additional 120 million women worldwide between 2012 and 2020.[56]

To devise a goal that was sensitive to country interpretation (and as some targets could indicate pressure for population control), a Family Planning Metrics Group was established that would utilize modeling to assist in selecting the metric for the target and to set an ambitious but feasible numerical goal. The process used to select the FP2020 target was published, and many challenges were cited.

The metric for the target was originally intended to be "unmet need for family planning." It was determined, however, that this approach would present complications for tracking progress—shifts in childbearing desires, for example, or the need to administer lengthy surveys. Therefore, a global goal focusing on the number of people having access to contraceptives was selected, with the intention that countries set their own national targets (see Box 5).

HIV fast-track targets: "90-90-90" and "95-95-95"

As Table 3 shows, the HIV response has had numerous, arguably ambitious, targets.

In 2014, the Joint United Nations Programme on HIV/AIDS (UNAIDS) set the "fast-track" targets that operationalize what countries need to do, and what program coverage targets need to be attained at certain time points, to achieve the policy goal of ending the AIDS epidemic by 2030, as advocated in the SDGs. By 2020, countries are to have met the following targets:

- 90 percent of people living with HIV (PLHIV) diagnosed
- 90 percent of those diagnosed with HIV receiving treatment
- 90 percent of those on treatment having achieved viral suppression

For 2020 to 2030, these coverage targets shift to 95 percent.

56. Brown et al. 2014.

Box 5. Modeling to set the FP2020 target and estimate cost and impact

To set a global target for family planning, mathematical modeling was utilized based on an aggregate for all 69 participating low-income countries, recognizing that each would progress at a different rate and according to the provisions of its national plan.

The first challenges were encountered by the Futures Institute and the Guttmacher Institute, which identified a baseline estimate of contraceptive prevalence in the 69 countries in 2012 to guide setting the target but found that comparable up-to-date national estimates were scarcely available; the latest data from some settings were a decade old. A number of approaches were taken to provide updated estimates, including the use of regional averages, matching countries according to equivalent demographic and family planning profiles, taking estimates from contiguous countries, drawing upon earlier survey data containing the missing items, and drawing from published reports of subnational surveys from countries having little or no national survey information regarding particular items. The Futures Institute conducted linear projections to estimate the following for 2012 to 2020:

1. ***An achievable rate of growth in contraceptive prevalence:*** A doubling in the overall growth rate (from 0.7 percent to 1.4 percent) for all 69 countries by 2020 was selected as a modest and achievable rate of growth.
2. ***The amount of funds needed to realize that rate of growth:*** The needed funds were estimated at US$4.3 billion, including costs of commodities, supply, labor, and systems and programs, using unit costs at the country level and then aggregating to the global level. This amount was in addition to the approximate US$10 billion required to maintain services for the existing 258 million contraceptive users in the 69 countries through 2020.
3. ***The impact from achieving the goal:*** An estimated 116 million unintended pregnancies, 52 million abortions, 212,000 maternal deaths, and 2.8 million infant deaths (for 2013–20, inclusive) would be averted

Sources: Brown et al. 2014; Silverman and Glassman 2016.

Table 3. Overview of global HIV targets

Target	Time frame	Set by
"3 by 5": 3 million people on ART by 2005	2003–5	WHO / UNAIDS
MDG goal 6: The spread of HIV/AIDS halted and reversal begun by 2015	2000–2015	UN
"15 by 15": 15 million people on ART by 2015	2011–15	UNAIDS
Reduction of new HIV infections among children by 90 percent	2011–15	WHO
Voluntary medical male circumcision services for 20 million men (subsequently 27 million)	2011–16 (by 2020)	WHO / UNAIDS
SDG target 3.3: End the epidemics of AIDS, tuberculosis, malaria, and neglected tropical diseases, and combat hepatitis, waterborne diseases, and other communicable diseases.	2015–30	UN
Fast-track:		
90-90-90: 90 percent of PLHIV to be aware of their status; 90 percent of those on treatment; 90 percent of those achieving viral suppression	2015–20	UNAIDS
95-95-95: 95 percent for each of these three metrics	2015–30	UNAIDS
HIV Prevention Roadmap goal to reduce new infections by 75 percent	2017–20	UNAIDS

Box 6. Modeling to set fast-track targets and estimate cost and impact

As targets were selected prior to modeling, future trends were modeled using the Goals model (from the Spectrum software package) and the Resource Needs Model to estimate the following:

1. ***The impact from achieving fast-track targets (that is, whether targets would be achieved to end AIDS by 2030):*** An estimated 1 million AIDS-related deaths and 18 million new HIV infections would be averted globally during the period 2016–30 (a reduction of nearly 80 percent).
2. ***The amount of funds that would be needed to realize fast-track targets:*** An estimated $26.1 billion per year would be needed globally. This figure exceeds the estimated $19 billion mobilized for the HIV response at that time.

Sources: United Nations Programme on HIV/AIDS 2016; Stover 2004; Kerr et al. 2015; Stover et al. 2016.

Unlike FP2020, the fast-track targets for HIV are intended to be adopted by all countries without translation to local contexts.

Also, unlike FP2020, the fast-track targets were not set using modeling so they would be "ambitious but feasible." Instead, targets were set arbitrarily, and modeling was conducted afterwards to explore whether they would achieve the policy goal of ending the AIDS epidemic by 2030 (in addition to achieving the 90-90-90 prevention goals). The modeling conducted is summarized in Box 6.

The modeling was not used to assess whether the goals were cost effective and could actually be afforded within available budgets.

Appendix 4.
Country experiences: What do guidelines and goals mean for health care delivery?

Below we explore some of the challenges guidelines and goals present for health care delivery in LMICs.

Challenges for countries in responding to guidelines and goals

In many instances following the release of global guidelines and goals, development partners make resources available to LMICs so they may respond. The response in these countries is often greater than in high-income countries, as the receipt of such assistance may depend on the adoption of guidelines or goals, and the offer of technical and financial assistance may be impossible for them to pass up. Anecdotal evidence exists, for example, of funding requests to the Global Fund being rejected if they do not align with key global goals. The U.S. President's Emergency Plan for AIDS Relief (PEPFAR) has also been said to decline to release funds until national guidelines have been revised.[57]

Where technical assistance is offered, it is often done in the absence of technical capacity at the national level. This dynamic results in external partners' advising national policymakers what to do, with those at the national level not having the technical expertise to consider alternatives.

In recent years, as global financing for health has been in decline, efforts have been made to boost domestic revenues. Some development partners have been utilizing matched funding or co-funding arrangements as part of their provision of development assistance to encourage domestic resource mobilization strategies, which may exacerbate misallocations. Diseases or issues with non-vocal constituents may lose out as domestic resources are reallocated.

Challenges in responding to goals and guidelines in LMICs are exacerbated by lack of country-specific data and limited resource mapping. These are summarized in comparison to an ideal process in Figure 5.

Threats of a reduction in funding by large donor organizations, such as PEPFAR,[58] also significantly affect the planning process and prevent sustainable implementation of country plans.

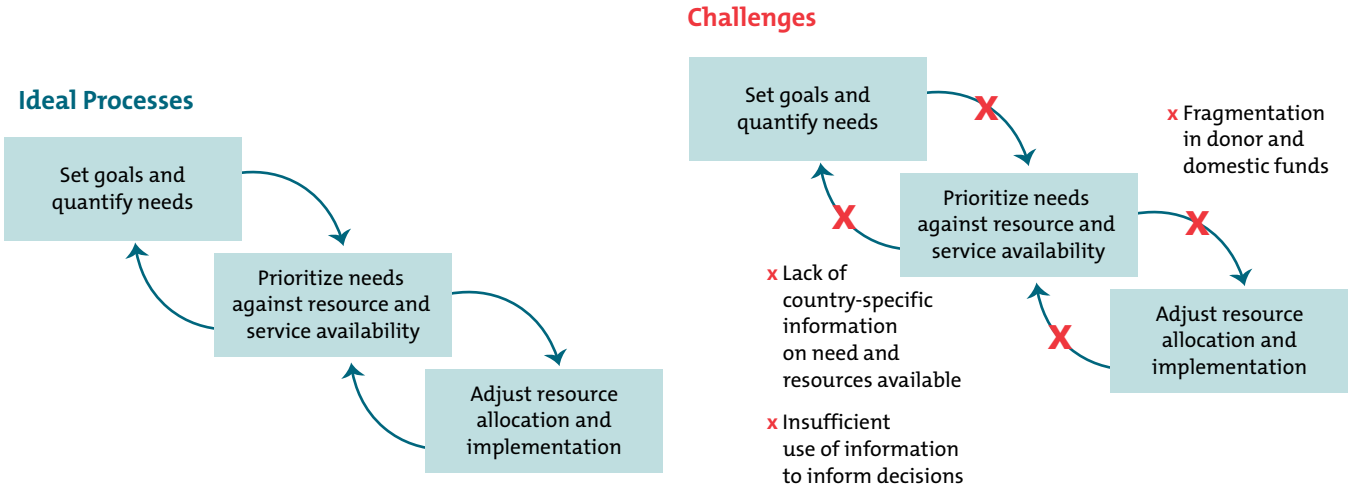
Challenges specific to how guidelines are translated

The current approach to guidelines developed by WHO leads to binary outcomes (an intervention is "recommended" or "cost effective"), even though epidemics, health systems, and resource constraints are, in reality,

57. McRobie et al. 2017.

58. Harris 2017.

Figure 5. Goal setting and prioritization



diverse, and an intervention can only ever be said to be "cost effective" in comparison to a specified alternative or alternatives and considered whilst recognizing other calls on limited resources. Consequently, guidelines—much like the Essential Medicines List—are treated as endorsements to be taken up at the national level despite this diversity of conditions.

Challenges specific to how targets are translated

Specific, narrow targets like 90-90-90 that are set with the intention that countries can attain the same coverage levels are likely to generate more issues than those like the FP2020 targets or SDGs that encourage local adaptation of the targets and the setting of what is realistic, given local epidemiology and budget constraints.

To meet such high coverage levels as 90-90-90/95-95-95, a substantial amount of resources may be required, and these may be better utilized elsewhere in the health care system. The target is thus set regardless of how feasible it is within the budget or other health system constraints the country faces. Indeed, some countries have nearly achieved the 90-90-90 targets, but this is not at all a uniform improvement globally.[59]

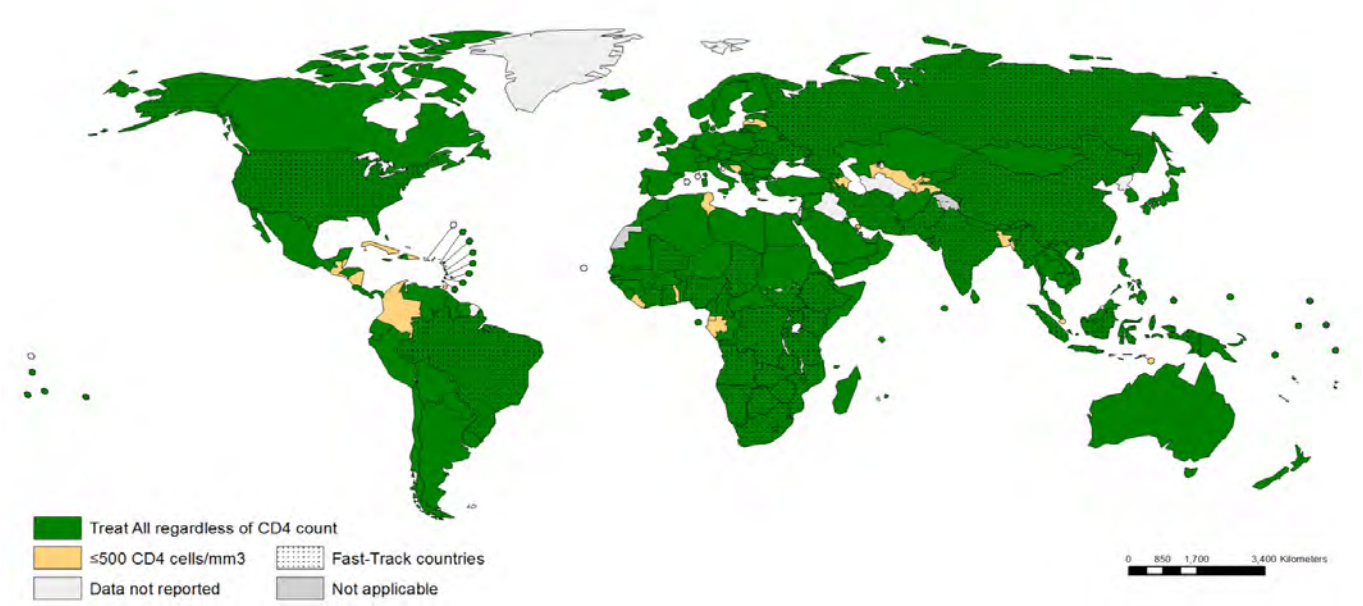
The 90-90-90 target is incredibly complex, as it requires a shift from a generalized national scale-up of ART programs to programs that target specific populations and geographical areas. Thus, the response would benefit from national-level modeling to identify where to target interventions for the best allocation of limited resources.

Many countries with limited resources and technical capacity need to rely on externally provided technical assistance to guide their responses to the targets. The models used and measures taken to assist them can vary substantially, and more needs to be done to ensure the process is collaborative, a national budget holder is present, and efforts are made to utilize national data (and work with local decision makers to discuss future data collection needs). Furthermore, modelers should ensure country decision makers are aware of the different outputs of the different modeling analyses and assumptions used.

In 2017, WHO and the World Bank published a report on progress towards universal health care coverage in response to target 3.8 of the Sustainable Development Goals (3.8.1 on coverage of essential health services and 3.8.2 on the proportion of a country's population with

59. Marukutira et al. 2018.

Figure 6. Uptake of WHO policy for Treat All ART initiation among adults and adolescents living with HIV (situation as of mid-2018)



Source: Global AIDS Monitoring (UNAIDS/WHO/UNICEF) and WHO HIV Country Intelligence Tool, 2018.

catastrophic spending on health). Whilst data were still being collected, they estimated that approximately 50 percent of the world's population did not have access to all essential health services, and many faced catastrophic health expenditures.[60]

Data on a number of tracer indicators are available. Whilst the average increase in coverage across a range of nine tracer indicators from 2000 to 2015 was 1.3 percent a year (approximately 20 percent over the time period), rapid rates of increase were seen in coverage of antiretroviral treatment for HIV (from 2 percent in 2000 to 53 percent in 2016) and the use of insecticide-treated nets for malaria prevention (from 1 percent in 2000 to 54 percent in 2016).

These figures demonstrate the substantial impact on certain diseases arising from the success of international advocacy and the presence of development assistance for these particular activities, whilst overall access to essential health services has been somewhat overlooked. Below we provide two examples of national responses to goals and guidelines.

Malawi's response to HIV and family planning goals and guidelines

Malawi is faced with significant health financing challenges, given that its allocated per-person health budget at US$26 per year is the lowest of all sub-Saharan African countries (although this amount actually represents the highest regional expenditure on health as a percentage of gross domestic product).[61] Given the scarcity of resources for health, Malawi continues to rely heavily on contributions from development partners: between 2012–13 and 2014–15, 61.6 percent of total health expenditure was provided by development

60. World Health Organization and World Bank 2017; 2015.

61. United Nations Programme on HIV/AIDS 2017.

partners, 25.5 percent by government, and 12.9 percent by households.[62]

Regardless of the financial challenges facing Malawi, the HIV program there has historically been very responsive to WHO treatment guidelines and aligned to globally set targets.[63]

Malawi was one of the first sub-Saharan countries to adopt a "public health approach" to HIV treatment scale-up, as promoted by the World Health Organization to encourage rapid ART initiation for people living with HIV (PLHIV),[64] and a 2015 study of the national adoption of WHO HIV guidelines demonstrated that Malawi has developed explicit policy largely in response to guidance from WHO for many aspects of care along the HIV continuum.[65] Notably, however, Malawi adopted Option B+ in 2011 before the WHO guidance was developed, as this was pioneered in the country.

Most recently, Malawi has adopted the 90-90-90 targets and, as of this writing, was on track to meet them. The country's National Strategic Plan for HIV and Aids, 2015–20, presents budget projections for achieving 90-90-90—alongside other NSP activities—within its investment case analysis; the cost is estimated at $1.39 billion over the five-year period, compared against an anticipated $1.1 billion funding envelope (including funds from the Global Fund that were unsecured at the time). The individual country cost estimate for meeting the fast-track targets was $1,415,365,939 between 2015 and 2030.[66]

The response to targets and guidelines in Malawi would clearly not be possible without support from development partners. The HIV program is heavily supported by them, with 74 percent of funding received from the Global Fund (for procurement and distribution of antiretrovirals and key commodities and supply chain management) and a further 12 percent from other donor resources.

Table 4. Malawi development indicators

	Baseline	Target
Maternal mortality ratio per 100,000 live births	510 (MDG)	155 (MDG)
Newborn death rate per 1,000 live births	44.3 (MICS)	78 (MDG)
Total fertility rate	57% (DHS)	4 (National Sexual and Reproductive Health Strategy, 2011–2016)
Unmet need (married women)	26.1% (DHS)	20% (National Sexual and Reproductive Health Strategy, 2011–2016)
Modern contraceptive prevalence rate (married WRA)	42.2%	60% (FP2020)

Source: Government of the Republic of Malawi 2015.

Malawi has also made commitments to global targets for family planning (see Table 4). Most recently, as a participant in the July 2017 About Family Planning Summit in London, the government of Malawi made 11 commitments to FP2020, notably setting a goal of 60 percent modern contraceptive prevalence rates (CPRs) among married and sexually active women of reproductive age. To achieve this, Malawi will need to increase funding for family planning significantly. As of 2015, the country relied heavily on donor funding to finance 80 percent of contraceptives.[67]

The Malawi Essential Health Package (EHP) was revised in 2017, using cost-effectiveness analysis to prioritize interventions that will, as far as possible, maximize population health. The total cost of the package still exceeds available resources, but the absolute shortfall (that is, short of 100 percent coverage) varies widely across diseases; the total of available resources for HIV in 2015–16 was US$81,670,857, whereas the cost of implementing the EHP for HIV was estimated at only $46,251,124. Comparatively, resources available for

62. Government of the Republic of Malawi 2017.
63. Jahn et al. 2016; Libamba et al. 2007.
64. Dasgupta et al. 2016.
65. Church et al. 2015.
66. Stover et al. 2016.
67. Government of the Republic of Malawi 2015.

malaria for the same time period totaled $13,440,439; however, an estimated $30,020,036 was needed for implementation of the EHP for the disease. This demonstrates the vast discrepancies between resource needs and availability by disease area. Overall, total resource availability was $141,866,109, while $247,042,586 was needed for the total implementation, again showing how HIV is largely over-resourced relative to the overall needs for delivering the EHP.[68]

Uganda's response to HIV and family planning goals and guidelines

Uganda, similar to Malawi, faces severe resource constraints in delivering health care. The most recent national health account data, published in 2013–14, gave the total health expenditure in Uganda in 2012–13 as U Sh 4,866 billion, translating to a per capita spending of U Sh 144,374 (US$55).[69] The primary sources of health care financing were households (37 percent—mostly out-of-pocket expenditure, far exceeding WHO's target of 20 percent), development partners (45 percent), and government (15 percent).[70] Private insurance constituted a small proportion of total health expenditure. Most of the development partner assistance was off-budget, as funded through PEPFAR.[71]

Regardless of these budget constraints, Uganda has, like Malawi, been very responsive to HIV goals and guidelines since its initial response to "3 by 5." Uganda has met the global milestone for the elimination of mother-to-child transmission and is reportedly on track to meet the 90-90-90 targets.[72] It is thought, however, that modeling to guide program planning in response to 90-90-90 aided the selection of slightly lower coverage targets, based on estimates of resource availability. Resource needs for meeting 90-90-90 were estimated to exceed availability of resources for the time period of the target.

The additional resources provided by donor partners to meet the targets were minimal. Instead, resources were front loaded or reallocated within existing grants, and novel domestic resource allocation approaches were utilized (although domestic financial gains were also minimal) in an attempt to reach the target. In addition, an approach was used that sought efficiencies by targeting populations and geographical areas, which were identified by modeling conducted for PEPFAR. Government resources are not thought to have been reallocated to meet these targets, as these activities are donor funded, while government resources are focused on recurrent human resource costs.

A 2015 study of national adoption of WHO HIV guidelines demonstrated that Uganda had largely developed explicit policy in response to guidance from WHO for many aspects of care along the HIV continuum;[73] however, fewer explicit policies had been adopted relating to retention in care.[74] High ART coverage levels have been attainable given substantial donor investment, with 90 percent of HIV commodities historically provided through PEPFAR and the Global Fund.

Financing of the HIV program domestically is unsustainable in Uganda. To meet 90-90-90 targets, it was necessary to adopt WHO guidance to initiate all HIV-positive individuals into ART, regardless of their CD4 cell count. It is known that PEPFAR required the update of the antiretroviral guidelines before it would disburse funds, putting Uganda in the position of having to accept the offer despite knowing its funding of ART in the long term was unsustainable.

The government of Uganda has also made commitments to meet family planning targets, stating its intention to lower unmet need for family planning by 10 percent by 2020 and increase the contraceptive prevalence rate to 50 percent in response to FP2020. This commitment included raising the budget allocation for family planning supplies from US$3.3 million to $5 million for the next five years and to mobilize

68. Government of the Republic of Malawi 2017.
69. Cited by Dedios et al. 2017.
70. Republic of Uganda, Ministry of Health 2016.
71. U.S. President's Emergency Plan for AIDS Relief 2017; Republic of Uganda, Ministry of Health 2018.
72. McRobie et al. 2017.
73. Church et al. 2015.
74. Hallett et al. 2014; World Health Organization 2016b.

an additional $5 million a year through donor financing. Even with this effort, however, a resource gap of approximately $10 million per year will remain.

Looking more broadly at the whole range of health care provision in Uganda, the same problems of affordability and sustainability are evident. Uganda first established its National Minimum Health Care Package (UNMHCP) in 1999–2000. The most recent revision of the UNMHCP estimated the per capita cost to deliver the package at $41.20, which is substantially higher than current per capita spending on health available from public resources, thus resulting in implicit rationing.

Summary of experiences in Malawi and Uganda

Regardless of significant financial challenges, both Malawi and Uganda have responded to global goals and guidelines. Notably, different target levels for contraceptive prevalence rate (CPR) were set by the two countries (60 percent for Malawi versus 50 percent for Uganda), whereas 90-90-90 appears to have had a significant impact, with both deemed to be on track to meet the targets, demonstrating significant investment and policy change.

In both Malawi and Uganda, allocation of resources to different diseases is highly variable and does not necessarily correspond to where resources could best be spent to increase population health as much as possible. This is indicated in Malawi by vast discrepancies in resource shortfalls for provision of the EHP, with non-vocal constituents receiving less funding. In each country, resource needs estimates for meeting the fast-track targets are much greater than the total health expenditures in each country (that is, insufficient resources are available to meet the targets).

Targets and guidelines seem to be having both positive and negative impacts in Malawi and Uganda. In Uganda, for example, 90-90-90 appears to have invigorated novel domestic financing mechanisms and encouraged program efficiency; however, international organizations appear to have put pressure on the country to respond, and matched funding or co-funding arrangements may exacerbate misallocations.

References

Akhlaq, A., B. McKinstry, K. B. Muhammad, and A. Sheikh. 2016. "Barriers and Facilitators to Health Information Exchange in Low- and Middle-Income Country Settings: A Systematic Review." *Health Policy and Planning* 31 (9): 1310–25.

Allcott, H., and S. Mullainathan. 2012. "External Validity and Partner Selection Bias." Working paper 18373. National Bureau of Economic Research, Cambridge, MA. September. https://web.stanford.edu/group/SITE/SITE_2012/2012_segment_5/2012_segment_5_papers/allcott.pdf.

Baltussen, R., and L. Niessen. 2006. "Priority Setting of Health Interventions: The Need for Multi–Criteria Decision Analysis." *Cost Effectiveness and Resource Allocation* 4 (1): 14.

Boerma, T., C. Victora, and C. Abouzahr. 2018. "Monitoring Country Progress and Achievements by Making Global Predictions: Is the Tail Wagging the Dog?" *The Lancet* 392 (10147): P607–9.

Brown, W., N. Druce, J. Buånting, S. Radloff, D. Koroma, S. Gupta, et al. 2014. "Developing the '120 by 20' Goal for the Global FP2020 Initiative." *Studies in Family Planning* 45 (1): 73–84.

Burda, B., A. Chambers, and J. Johnson. 2014. "Appraisal of Guidelines Developed by the World Health Organization." Public Health 128 (5): 444–74.

Cairncross, S., H. Periès, and F. Cutts. 1997. "Vertical Health Programmes." The Lancet 349:S20–S1.

Church, K., F. Kiweewa, A. Dasgupta, M. Mwangome, E. Mpandaguta, F. X. Gómez-Olivé, et al. 2015. "A Comparative Analysis of National HIV Policies in Six African Countries with Generalized Epidemics." *Bulletin of the World Health Organization* 93:457–67.

Claridge, J. A., and T. C. Fabian. 2005. "History and Development of Evidence-Based Medicine." *World Journal of Surgery* 29 (5): 547–53.

Culyer, A. J., and J. Lomas. 2006. "Deliberative Processes and Evidence-Informed Decision Making in Healthcare: Do They Work and How Might We Know?" *Evidence & Policy: A Journal of Research, Debate and Practice* 2 (3): 357–71.

Dasgupta, A. N., A. Wringe, A. C. Crampin, C. Chisambo, O. Koole, S. Makombe, et al. 2016. "HIV Policy and Implementation: A National Policy Review and an Implementation Case Study of a Rural Area of Northern Malawi." *AIDS Care* 28 (9): 1097–109.

Deaton, A. S. 2009. "Instruments of Development: Randomization in the Tropics, and the Search for the Elusive Keys to Economic Development." National Bureau of Economic Research.

Dedios, M. C., A. Esperato, L. M. De-Regil, J. P. Peña-Rosas, and S. L. Norris. 2017. "Improving the Adaptability of WHO Evidence-Informed Guidelines for Nutrition Actions: Results of a Mixed Methods Evaluation" *Implementation Science* 12 (1): 39.

Drummond, M. F., and L. Davies. 1991. "Economic Analysis Alongside Clinical Trials: Revisiting the Methodological Issues." *International Journal of Technology Assessment in Health Care* 7 (4): 561–73.

Drummond M., and A. McGuire. 1997. *Methods for the Economic Evaluation of Health Care Programmes*. 2nd ed. Oxford: Oxford University Press.

Drummond, M. F., M. J. Sculpher, K. Claxton, G. L. Stoddart, and G. W. Torrance. 2015. *Methods for the Economic Evaluation of Health Care Programmes*. Oxford: Oxford University Press.

Easterbrook, P. J., M. C. Doherty, J. H. Perriëns, J. L. Barcarolo, and G. O. Hirnschall. 2014. "The Role of Mathematical Modelling in the Development of Recommendations in the 2013 WHO Consolidated Antiretroviral Therapy Guidelines." *AIDS* 28: S85–S92.

Eaton, J. W., N. A. Menzies, J. Stover, V. Cambiano, L. Chindelevitch, A. Cori, et al. 2014. "Health Benefits, Costs, and Cost-Effectiveness of Earlier Eligibility for Adult Antiretroviral Therapy and Expanded Treatment Coverage: A Combined Analysis of 12 Mathematical Models." *The Lancet Global Health* 2 (1): e23–e34.

Edejer, T. Tan-Torres. 2003. *WHO Guide to Cost-Effectiveness Analysis*. Geneva: WHO. http://www.who.int/choice/publications/p_2003_generalised_cea.pdf.

El–Sadr, W. M., C. B. Holmes, P. Mugyenyi, H. Thirumurthy, T. Ellerbrock, R. Ferris, et al. 2012. "Scale-Up of HIV Treatment through PEPFAR: A Historic Public Health Achievement." *Journal of Acquired Immune Deficiency Syndromes* 60 (Suppl 3): S96–104.

Ford, N., A. Ball, R. Baggaley, M. Vitoria, D. Low-Beer, M. Penazzato, et al. 2018. "The WHO Public Health Approach to HIV Treatment and Care: Looking Back and Looking Ahead." *The Lancet Infectious Diseases* 18 (3): e76–e86.

Gilks, C. F. V. 2006. *Marco Antiretroviral Therapy for HIV Infection in Adults and Adolescents: Recommendations for a Public-Health Approach*. Geneva: World Health Organisation.

Gilks C. F., S. Crowley, R. Ekpini, S. Gove, J. Perriens, Y. Souteyrand, et al. 2006. "The WHO Public-Health Approach to Antiretroviral Treatment against HIV in Resource-Limited Settings." *The Lancet* 368 (9534): 505–10.

Glassman, A., and K. Chalkidou. 2012. *Priority-Setting in Health: Building Institutions for Smarter Public Spending*. Washington, DC: Center for Global Development.

Godah, M. W., R. A. A. Khalek, L. Kilzar, H. Zeid, A. Nahlawi, L. C. Lopes, et al. 2016. "A Very Low Number of National Adaptations of the World Health Organization Guidelines for HIV and Tuberculosis Reported Their Processes." *Journal of Clinical Epidemiology* 80: 50–6.

Gopalappa, C., J. Stover, N. Shaffer, and M. Mahy. 2014. "The Costs and Benefits of Option B+ for the Prevention of Mother-to-Child Transmission of HIV." AIDS 28:S5–S14.

Guyatt, G., Oxman, E. A. Akl, R. Kunz, G. Vist, J. Brozek, et al. 2011. "GRADE Guidelines: Introduction—GRADE Evidence Profiles and Summary of Findings Tables." *Journal of Clinical Epidemiology* 64 (4): 383–94.

Guyatt, G. H., A. D. Oxman, H. J. Schünemann, P. Tugwell, and A. Knottnerus. 2011. "GRADE Guidelines: A New Series of Articles in the Journal of Clinical Epidemiology." *Journal of Clinical Epidemiology* 64 (4): 380–2.

Guyatt, G. H., A. D. Oxman, G. E. Vist, R. Kunz, Y. Falck-Ytter, P. Alonso-Coello, et al. 2008. "GRADE: An Emerging Consensus on Rating Quality of Evidence and Strength of Recommendations." *British Medical Journal* (clinical research edition) 336 (7650): 924–6.

Hallett, T. B., N. A. Menzies, P. Revill, D. Keebler, A. Bórquez, E. McRobie, et al. 2014. "Using Modeling to Inform International Guidelines for Antiretroviral Treatment." *AIDS* 28: S1–S4.

Harris, G. 2017. "Cuts to AIDS Treatment Programs Could Cost a Million Lives." *New York Times*, May 23. https://www.nytimes.com/2017/05/23/world/africa/cuts-to-aids-treatment-programs-could-cost-a-million-lives.html.

Hartman, E., R. Grieve, R. Ramsahai, and J. S. Sekhon. 2015. "From Sample Average Treatment Effect to Population Average Treatment Effect on the Treated: Combining Experimental with Observational Studies to Estimate Population Treatment Effects." *Journal of the Royal Statistical Society: Series A (Statistics in Society)* 178 (3): 757–78.

Imbens, G. W. 2010. "Better LATE than Nothing: Some Comments on Deaton (2009) and Heckman and Urzua (2009)." *Journal of Economic Literature* 48 (2): 399–423.

Jahn, A., A. D. Harries, E. J. Schouten, E. Libamba, N. Ford, D. Maher, et al. 2016. "Scaling-Up Antiretroviral Therapy in Malawi." *Bulletin of the World Health Organization* 94 (10): 772.

Keebler, D., P. Revill, S. Braithwaite, A. Phillips, N. Blaser, A. Borquez, et al. 2014. "Cost-Effectiveness of Different Strategies to Monitor Adults on Antiretroviral Treatment: A Combined Analysis of Three Mathematical Models." *The Lancet Global Health* 2 (1): e35–e43.

Kerr, C. C., R. M. Stuart, R. T. Gray, A. J. Shattock, N. Fraser-Hurt, C. Benedikt, et al. 2015. "Optima: A Model for HIV Epidemic Analysis, Program Prioritization, and Resource Optimization." *Journal of Acquired Immune Deficiency Syndromes* 69 (3): 365–76.

Libamba, E., S. D. Makombe, A. D. Harries, E. J. Schouten, J. K.-L. Yu, O. Pasulani, et al. 2007. "Malawi's Contribution to '3 by 5': Achievements and Challenges." *Bulletin of the World Health Organization* 85 (2): 156–60. https://www.who.int/bulletin/volumes/85/2/05-033688.pdf

Malawi, Government of the Republic of. 2015. *Malawi Costed Implementation Plan for Family Planning, 2016–2020*. Lilongwe: Government of the Republic of Malawi.

———. 2017. *Health Sector Strategic Plan 2 2017–2022: Towards Universal Health Coverage*. Lilongwe: Government of the Republic of Malawi.

Marukutira T., M. Stoové, S. Lockman, L. A. Mills, T. Gaolathe, R. Lebelonyane, et al. 2018. "A Tale of Two Countries: Progress towards UNAIDS 90-90-90 Targets in Botswana and Australia." *Journal of the International AIDS Society* 21 (3): e25090.

McRobie, E., F. Matovu, A. Nanyiti, J. Nonvignon, D. N. Y. Abankwah, K. K. Case, et al. 2017. "National Responses to Global Health Targets: Exploring Policy Transfer in the Context of the UNAIDS '90–90–90' Treatment Targets in Ghana and Uganda." *Health Policy and Planning* 33 (1): 17–33.

National Institute for Health and Care Excellence. 2014. Developing NICE Guidelines: The Manual. London: NICE.

———. 2018. *Hearing Loss in Adults: Assessment and Management*. London: NICE.

Norheim, O. F. 1999. "Healthcare Rationing—Are Additional Criteria Needed for Assessing Evidence Based Clinical Practice Guidelines?" *British Medical Journal* 319 (7222): 1426.

Norris, S. L., and N. Ford. 2017. "Improving the Quality of WHO Guidelines over the Last Decade: Progress and Challenges." *The Lancet Global Health* 5 (9): e855–e6.

Silverman, R., and A. Glassman. 2016. *Aligning to 2020: How the FP2020 Core Partners Can Work Better Together*. Final report of the Working Group on Alignment in Family Planning. Center for Global Development, November 3. https://www.cgdev.org/publication/aligning-2020.

Sinclair, D., R. Isba, T. Kredo, B. Zani, H. Smith, and P. Garner. 2013. "World Health Organization Guideline Development: An Evaluation." *PloS One* 8 (5): e63715.

Spyridonidis, D., and M. Calnan. 2011. "Opening the Black Box: A Study of the Process of NICE Guidelines Implementation." *Health Policy* 102 (2–3): 117–25.

Stenberg, K., O. Hanssen, T. T.-T. Edejer, M. Bertram, C. Brindley, A. Meshreky, et al. 2017. "Financing Transformative Health Systems towards Achievement of the Health Sustainable Development Goals: A Model for Projected Resource Needs in 67 Low-Income and Middle-Income Countries." *The Lancet Global Health* 5 (9): e875–e87.

Stover, J. 2004. "Projecting the Demographic Consequences of Adult HIV Prevalence Trends: The Spectrum Projection Package." *Sexually Transmitted Infections* 80 (suppl 1): i 14–i8.

Stover, J., L. Bollinger, J. A. Izazola, L. Loures, P. DeLay, P. D. Ghys, et al. 2016. "What is Required to End the AIDS Epidemic as a Public Health Threat by 2030? The Cost and Impact of the Fast-Track Approach." *PloS One* 11 (5): e0154893.

Summerskill, W. 2005. "Cochrane Collaboration and the Evolution of Evidence." *The Lancet* 366 (9499): 1760.

Uganda, Republic of, Ministry of Health. 2016. *Consolidated Guidelines for Prevention and Treatment of HIV in Uganda*. https://aidsfree.usaid.gov/sites/default/files/uganda_hiv_gl_2016.pdf.

———. 2018. *Uganda Health Accounts: National Health Expenditure, Financial Years 2016/17 and 2017/18*. http://library.health.go.ug/sites/default/files/resources/NHA_FINAL%20-UGANDA-1%20FY%202016-17_2017-18%20final%20%20%202018-1.pdf.

———. 2016. *Uganda Health Accounts: National Health Expenditure, Financial Years 2012/13 and 2013/14*. http://health.go.ug/sites/default/files/Uganda%20Health%20Accounts_-%20FINAL%20%20REPORT-2013-14.pdf.

United Nations Programme on HIV/AIDS. 2016. *Fast-Track Commitments to End AIDS by 2030*. Geneva, Switzerland: UNAIDS.

———. 2017. *Ending AIDS: Progress towards the 90-90-90 Targets*. Geneva, Switzerland: UNAIDS.

United Nations Programme on HIV/AIDS and World Health Organization. 2018. *Annual Consultation with Pharmaceutical Companies, Partner Organisations and Stakeholders*. Geneva: WHO.

United Nations. 2000. *United Nations Millenium Summit: Declaration of Millennium Development Goals*. New York: United Nations.

——. 2015a. *The Millenium Development Goals Report 2015*. New York: United Nations.

——. 2015b. *Transforming Our World: The 2030 Agenda for Sustainable Development*. Stat. A/RES/70/1. October 21. https://sustainabledevelopment.un.org/content/documents/21252030%20Agenda%20for%20Sustainable%20Development%20web.pdf.

U.S. President's Emergency Plan for AIDS Relief. 2017. *Country Operational Plan 2017: Strategic Direction Summary*. Uganda: PEPFAR. https://www.pepfar.gov/documents/organization/273638.pdf.

Vitoria, M., A. Rangaraj, N. Ford, and M. Doherty. 2019. "Current and Future Priorities for the Development of Optimal HIV Drugs." *Current Opinion in HIV and AIDS* 14 (2): 143–9.

Wang, Z., S. L. Norris, and L. Bero. 2015. "Implementation Plans Included in World Health Organisation Guidelines." *Implementation Science* 11 (1): 76.

Woods, B., P. Revill, M. Sculpher, and K. Claxton. 2016. "Country-Level Cost-Effectiveness Thresholds: Initial Estimates and the Need for Further Research." *Value Health* 19 (8): 929–35.

World Health Organization. 2011. *Global Price Reporting Mechanism (GPRM).* Geneva: WHO. http://apps.who.int/hiv/amds/price/hdd/.

——. 2013. *WHO Consolidated ARV Guidelines.* Geneva: WHO.

——. 2014a. *Guidelines for the Screening, Care and Treatment of Persons with Hepatitis C Infection.* Geneva, Switzerland: WHO.

——. 2014b. *WHO Handbook for Guideline Development*. 2nd ed. Geneva: WHO.

——. 2016a. *Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection: Recommendations for a Public Health Approach.* 2nd ed. Geneva: WHO.

——. 2016b. *Guidelines for the Screening, Care and Treatment of Persons with Chronic Hepatitis C Infection (Updated)*. Geneva: WHO.

——. 2018a. *Updated Recommendations on First-Line and Second-Line Antiretroviral Regimens and Post-Exposure Prophylaxis and Recommendations on Early Infant Diagnosis of HIV: Interim Guidelines: Supplement to the 2016 Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection*. Geneva, Switzerland: WHO.

——. 2018b. *WHO Recommendation: Calcium Supplementation during Pregnancy for Prevention of Preeclampsia and its Complications*. Geneva: WHO.

——. 2018c. *WHO Recommendation on Duration of Bladder Catheterization after Surgical Repair of Simple Obstetric Urinary Fistula*. Geneva: WHO.

——. 2019a. *Thirteenth General Programme of Work 2019–2023.* Geneva: WHO. February 15. https://www.who.int/about/what-we-do/gpw-thirteen-consultation/en/.

——. 2019b. *WHO 13th General Programme of Work (GPW13) Impact Framework: Targets and Indicators*. Geneva, Switzerland: WHO. https://www.who.int/about/what-we-do/thirteenth-general-programme-of-work-2019-2023.

World Health Organization and World Bank. 2015. *Tracking Universal Health Coverage: First Global Monitoring Report.* WHO and International Bank for Reconstruction and Development/World Bank. https://www.who.int/healthinfo/universal_health_coverage/report/2015/en/.

——. 2017. *Tracking Universal Health Coverage: 2017 Global Monitoring Report*. WHO and International Bank for Reconstruction and Development/World Bank. December 13. https://www.worldbank.org/en/topic/universalhealthcoverage/publication/tracking-universal-health-coverage-2017-global-monitoring-report.

Zhang, P., X. Zhang, J. Brown, D. Vistisen, R. Sicree, J. Shaw, et al. 2010. "Global Healthcare Expenditure on Diabetes for 2010 and 2030." *Diabetes Research and Clinical Practice* 87 (3): 293–301.

2055 L Street NW, Floor 5
Washington DC 20036

CGD Europe
1 Abbey Gardens
Westminster
London SW1P 3SE

www.cgdev.org