GUIDANCE NOTE
for the development of national investment cases for neglected diseases

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Acknowledgements: This Guidance Note was commissioned by Uniting Efforts for Innovation, Access and Delivery (Uniting Efforts) and its three core partners – the Government of Japan, the Global Health Innovative Technology (GHIT) Fund, and the United Nations Development Programme (UNDP)-led Access and Delivery Partnership (ADP), implemented by the World Health Organization (WHO), the Special Programme for Research and Training in Tropical Diseases (TDR), PATH and UNDP.

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The views expressed in this publication are those of the authors and do not necessarily represent those of the partners of Uniting Efforts for Innovation, Access and Delivery or the expert contributors or reviewers.

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**Acronyms and abbreviations**

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<tr>
<th>Acronym</th>
<th>Definition</th>
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<tr>
<td>ADP</td>
<td>Access and Delivery Partnership</td>
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<tr>
<td>AIDS</td>
<td>acquired immunodeficiency syndrome</td>
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<td>BCA</td>
<td>benefit-cost analysis</td>
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<td>CEA</td>
<td>cost-effective analysis</td>
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<td>CMA</td>
<td>cost-minimization analysis</td>
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<td>COVID-19</td>
<td>coronavirus disease</td>
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<td>DAH</td>
<td>development assistance for health</td>
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<td>DALYs</td>
<td>disability-adjusted life years</td>
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<td>ECEA</td>
<td>extended cost-effectiveness analysis</td>
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<tr>
<td>GDP</td>
<td>gross domestic product</td>
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<td>Global Fund</td>
<td>Global Fund to Fight AIDS, Tuberculosis and Malaria</td>
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<td>HIA</td>
<td>health impact analysis</td>
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<tr>
<td>ICA</td>
<td>institutional and context analysis</td>
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<td>IHME</td>
<td>Institute for Health Metrics and Evaluation</td>
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<td>LMICs</td>
<td>low- and middle-income countries</td>
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<td>MDA</td>
<td>mass drug administration</td>
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<td>MoH</td>
<td>Ministry of Health</td>
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<td>MRA</td>
<td>medical regulatory authorities</td>
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<td>NCD</td>
<td>noncommunicable disease</td>
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<td>NTDs</td>
<td>neglected tropical diseases</td>
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<td>R&amp;D</td>
<td>research &amp; development</td>
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<tr>
<td>ROI</td>
<td>return on investment</td>
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<td>SDG</td>
<td>Sustainable Development Goal</td>
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<td>SROI</td>
<td>social return on investment</td>
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<td>TB</td>
<td>tuberculosis</td>
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<td>UHC</td>
<td>universal health coverage</td>
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<td>UNDP</td>
<td>United Nations Development Programme</td>
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<td>Uniting Efforts</td>
<td>Uniting Efforts for Innovation, Access and Delivery</td>
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<td>WASH</td>
<td>Water, Sanitation and Hygiene</td>
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<td>WHO</td>
<td>World Health Organization</td>
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<td>WHO FCTC</td>
<td>WHO Framework Convention on Tobacco Control</td>
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Universal health coverage (UHC) is a critical component of the 2030 Agenda for Sustainable Development. The development benefits of UHC go beyond health, cutting across many of the Sustainable Development Goals (SDGs), from poverty reduction, economic growth and women’s empowerment to greater equality and human security. It is now well recognized that health is both a driver and outcome of sustainable development; whereby sustainable and resilient health systems are regarded as foundations for protecting health, well-being and economic productivity [1,2]. Moreover, coronavirus disease (COVID-19) has shown beyond the shadow of a doubt that health is central to development.

Good population health to better social and economic outcomes, disease prevention and treatment remain underfunded in many countries [3,4]. This pattern is even more pronounced for diseases that primarily affect the poor – such as neglected diseases. SDG 3, through its Target 3.3, challenges the world to end the epidemics of AIDS (acquired immunodeficiency syndrome), tuberculosis (TB), malaria and neglected tropical diseases (NTDs), and to lower the burden of other communicable diseases by 2030. The ongoing COVID-19 pandemic has already had an historic impact on economies and health systems worldwide. For countries already affected by neglected diseases, the pandemic is likely to negatively impact programmes to prevent, diagnose and treat neglected diseases. The economic impact of the COVID-19 pandemic on all countries could also negatively affect the resources that the public and private sectors can dedicate to address neglected diseases and further de-prioritize the necessary investments in neglected diseases, making them even more neglected. Even as countries respond to the COVID-19 pandemic, it will be crucial to adopt measures to mitigate any reversal in the progress towards the targets of ending the epidemics of TB, malaria and NTDs, as set out in the SDGs.

This Guidance Note was commissioned by the three core partners – Government of Japan, GHIT (Global Health Innovative Technology) Fund, and the United Nations Development Programme (UNDP)-led Access and Delivery Partnership (ADP) – of Uniting Efforts for Innovation, Access and Delivery (Uniting Efforts). Uniting Efforts, a global platform launched in 2019, aims to facilitate dialogue and foster collaboration among a range of stakeholders (governments, funders, innovators, product development partnerships, the private sector, civil society and other stakeholders) in the field of neglected diseases to accelerate and improve innovation, access and delivery of medicines, vaccines, diagnostics and other health technologies for unmet health needs in low- and middle-income countries (LMICs). Recognizing the importance of improving financing for health technology uptake, Uniting Efforts is focusing on sustainable financing of access and delivery of medicines, diagnostics and other health technologies for neglected diseases [4].

For the purposes of Uniting Efforts, neglected diseases include TB, malaria and NTDs. While recognizing that TB, malaria and NTDs represent a diverse set of neglected diseases, this Guidance Note seeks to provide a common framework for governments and partners interested in developing national investment cases for neglected diseases.

This Guidance Note is complementary to other resource mobilization tools for neglected diseases, including the upcoming global investment case for the World Health Organization (WHO) NTD Roadmap 2021–2030, as well as strategies to improve the financing and funding for malaria and TB, and UHC more broadly.

National investment cases for other diseases and health priorities have proven to be useful advocacy and evidence-based tools prompting resource mobilization and spurring programme implementation [5,6]. This Guidance Note is not itself an investment case for neglected diseases – it describes the purpose and process of a potential national investment case for selected neglected diseases. If countries and partners are interested in the use of investment cases for neglected diseases, the next step, as the conclusion explains,
should be the development of the terms of reference and methodology of national investment cases for neglected diseases. The methodology and investment cases could be for one or more neglected diseases, and could include groups of related diseases, including NTDs.

The Guidance Note aims to answer three main questions:

- What is an investment case?
- Why develop national investment cases for neglected diseases?
- How should national investment cases for technology uptake in neglected diseases be designed?

**What is an investment case?** An investment case evaluates the costs and benefits of implementing and scaling up country-prioritized and cost-effective health interventions and policies for a specific population. It is a flexible tool that provides a process and results that can be influential in opening or exploiting a policy window. National investment cases for neglected diseases could draw attention and funding to a neglected set of diseases that impact the world’s most vulnerable populations. It would aim to situate a stronger national neglected diseases response within UHC funding strategies and it would quantify the costs and benefits of feasible prospective control scenarios.

**Why develop national investment cases for neglected diseases?** *Uniting Efforts* notes that progress on SDG 3.3 requires increased domestic investment in countries affected by TB, malaria and NTDs. In addition, programmatic and technology changes are needed to reduce existing obstacles and facilitate cost-effective TB, malaria and NTD technology introduction, delivery and uptake. In part three, the Guidance Note summarizes how an investment case can: provide the rationale for investment in each of the major steps in the value chain of access and delivery of health technologies; show where particular enablers and incentives may be critical to progress; and demonstrate connections between improved technology access and delivery and health, social and economic impacts. The main audiences for these results are national governments facing choices about how far and how fast to scale up existing and new interventions for a single disease or set of related diseases.

**How should national investment cases for technology uptake in neglected diseases be designed?** The emphasis in this Guidance Note is on developing a framework that can encompass a broad range of changes in the status quo, ranging from introducing new technology to shifting the delivery modality for existing technologies. As such, it suggests that investment cases for neglected diseases should focus less on incremental tradeoffs between prevention and treatment interventions – as noncommunicable disease (NCD) investment cases do, for example – and more on describing and quantifying the impacts of promising interventions and processes that would dramatically improve the landscape for control and elimination. Without wishing to be prescriptive, part four of this Guidance Note suggests what an investment case for neglected diseases could include. Decisions are required about the perspective (i.e. social vs. health sector) and timeline to use for economic analysis, the breadth of the diseases to be included, which potential outcomes are relevant in a country, an initial list of interventions and technologies to be considered, targeted populations, and the data that should form the foundation of the analysis. Further, an investment case for neglected diseases should speak to the range of players who are instrumental in improving access to technology, including affected communities, technology developers and funders.

The Guidance Note begins with a discussion of terminology and examples of how governments, UNDP and WHO and their partners have used investment cases to increase and prioritize funding for specific health needs and to inform government planning, budgeting and health priority setting (i.e. in the areas of HIV, TB, malaria and NCDs among others). These examples are offered to help the *Uniting Efforts* partners - especially national governments - consider the value of developing investment cases to improve access and delivery of health technologies for neglected diseases and support implementation of national programmes.
2. What is an investment case?

2.a. The scope of investment cases for health

Investment cases are borne of a desire to make strategic and well-informed decisions about how to use limited resources when faced with competing demands for funding. They differ from other decision analysis tools in purpose and type of decision-maker they are directed to (see Table 1 for a selection of tools used in health decision-making) [7].

Investment cases begin by defining a specific goal – such as a stage of disease elimination – and then assess the options for achieving that goal in a cost-effective and feasible way. Once policy and programme options are well-defined, they are costed at different levels of coverage and scale-up, and the health impacts are calculated. The results show how investment decisions generate different short- to long-term returns and suggest how decision-makers may prioritize actions based on which ones will have the largest impact.

Table 1. Differences between investment cases and other similar types of analysis

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<tr>
<th>Type of analysis and description</th>
<th>Example</th>
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<tr>
<td><strong>Investment case</strong>: Investment cases for health are conducted using a societal perspective that draws attention to the connections between good health and other societal, economic and environmental goals. National investment cases conducted using a UNDP/WHO framework pair a political economy analysis with quantitative valuation and costing techniques to inform local planning and decision-making. Quantitative analyses assess the current social and economic burden of disease and evaluate the costs and consequences of implementing or scaling health interventions.</td>
<td>Hutchinson et al (2019). The investment case as a mechanism for addressing the NCD burden: Evaluating the NCD institutional context in Jamaica, and the return on investment of select interventions [5]. <a href="#">Link</a></td>
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<td><strong>Business case</strong>: A business case captures the rationale for making a specific investment from a business portfolio perspective. While the term “business case” is sometimes used interchangeably with investment case, a business case typically focuses only on the financial consequences of a given action, including risk analysis. It does not take into account wider positive or negative consequences to social or environmental outcomes.</td>
<td>Swensen et al (2013). The business case for health-care quality improvement [8]. <a href="#">Link</a></td>
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<td><strong>Social return-on-investment analysis (SROI)</strong>: An organizational method of accounting for value creation, SROI enables organizations to measure change by tracking relevant social, environmental and economic outcomes. While SROI builds upon the logic of economic cost-benefit analysis, it is different in that it is explicitly designed to inform decision-making of enterprise managers and investors who are focused on optimizing their social and environmental impacts. By contrast, cost-benefit analysis (CBA) is a technique rooted in social science that is most often used by funders outside an organization to determine whether their investment or grant is economically efficient, although economic efficiency also encompasses social and environmental considerations.</td>
<td>Goudet et al (2018). Social value of a nutritional counselling and support programme for breastfeeding in urban poor settings, Nairobi. [9]. <a href="#">Link</a></td>
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Within the context of health decision-making, an investment case:

- describes the current disease burden (social and economic impact);
- identifies programme goals, and locates issues (bottlenecks) of access, affordability and acceptability that exist within health systems and policy spheres;
- identifies effective, evidence-based and locally relevant interventions for analysis;
- surveys the policy environment to assess the feasibility of specific actions;
- analyses the costs and benefits of interventions, and compares them to assess the return on investment; and
- frames current levels of health spending against the cost of interventions, and provides input on how to close the funding gap.

Investment cases have played a role in shaping the funding, budgeting and delivery of health services worldwide. Investment cases for health are typically limited to multiple interventions that target specific diseases or closely related disease sets occurring in a specific population. They have been used to inform investments in HIV and AIDS, TB and malaria [12]; reproductive, maternal, newborn and child health [13]; NCDs [5, 10, 14]; mental health conditions [5, 15]; NTDs [16]; tobacco control [17] and other health needs. Section 2.c. provides examples of how investment cases have been used in other areas of global health.

Investment cases for health often articulate investment needs at the global or national level and are conducted using a societal perspective that draws attention to the connections between good health and other societal, economic and environmental goals. In doing so, investment cases can target stakeholders who may have a say in the decision-making process, but who have missions or interests that do not directly align with health. Sometimes a narrower health sector perspective is taken. Communicating the positive multiplier effects of improved public health and emphasizing the direct impact on non-health interests can align stakeholders behind the policy process. SDG 3: Good health and well-being interacts with virtually every other SDG, and achieving good health has clear benefits on multiple development outcomes, including reducing poverty and inequalities, and increasing educational attainment and economic growth [18].

2.b. The national investment case framework: what is included

Investment cases typically consist of two components: an economic analysis and an institutional and context analysis (ICA) [19]. The economic component is a quantitative analysis of the current burden of disease, and the extent to which the burden can be reduced through the implementation and scale up of selected interventions. The ICA is a qualitative analysis that aims to uncover promising policy pathways, political will and opportunity – as well as challenges to implementation. The economic and institutional and context analyses are complementary and together present a rationale and road map for action.
Through desk research, data stocktaking and interviews with key stakeholders, the ICA uncovers the main human-influenced disease drivers and modifiers. These may include: socio-economic conditions; geography and infrastructure; culture and knowledge; availability, affordability, or accessibility issues that affect coverage rates of critical interventions; available international and domestic financing; and the power dynamics between different stakeholders – allies and opponents – that drive the status quo. By naming drivers, barriers and bottlenecks, the ICA informs the ways to alter the conditions that cause disease burden.

Informing the ICA, the economic analysis first quantifies the health and economic consequences of maintaining the status quo. The disease burden may be expressed not only in health terms (e.g. the number of lives lost, years lived in a state of ill health), but also, following the approach of cost of illness studies, as enumeration of the total cost of ill health – inclusive of direct (e.g. health expenditures) and indirect costs (e.g. missed days of work or school, patient time costs, dropout from the workforce due to disability). By placing a monetary value on productivity costs, the investment case encompasses the total economic burden caused by a specific disease or disease set. The extent of the problem can be compellingly framed (e.g. the total economic burden as a percent of gross domestic product (GDP)) to further clarify or emphasize the extent of the problem and draw attention to the need for action. Impacts on equity or poverty reduction, such as reduction in out-of-pocket costs, may also be measured and communicated.

A valuable aspect of an investment case is the opportunity to make a connection between existing goals – whether health or economic – that have been established for government programmes or for the economy. The economic impacts calculated for the investment case can show how poor health may be inhibiting achievement of national economic goals (the economic consequences of maintaining the status quo) and how improvements to health will contribute to national economic targets. The same can be said of the calculated health impacts and programmatic goals. Aligning the investment case with existing or new national goals and targets will increase its relevance and usability as a guide to national policy decisions.

Dialogue is then needed with a range of stakeholders to determine the desired set of interventions for analysis. An investment case generally utilizes standardized interventions with proven cost-effectiveness and/or that are recommended according to international standards (e.g. WHO ‘Best Buys’), but it is also possible to let local circumstances shape the definition of interventions – including possible avenues for meeting the programmatic and economic goals. Interventions can be implemented at any point in the supply chain, and options may range widely, from the provision of entirely new services or technologies, to scale-up of existing technologies, to implementation of new policies (e.g. regulatory harmonization), supply chain management, alternative delivery modalities, or other services to facilitate uptake. An investment case may incorporate results of a business case developed for a new technology, for example, but generally examines a broader range of possible choices. The institutional and context analysis (ICA) works to vet the prescribed list for feasibility, including political feasibility and outlines the challenges that must be overcome to meet stated goals. Low feasibility may omit some interventions from the analysis or suggest actions that must occur to increase the potential for uptake. The investment case should include the full range of intervention, policy and technological choices that confront the decision-maker.

A key economic step of the investment case is to assess the cost of each proposed activity, year-by-year as the interventions are scaled up or shifted to accommodate changing epidemiology. The cost for the full set of proposed activities at a given scale can be compared to existing funding levels. Changes in the funding landscape can also be explored, ideally through a systematic analysis of future funding and macroeconomic conditions. A financing component should be included in the investment case to determine whether known funding mechanisms at the national and international levels can close the funding gap, or whether aspirations for the intervention package need to be adjusted. This helps ensure that challenging realities for mobilizing resources are considered and addressed as part of the investment case process.

The economic evaluation component employs a return on investment (ROI) analysis. Figure 1 illustrates different economic evaluation methods that may provide evidence for the investment case. A ROI analysis demonstrates
where the most value can be obtained for the money invested, an important – though not the only – criterion for decision-making. An ROI analysis compares the current status quo against intervention scenarios, the impacts of which are modelled over a time frame that is long enough to capture the significant benefits and costs.

**Figure 1. Types of economic evaluations of health care programmes**

**Cost-minimization analysis (CMA)**

In CMA, the consequences of two or more alternative courses of action are presumed to be the same, and thus the analysis only compares the costs. The option with the lowest cost is the most efficient.

**Cost-effectiveness analysis (CEA)**

CEA compares the costs of health programmes, against the consequences (health outcomes) that they generate. The analysis may examine the impact of a programme on immediate outcomes (e.g. reduction in fasting blood glucose levels for patients with diabetes) or distal outcomes (e.g. the number of lives saved or disability-adjusted life years avoided) per X dollars spent. CEA usually does not include non-health care sector outcomes such as the educational benefits of a health intervention.

**Benefit-cost analysis (BCA)**

BCA is defined by its attempt to measure all health and non-health consequences of a programme, and to monetize the value of those consequences in order to express the programme’s total social value. Thus, a BCA examines the total impact of a programme across all sectors—health, economic, education, legal, environmental, etc.—and then places a dollar value on that outcome. This allows for comparison of a programme’s benefits across sectors, and also a direct comparison of the benefits of a programme to its costs. Final outcomes of a programme are usually expressed as net social benefit (total value of the consequences, minus the costs) or as a benefit-cost ratio.

**Return-on-investment (ROI) analysis**

Within the context of UNDP investment cases, ROI analyses mirror BCAs, but place emphasis on the differential timing of costs and consequences to show how a programme becomes more or less efficient over time. This allows decision-makers to examine considerations of timing that may affect decision-making, such as the break-even point when programme benefits begin to outweigh costs. ROI analyses express outcomes as total costs, total monetary benefits, and as ratios that show the monetary benefits that can be achieved for every dollar spent.
To further elucidate the components and sequence of a generic investment case for illustrative purposes, the usual UNDP/WHO process to support national investment cases is described in Table 2. UNDP and WHO have been jointly supporting the development of national investment cases for other diseases and health priorities – through, for example, the WHO-UNDP Global Joint Programme to Activate National Responses to Noncommunicable Diseases – and they typically consist of four distinct stages that occur over the course of four to six months.

Table 2. Activities undertaken in typical WHO-UNDP-supported national investment cases

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<th>STEP</th>
<th>ACTIVITIES</th>
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| **PRE-MISSION: INITIATION OF INVESTMENT CASE** | • Agreement on mission terms of reference by UNDP and WHO and country government officials.  
• Identification of investment case team, with focal points from UNDP, WHO, RTI International, WHO Framework Convention for Tobacco Control (WHO-FCTC) Secretariat, the ministry of health (MoH) and potentially other key ministries. A lead economist is contracted and, if the government considers it necessary, a national economist.  
• Agreement on investment case objectives, process, timelines, roles and logistics for first mission.  
• Drafting of first mission programme and submission of bilateral meeting requests with relevant government and non-government stakeholders. |
| **PRE-MISSION: PREPARATIONS** | • Review of academic literature, and publicly available country reports and data for background.  
• Compile and share background material and pre-populated data-request forms with national partners. Identify in-country focal point for data collection.  
• Query national partners about background and preferences for the analysis. Obtain country consent on acceptability and extent of use of data that comes from international sources.  
• Confirm first mission bilateral meetings and finalize the agenda for the initial mission. |
| **INITIAL MISSION** | • Hold sensitization meetings with key counterparts (MoH leads). MoH and other representatives present background information, and communicate goals for the mission and overall exercise. The investment case team and other relevant persons introduce the investment case and methodology, and discuss data acceptability. Reach agreement on analysis parameters, including the set of relevant national interventions to be included in the analysis.  
• Conduct bilateral interviews to inform the ICA.  
• Consider a multi-stakeholder event to raise the profile of the investment case. |
| **POST-MISSION** | • Convene a call or video-conference with the investment case team to provide a brief on the findings of the ICA and discuss next steps.  
• Agree on draft recommendations and key messages.  
• Discuss options for dates to present the final investment case deliverables.  
• Continued collection of data. |
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| **ANALYSIS**                | • Lead economists conduct the investment case economic analysis.  
• Lead institutional and context analysts begin drafting an advocacy brief and PowerPoint presentation with key ICA messages. |
| **FINALIZATION OF ANALYSIS AND OUTPUTS** | • Economists and institutional analysts share a draft of analysis outcomes with the greater investment case team. If needed, economic analysts convene a workshop (remote or in country) to brief national health economists on the methodology, data sources and assumptions used, and findings from the analysis. Consider external peer review (international and national).  
• Comments on each form of analysis, including from MoH, are consolidated. Revisions occur where needed and are resubmitted for final approval from local authorities.  
• Draft of the investment case report, PowerPoint presentation, and one-to-two page infographic are submitted to the MoH for review.  
• MoH provides feedback on the draft report. Convene a call to confirm clearance of the findings and recommendations.  
• Report, PowerPoint presentation, infographic and other materials (e.g. advocacy brief and media release) are finalized. |
| **HANDOVER (SECOND MISSION) PREPARATIONS** | • Translate (if necessary) all final deliverables.  
• Agree on logistics for handover mission.  
• Plan launch event:  
  High-level interactions with key influencers (parliamentarians, cabinet-level officials).  
  Work with MoH and UNDP and WHO Country Offices on a communications and media plan.  
  Schedule bilateral briefing meetings with key counterparts. |
| **HANDOVER MISSION** | Key events:  
  Hold an initial planning meeting.  
  Presentation to the MoH on the modelling, findings, assumptions, limitations, key messages and partners to target.  
  Handover event – government-focused, multi-sectoral, as high-level as reasonable.  
  Bilateral debriefings with key ministries.  
  United Nations country team debriefing.  
  Consider a public event with media.  
• Send copies of investment case report and infographics to all key ministries and other relevant stakeholders (e.g. private sector, civil society and academic institutions). |

2.c. Investment case outcomes from real life

Investment cases in global health (see Figure 2 for examples) have been used by multilateral development organizations, governments and non-governmental organizations to identify and communicate synergies between sectors, advocate for investment in health, assess resource requirements, and inform discussion or strategies and policies under consideration. Recent lessons from UNDP/WHO-supported national investment cases conducted in 28 countries illustrate how investment cases have been used to identify barriers, advocate for health priorities, build health coalitions, create resonant messaging and advance policies.
Identify barriers and opportunities

The process of conducting an institutional and context analysis uncovers cultural, historical, political, governance and other barriers or opportunities, both evident and not. For instance, in one country covered by the WHO Regional Office for the Western Pacific (WPRO), the ICA found that pressure from international finance institutions to raise taxes provided an opening to talk about the revenue-raising potential of health taxes to the ministry of finance.

Advocate for public health priorities

MoHs use investment case findings to draw attention to public health needs, amid the cacophony of other public sector demands. For instance, in Jamaica, the Minister of Health used the investment case findings to support health priorities in a speech to the House of Representatives in June 2018, and the results were featured in a national sector report highlighting progress on major health programmes [20]. In El Salvador, the MoH has used the investment case on tobacco-control measures to communicate to local media [21].

Build a health coalition

Investment cases speak the language of sectors outside of health by providing evidence on social, economic and environmental needs that are interwoven with health issues. Ministries of labour will be interested in the productive capacity lost to poor health (e.g. work days missed, or health-induced disability or premature death of working-age individuals). Ministries of finance, concerned with public sector investment and efficiency, may find estimates of disease-attributable health care expenditures and potential savings compelling. The impact of ill health on students may induce attention from the ministry of education, and ministries of social affairs may find the equity implications of improvements in health persuasive. Evidence that addresses the individual mandates of diverse actors can produce surprising coalitions to advance health priorities.

Create messaging that resonates

A systematic review of empirical studies that examined how health evidence becomes policy pointed to a need to identify ‘sweet spots’ where health and political priorities overlap [22], an investment-case aim. For instance, in Jamaica, a review of government plans revealed the goal to grow GDP by four percent in five years (the ‘5 in 4’ plan), previously announced by the Prime Minister. However, within the plan, health was not mentioned as a potential growth contributor. Recognizing the potential synergy between health and broader government goals, the Jamaica investment case framed the economic benefits of scaling up clinical interventions that target NCDs in terms of how much they could contribute to the existing ‘5 in 4’ goal. By using information from ICAs to frame economic results, investment cases seek to create messaging that resonates within a country’s existing context.

Advance policies and interventions

Investment cases are not always expected to lead directly to policy change – at least, not immediately. But investment cases have frequently contributed to policy action. National tobacco control investment cases in Cabo Verde, Georgia and Zambia have been used in discussions to advance legislation. The results from the Georgia tobacco control investment case study were provided to the Government of Georgia to assist its Parliament in considering new comprehensive tobacco policy legislation. The Zambia investment case is being submitted as part of an official government regulatory impact assessment in anticipation of a comprehensive tobacco control law. In Jordan, after investment case results were presented at a cabinet meeting, the Prime Minister directed the Ministry of Health to consider a new tobacco-control measure (plain packaging) and move toward signing the protocol on illicit trade in tobacco products.
**Figure 2: Examples of health investment cases**

**HIV and AIDS, TB and Malaria**

The Global Fund to Fight AIDS, Tuberculosis and Malaria commissions investment cases to support its replenishment rounds. The Sixth Replenishment 2019 case for investment in prevention and control of HIV, TB, and malaria examines the health (incidence, mortality) and economic benefits (gains in productivity due to avoided premature death and disease morbidity) of scaling interventions over the remaining time to the end of the SDG period, 2030 [12]. The case is designed to catalyse funding to fulfill investment needs for the period from 2020 to 2022 [23].

For HIV, the case includes scale up of preventative interventions (e.g. voluntary male circumcision, condom promotion and distribution, programmes to prevent mother-to-child transmission), ‘new approaches’ such as community-based testing and adherence-support groups, diagnostic self-testing, and new medications. For TB, the case models increased x-ray screening and diagnosis with rapid molecular tests, along with scale-up of preventive and restorative medicines. For malaria, the case models vector control strategies (e.g. long-lasting insecticidal nets), and chemoprevention and treatment. Facilitating improvements such as increased surveillance, and health and supply chain strengthening are also costed.

**Adolescent Risk Factor Investment Case**

Philanthropic and commercial entities with disease- or population-targeted global health interests have requested investment cases to support policy advocacy in their philanthropy and partnering. An RTI International investment case analysed the health and economic impacts of NCD risk prevention among adolescents worldwide [24]. The case analysed the extent to which exposure to school-based programmes and policies to control NCD risk factors (tobacco use, alcohol use, sugar consumption) during adolescence can change mortality outcomes over an individual’s life course.

**Tobacco Control**

The WHO Framework Convention on Tobacco Control (WHO FCTC) investment cases from the WHO FCTC Secretariat, UNDP and RTI quantify the health and economic burden of tobacco use and the ROI of implementing or intensifying tobacco control measures [25]. In addition to analysing the ROI of tobacco control measures, the cases examine other issues of national interest such as the extent to which the measures contribute to fulfilment of the SDGs, potential revenue gains and equity implications of raising taxes, and the impact of tobacco control measures on tobacco farmers.

**NCDs and Mental Health Conditions**

A series of UNDP and WHO-supported investment cases for the prevention and control of NCDs examines the impact of implementing or scaling up WHO ‘Best Buys’ over the short- (five years) and medium-term (15 years) [5]. The cases analyse the health and economic benefits of scaling up clinical interventions for NCDs (e.g. cardiovascular disease, diabetes) and mental health disorders (depression, anxiety), and policy measures that address NCD risk factors (tobacco, alcohol, salt consumption, physical inactivity).
3. Why develop national investment cases for neglected diseases?

3.a. Underinvestment threatens global goals and national plans

The near eradication of Guinea-worm disease, and a 92 percent reduction in cases of trypanosomiasis highlight significant recent successes against neglected diseases [26]. The SDGs envision additional achievements ahead, with SDG 3.3 calling for an end to the epidemics of AIDS, TB, malaria and NTDs. In addition, the WHO NTD Roadmap 2021–2030 specifies a 60 percent decline in the incidence of vector-borne NTD cases and 75 percent fewer vector-borne NTD deaths by 2030 [27]. Additional global goals are laid out in the Roll Back Malaria Global Malaria Action Plan 2 and the WHO End TB Strategy. All need sufficient international and domestic investment to be realized. Achieving these goals will require a concerted effort – and additional financing – to scale up interventions to prevent and treat the diseases. Worldwide, over 1.7 billion people are at risk of infection from NTDs [28], and about 218 million people contract malaria or TB annually [29]. Neglected diseases are responsible for over 107 million disability adjusted life years (DALYs) and cause over 1.9 million deaths annually, more than 99 percent of which occur in LMICs [29].

Despite their contribution to the global health burden, financing for neglected diseases remains a challenge. Figure 3 shows that infectious diseases that primarily affect low-income populations in LMICs – such as TB, malaria and NTDs – continue to lag far behind HIV in dollars of research and development (R&D) and development assistance for health (DAH) per DALY.

**Figure 3.** Combined R&D and DAH dollars per global DALY for NTDs, malaria, TB and HIV and AIDS

<table>
<thead>
<tr>
<th></th>
<th>DAH [22]</th>
<th>R&amp;D [23]</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV and AIDS</td>
<td>10,400.0</td>
<td>1,102.3</td>
<td>11,502.3</td>
</tr>
<tr>
<td>Malaria</td>
<td>2,400.0</td>
<td>576.4</td>
<td>2,976.4</td>
</tr>
<tr>
<td>TB</td>
<td>1,900.0</td>
<td>568.1</td>
<td>2,468.1</td>
</tr>
<tr>
<td>NTDs</td>
<td>368.6*</td>
<td>605.1</td>
<td>973.7</td>
</tr>
</tbody>
</table>

**Source:** RTI calculations based on numbers included in the G-Finder survey of global public, private and philanthropic research [30] and development funding for NTDs and the Institute for Health Metrics and Evaluation (IHME) 2017 Financing Global Health study [31] tracking DAH – “financial and in-kind resources that are transferred through major health development agencies to low- and middle-income countries with the primary purpose of maintaining or improving health” [32 p. 17].

*Author estimate of DAH for NTDs based on the following: IHME reports US$1.7 billion in funding for the category “Other infectious diseases”, which includes NTDs, polio and many other infectious diseases. Because a breakdown is not given, we estimate DAH for NTDs as follows: United States funding for NTDs is reported to be $100 million in 2017, about 21.7 percent of what IHME reports as the contribution of the United States to “other infectious disease”. Assuming that the United States percentage directed toward NTDs holds for all other funders, DAH for NTDs is $368.6 million (21.7 percent * $1.7 billion = $368.6 million).

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* Malaria incidence in 2017: 209 million; TB incidence in 2017: 9 million
The Global Fund to Fight AIDS, Tuberculosis and Malaria has been a significant source of funding to support programmes to accelerate the end of the epidemics of malaria and TB, channeling $2.3 billion to this work in 2017. In addition, global spending on R&D of new technologies for malaria and TB continues to grow. However, funding for diseases covered by the Global Fund still falls short of what is needed to meet SDG targets. For instance, $1.3 billion more in global annual spending on TB research is needed to meet TB targets [33].

Funding for NTD programming and product R&D, access and delivery is tiny by comparison. To date, NTD programmes have largely been funded by international donors (mainly USAID (United States Agency for International Development), DFID (United Kingdom Department for International Development), and the Bill & Melinda Gates Foundation) [31]; the medical and pharmaceutical industries donate more than $130 million per year in medicines, supplies and diagnostics for NTD programmes [34]. These public and private investments have been key to reducing the NTD burden; however, these gains require continued investment to prevent recrudescence; moreover, an additional 500 million people beyond those currently receiving interventions are in need of treatment [34]. While estimates vary, one study indicates that the costs to scale NTD interventions to the degree necessary to achieve global goals are relatively affordable for countries worldwide, representing about 0.1 percent of health spending in endemic countries [16].

With international funding precarious and new priorities introduced by coronavirus disease (COVID-19), additional means are needed to catapult progress towards SDG 3.3. Funding gaps of more than $3 billion annually are forecast for malaria and TB [35]. United States government budget requests to Congress to support global NTDs in fiscal year 2020 were 25 percent below 2014–2019 levels [36]. Pointedly, increased and sustained domestic resources must be prioritized, yet domestic funding currently covers less than half of the programme costs for malaria and TB. But reliance on external funders is not a given and many countries are exploring alternative funding streams [35].

3.b. Ensure current and future investments are realized

Defeating neglected diseases depends not only on expanding existing efforts but also changing the trajectory of disease transmission. For example, strong growth in funding for neglected diseases research and product development in recent years – especially through product development partnerships and philanthropic funders – means that new technological innovations are being introduced [37]. Ensuring that these products reach populations in need offers new routes to success in the 2030 agenda. Yet, few countries have invested in the kind of capacity that would facilitate access to and delivery of these technologies [38].

The UNDP-led Access and Delivery Partnership (ADP), with core partners WHO, TDR and PATH, is one of the three co-conveners of Uniting Efforts. ADP has identified bottlenecks and key interventions across the access and delivery value chain for health technologies (see Figure 4). The presence of these bottlenecks and the costs of reducing them can be integrated into country investment cases for neglected diseases, shifting the calculus on the expected benefits of interventions. Major bottlenecks and interventions needed are present in: regulatory approval processes; selection and prioritization of health technologies; procurement; distribution and storage; service delivery; and patient uptake. Table 3 further explores these bottlenecks and interventions in the context of neglected diseases.

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b For example, the USAID ENVISION global health project delivered $16 billion in donated medicines between 2012 and 2019, resulting in: the elimination of trachoma as a public health problem in three countries and the elimination of lymphatic filariasis in two countries; and over 1.4 billion treatments for people in 16 countries [39].

c Personal communication from Sultani Hadley Matendechero, Head, Division of Vector Borne and NTDs, Ministry of Health, Nairobi, 16 April 2020.
Guidance Note for the development of national investment cases for neglected diseases

Figure 4. The ADP access and delivery value chain

Table 3. Bottlenecks in the value chain for access and delivery of health technologies for neglected diseases

Novel medicines for neglected diseases are largely developed and deployed for use in developing countries, meaning that medical regulatory authorities (MRAs) in developed countries are not asked to approve these products. Thus, the process of registering, licensing, approving (for quality and safety), and authorizing and overseeing clinical trials and appeals falls to MRAs in endemic countries. Unclear or inhibiting legislative frameworks to these processes, under-resourced MRAs, and dispersion of regulatory responsibility among a multitude of institutions have all been identified as barriers preventing the approval and delivery of life-saving medicines and technologies [40]. Funding and strengthening these institutions, and harmonizing regulations both at the national and regional levels, would act to both incentivize research and product development, and facilitate the uptake of quality, safe and effective medicines and technologies.

Informed decisions by policy-makers depend on comprehensive evaluations of the impact of new medicines and technologies on issues such as health, social and ethical values, budgets, and existing systems and capacities (feasibility) [41]. HTAs serve these needs by evaluating the effectiveness of a technology in a specific context and determining whether it justifies reimbursement from the public sector. In a WHO survey of 111 countries, two out of every three countries identified a national HTA entity that provided assessments directly to the MoH [42]. However, the countries that lack HTA capacity are generally the poorest and also those most likely to have endemic neglected diseases. Even in countries with an HTA entity, these agencies face budget, human resources and infrastructure scarcities, as well as challenges aligning analysis with the priorities of other public institutions [42–44]. HTAs and other priority-setting processes (such as investment cases) provide a transparent and evidence-based choice framework.
Affordability and accessibility of medications depends on an effective procurement process. Demand forecasting is paramount; however, poor disease surveillance and lack of information systems to track drug distribution and waste can make quantification of demand difficult [45]. Until now, many NTD medications have been donated or prices are negotiated at the international level. But as countries more closely align with the WHO NTD Roadmap 2021–2030 calls to mainstream NTDs in health sector plans and budgets, and plan for scale-ups to achieve elimination, their use of global tools to evaluate value for money, quantify demand and procure technologies will be ever more important. This could include managed entry agreements to establish sustainable pricing for technologies, local production and generic competition as well as pooled procurement.

Medications and technologies for neglected diseases also encounter distribution bottlenecks along the supply chain: from customs to distribution at the local level. A review of 24 missed or delayed mass drug administrations (MDAs) for the Children Without Worms programme identified frequent customs challenges. Leading factors included fluctuating clearance requirements, consignees untrained to navigate complex clearance processes and under-budgeting of customs clearance costs [46]. Post-customs, deficiencies in supply chain design such as excessive tiering, uneven geographic distribution of capacity, and lack of payment and reimbursement processes undermine the reliability and sustainability of product distribution [45]. Often, independent supply chains exist for a limited number of medications, creating inefficiencies (e.g. separate logistics management information systems) that prevent coordination and increase costs [47]. Because many NTD campaigns only occur annually, few supply chain experts are assigned to oversee NTD supply chains, with repercussions for management and standard operating procedures, particularly efficient tracking and ordering [48]. In addition, forecasting of medicine needs is hampered by poor or non-existent logistic information management systems, and a lack of supply chain and delivery staff who are trained – or properly incentivized – to collect and log the information that can lead to an equilibrium between supply and demand [47–49]. Country-level analysis to understand “the journey of the pill/product” can pinpoint where efficiencies can be gained and provide information for costing improvements.

When medicines do make it to last mile storage and distribution facilities, the final patient delivery mechanism – or the reliability/acceptability of deliverers – may impact whether patients are contacted and/or accept treatment [50]. MDAs may miss certain demographic groups who tend to be absent during the time of administration (e.g. men during fishing season, rural groups during the rainy season), and the point-of-delivery (e.g. house-to-house, central community location, schools) or person-of-delivery can also impact who receives products [51]. In addition, the training of deliverers, and their incentive structure, can also affect delivery rates. Resource constraints leading to low pay for community health workers have been identified as major challenges to programme efficiency [47, 51, 52]. There are opportunities to identify synergies between existing, separate neglected diseases programmes, and also to strategically identify components of programmes that can be drawn into the greater health system [53]. Integrating multiple NTD streams into a single programme has been well demonstrated by the USAID ENVISION project [54], and potential exists to integrate neglected diseases’ delivery platforms within existing health system platforms (e.g. primary care; community health days; water, sanitation and hygiene (WASH) programmes; etc.) [55–57]. Further, surveillance technology is changing (e.g. image recognition) and may improve ability to track low-prevalence diseases.

Final uptake by patients is determined in part by the acceptability of the intervention. Hindrances include issues such as programme design that conflicts with beliefs, or medication side-effects. Packaging and formulations can deter efficient use of medications and supplies in the field. Consideration of social, cultural, economic and other contexts can improve programme design and delivery. Pharmacovigilance guidelines and systems can help monitor side-effects of medications and improve communication of expected side-effects as well as mitigation [51].
3.c. Demonstrate the social and economic benefits of reducing neglected diseases

Neglected diseases cause disability and death, often among the world’s most vulnerable populations. Globally, in 2017, neglected diseases caused 1.9 million deaths, and the loss of nearly 107 million DALYs [29]. Targeting and accelerating action on neglected diseases will improve health, which has been shown to have reverberating social and economic impacts. Figure 5 enumerates ways that lowering the neglected diseases’ health burden can decrease poverty, hunger, ill health and inequity, and increase educational attainment, employment and economic growth [58]. A key purpose of national investment cases is quantifying those broad impacts so that stakeholders outside the health sector – including ministries of finance and development organizations - can better evaluate the value of improved health.

**Figure 5. Select health and non-health impacts of neglected diseases**

<table>
<thead>
<tr>
<th>Health</th>
<th>Education</th>
<th>Employment and Economic growth</th>
<th>Poverty and inequality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neglected diseases caused 1.9 million deaths globally in 2017 [29].</td>
<td>Neglected diseases have a significant impact on educational attainment. Treatment for malaria was demonstrated to increase educational attainment in The Gambia (by 0.5 years) [65], and for every 10 percent decrease in malaria incidence in Paraguay and Sri Lanka, female education is estimated to increase by 0.1 years [66]. De-worming programmes increased Kenyan girls’ educational attainment by about a quarter of a year [67].</td>
<td>Given increased risk of disability, patients with neglected diseases have lower odds of maintaining or obtaining employment [68]. In Guinea, 38 percent of individuals with onchocerciasis-attributable visual impairment – and 79 percent of those with blindness – reported that they were economically inactive [69].</td>
<td>Incidence and prevalence of neglected diseases are significantly higher among the world’s poorest populations [70–72]. Debt or medical impoverishment can result from high out-of-pocket costs to treat disease. In addition, sickness lowers individuals’ capacity to participate in formal or informal labour markets, reducing income-earning opportunities.</td>
</tr>
<tr>
<td>Infections lead to ill-health, and in severe cases long-term complications such as impaired pulmonary function for TB patients [59], brain injury and neurocognitive decline for individuals with cerebral malaria [60, 61], and visual or physical disabilities such as blindness for individuals with select NTDs [62].</td>
<td>Lower-educational attainment leads to lower earning capacity later in life, perpetuating cycles of poverty within the low-income populations where infections are most prevalent.</td>
<td>Ill-health may cause individuals to miss more work days. For instance, in Ethiopia, coffee estate workers with onchocerciasis skin disease were found to miss 25 percent more days of work than those without the disease [69].</td>
<td>Investment cases can measure the distributional effects of interventions and policies on specific segments of society with an equity analysis.</td>
</tr>
<tr>
<td>In addition, stigma and social exclusion of individuals with neglected diseases can lead to mental health conditions, including depression and anxiety [63, 64].</td>
<td>Investment cases can incorporate the sequelae of index diseases in evaluating costs and benefits of investments.</td>
<td>Lower rates of productivity and capital accumulation at the household level depress macro-level economic growth.</td>
<td>Investment cases quantify the economic impact of maintaining “business-as-usual” and compare it to better health alternatives.</td>
</tr>
</tbody>
</table>

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d Global deaths due to: malaria (619,000), TB (1.2 million), NTDs (100,000). DALYS due to: malaria (45.0 million), TB (44.7 million), NTDs (17.2 million) [IHME, 2017].

given global data on neglected diseases and their impacts.
3.d. Framing from neglected diseases experts on country role

During production of this Guidance Note, the authors conducted informal interviews with global neglected diseases experts (see Appendix 1), who provided their perspectives on the need for national investment cases for neglected diseases as well as on specific technical aspects. Broadly, experts conveyed: 1) a need to draw attention to diseases that are not well recognized or represented at the policy level; and 2) a neglected diseases landscape that is transitioning toward putting the onus on sustainable national programmes, with government-led financing and technical know-how as a pillar of sustainability. These interviews were primarily about NTDs, but most of the conclusions apply to malaria and TB as well.

Several experts based in LMICs described how NTDs can appear invisible at the national level, even in endemic countries, because they often only affect certain regions, and even then, sometimes only marginalized sub-populations within those regions. This is true as well for TB, where countries often face outbreaks among certain populations rather than generalized disease prevalence. Policy-makers, and others positioned in national-level decision-making spheres, are more likely to be removed from any threat of infection, and from experiences with individuals for whom – or settings within which – the consequences of neglected diseases are apparent. Moreover, government NTD programme managers and representatives may tend to have less political leverage, meaning that NTD priorities can receive little airing within power centres. Even when neglected disease priorities gain traction by integrating or pairing with parallel efforts for other diseases (e.g. HIV) or larger framing mechanisms (e.g. the SDGs), there is still a risk that NTDs are subsumed under funding and implementation directives that are oriented toward ‘higher priority’ diseases. The need to advocate for investment in neglected diseases, and to target information to parliamentarians and other decision-makers, is especially acute given that neglected-disease endemicity is tied to upstream development needs (e.g. water, sanitation, housing and hygiene) that can rarely be solved without government interventions.

The changing landscape of neglected diseases’ technology development and funding also provides framing for an investment case. Previously taken for granted, it is likely that important characteristics of neglected diseases (e.g. donated and highly subsidized medicines; limited development and availability of neglected-disease technologies) will change in the coming years. Interviewees explained that part of creating sustainability is ensuring the technology pipeline flows from funders to manufacturers to patients. That requires investments in new technologies, global and domestic financing backed by political will, procurement mechanisms, self-sufficient supply chains that can stand up for the long-run, and technical know-how to facilitate effective and efficient access and delivery platforms.

Some interviewees asserted that donor-driven financing is often conditional and dedicated to specific ends, such as programme delivery, that are led by international and donor partners. In this system, countries rarely grapple with difficult trade-offs on implementation choices. The hope was expressed that, as the system transitions to domestic-government financing, countries will experience greater flexibility in carrying out their strategies while also making progress on wider health system needs. Tough choices will need to be made and investment cases can bring those trade-offs to the forefront. Questions include: Which near-term emerging technologies should be brought in and integrated within neglected diseases national programmes, and within what time frame?; On what service delivery platforms should technologies be deployed?; and What will the costs and impact of these changes be?

As governments grapple with these questions and their growing role in delivering programmes, the importance of institutions for them to rely on – enabling regulatory frameworks, health technology assessment entities, pooled procurement through participation in supra-national organizations – is paramount. The choices that countries make must be informed by the costs and consequences they face. How for instance, should a government decide between a school-based programme that achieves control, versus a community-wide programme that breaks the cycle of transmission? What is the cost of professionalizing community distribution networks that once operated on a voluntary basis, and what kind of benefits may result? What kind of resources are needed to set up cross-government frameworks in which stakeholders such as ministries of finance, the environment, public works and health can work together on a cross-cutting issue such as NTDs? Realistic assessments must be made to understand what it will take to get to the end game.
4. How should national investment cases for neglected diseases be designed?

4.a. Adding value with country-level investment cases for neglected diseases

In the last decade, health-related investment cases have been prepared with sponsorship from different groups including global health institutions (The Global Fund, GAVI, UNDP, WHO), partnerships and consortia (Pediatric Praziquantel Consortium, WHO FCTC), and donors (Bill & Melinda Gates Foundation) (73)). For good reasons, these investment cases vary widely in scope and methods. Not all these investment cases have well-documented impact. Some investment cases are narrowly focused on mobilizing resources, some are aimed at galvanizing government agencies to take collective action, and some are used for awareness-raising on a neglected topic. Thoughtfully designed and intelligently used, an investment case can do all those things as well as solidify evidence. It is important to emphasize, however, that the results from investment cases are hypothetical in that costs and – especially – benefits are estimated using a series of assumptions. The most heroic assumptions relate to productivity benefits accruing from improved health. These productivity gains will arise only if labour markets are flexible enough to employ fully additional workers (compared to the status quo), pay them a standard wage, and employ them throughout their working lifetime. It also assumes that workers will choose to work more when they are healthier. Thus, estimated benefits should be considered as potential additions to GDP.

Many previous investment cases for neglected diseases have focused on assessing the health and economic returns to meeting strategic or global goals (see the example of a global NTD investment case in Box 1). These investment cases have provided broad global estimates of the cost to scale up interventions to prevent and treat neglected diseases (e.g. preventative chemotherapy, treatment of existing cases), and the impact of reaching a desired target population. We suggest that additional investment case analysis could beneficially move to the country level where decisions about future programmatic directions will increasingly reside, and that country investment cases should prominently feature the impacts of introduction and uptake of new technologies.


Fitzpatrick and colleagues (2017) [16] analysed the costs and benefits of meeting the 2030 SDG targets for NTDs. Globally, scaling uptake of preventative chemotherapy and disease management strategies was estimated to cost funders $8.4 billion between 2015 and 2030, and to generate $419.9 billion in economic benefits (in productivity gains and averted out-of-pocket health expenditures).

a “Integrated delivery of preventive chemotherapy medicines for lymphatic filariasis, onchocerciasis, schistosomiasis, soil-transmitted helminthiasis, and trachoma; also includes post-preventive chemotherapy surveillance and morbidity management and disability prevention” [16, Table 17.8].

b “Individual management of human African trypanosomiasis (HAT), leprosy, and visceral leishmaniasis (VL); also includes active case finding for HAT, leprosy, and VL, and vector control for VL; includes the cost of integrated disease surveillance in HAT-endemic areas” [16, Table 17.8].

National investment cases for neglected diseases – including on supporting health systems strengthening for technology uptake – can build on the foundation of previous investment cases, while innovating in five key areas.
First, previous neglected-disease investment cases were calls to global action. Building on that foundation, a new generation of investment cases for neglected diseases needs to be tailored to specific national contexts and conducted in partnership with local MoH officials. By taking a national perspective, these investment cases can catalyse national action. Investment cases will vary by country needs, goals and timelines.

Second, few investment cases have addressed bottlenecks to scale-up technology uptake along the entire supply chain in detail, nor quantified the costs of – and benefits to – removing the bottlenecks. A national investment case that seeks to locate issues within supply chains and health systems, survey the policy environment for feasible solutions, and analyse the benefits and costs of taking action can provide a road map for national actions, building on global guidance such as the WHO NTD Roadmap 2021–2030.

Third, while previous investment cases have quantified the health and economic benefits of taking action to address neglected diseases, few have grappled with the full range of social (health, education, equity) and economic consequences of neglected diseases. A holistic accounting of neglected-disease impacts will provide additional impetus to act.

Fourth, new investment case analysis should be able to show how integrated investments in access, delivery and disease management can accelerate the transition to UHC and the assumptions and methods should be chosen with an eye toward feeding into a broader UHC investment case analysis.

Fifth, uptake and utilization of new technologies offer both promise and challenge to countries on their path to achieve disease eradication and control. An investment case can sharpen the focus on the trade-offs inherent in adopting and rolling out new technologies and help countries lay the groundwork for successful adoption on a financially feasible timescale. It can also consider country-specific factors relevant to delivery modalities which a global delivery model steered by donors may not have considered.

**Figure 6. Investment cases for technology update for neglected diseases**

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Economic analysis - Methodological steps

1. **Step One**
   - Estimate mortality and morbidity from neglected diseases

2. **Step Two**
   - Estimate the total social and economic costs (direct and indirect costs) that result from neglected diseases

3. **Step Three**
   - Estimate the financial costs of implementing the interventions, and the social and economic benefits

4. **Step Four**
   - Estimate the impact of interventions to increase access to-and uptake of-technologies for neglected diseases

5. **Step Five**
   - Quantify the return on investment (ROI) of the interventions for neglected diseases

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**Final Results**
4.b. Conducting the economic analysis

A carefully scoped and conducted investment case can support major changes in the delivery and uptake of life-saving technologies through the gains outlined in Section 2.c. The framework of the economic analysis may consist of two components spanning five main methodological steps (see Figure 6). Assessing the current burden of disease is the first component and includes two methodological steps. This component provides information on the size of the social and economic problem caused by neglected diseases, providing a rationale for action. The second component prescribes ‘what to do’ about the problem.

Steps 3–5 assess costs and impact of taking specific actions to reduce the social and economic burden of neglected diseases. Previous reviews have summarized evidence on the costs of select interventions for TB [74], malaria [75] and NTDs [76]. An investment case should integrate this body of work, linking averted health events with averted health care costs. To the extent possible, averted health care expenditures can be broken down into those avoided by patients, government and other entities.

Each of the above-mentioned steps requires detailed discussions with multiple stakeholders about what is desirable, feasible and evidence-based within the local context, acknowledging existing commitments and goals. Sometimes these goals are very general and require greater specificity to identify costs and potential trade-offs. Other times they are imposed by some stakeholders but not fully socialized with others. This can be true both of external versus domestic stakeholders as well as across ministries within a single government. The investment case process has been shown to surface these gaps or divisions and can lead to a needed transparency in how goals are translated into the investment case. The flexible nature of investment cases works to advantage in choosing how far to carry this process.

As a starting point, Table 4 lays out some of the key features, data and decisions that are needed to perform the steps in Figure 6. The table uses NCD investment cases as an example and suggests parameters that could be incorporated in neglected diseases investment cases.

Table 4: Comparison of assumptions and data requirements for NCD and neglected diseases investment cases for technology uptake

<table>
<thead>
<tr>
<th>Investment Case Features</th>
<th>NCD Investment Case</th>
<th>Neglected Diseases Technology Investment Case</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perspective</td>
<td>Generally, NCD investment cases assume a societal perspective that accounts for costs and benefits accruing to – and experienced by – any members and sectors of society. Though often difficult to measure, efforts are made to include impacts on patients and households such as medical costs including out-of-pocket expenditures. A health sector perspective could also be taken, but in general, decisions to make public investments should reflect society's opportunity costs.</td>
<td>Societal or health sector with same proviso as NCD cases.</td>
</tr>
<tr>
<td>Comparator</td>
<td>NCD investment cases compare two scenarios. A baseline scenario assumes that no changes take place from the current status quo, and that coverage levels of interventions remain static throughout the time frame of the analysis. An intervention scenario examines the impact of scaled up coverage of clinical interventions, and intensification of policy measures targeting NCDs.</td>
<td>Comparators should be carefully selected with the country that is the focus of the investment case. A ‘baseline’ scenario may assume no changes in the current status quo over the time, or include projections of a country’s current expansion pathway. An intervention scenario may examine expansion of preventative or treatment-oriented interventions, potentially in reflection of the pathway needed to achieve SDG goals.</td>
</tr>
</tbody>
</table>
**Investment Case Features**

<table>
<thead>
<tr>
<th>NCD Investment Case</th>
<th>Neglected Diseases Technology Investment Case</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Timeline</strong></td>
<td>30 years – Frame investments in terms of current national five-year plans, or 10-year SDG or WHO treatment/diagnostic targets, expanding beyond that period where reasonable to assess the costs and benefits of breaking transmission (proceeding to elimination and eradication of diseases). Include emerging new technologies. The analysis timeline should fully capture the costs and consequences of neglected-disease programmes – including by tracing the impact on adolescents into adulthood – meaning that the analysis timeline may extend beyond elimination.</td>
</tr>
<tr>
<td>15 years, with the end date normally 2030, to align with the time frame of the SDGs.</td>
<td><strong>Target populations</strong></td>
</tr>
<tr>
<td>A shorter time frame would generally be harmful to the advocacy agenda as it would not fully account for all the benefits that take a longer time to accrue but would include full costs for each year including possible front-loaded costs.</td>
<td>Adults age 18+ with NCD risk factors (e.g. tobacco use, unhealthy diet), or existing diseases or conditions (e.g. diabetes, depression).</td>
</tr>
<tr>
<td>Some investment cases use a longer time frame. For instance, adolescent health investment cases evaluate the lifetime impacts of interventions applied in adolescence, projecting out 50 years or more.</td>
<td>• TB-, malaria- and NTD-endemic LMIC countries, potentially including a sub-national perspective to frame the problem at a relatable scale</td>
</tr>
<tr>
<td><strong>Interventions and Platforms</strong></td>
<td>• Children and adults at risk of contracting a neglected disease, and/or in need of treatment for existing disease</td>
</tr>
<tr>
<td>Starting point usually is the NCD ‘Best Buys’ from WHO that are well-evidenced and cost-effective interventions deemed to be feasible to apply in LMICs.</td>
<td>• Disaggregation by specific demographic groups (e.g. gender, or income or education quintiles) using an extended cost-effectiveness analysis approach.</td>
</tr>
<tr>
<td>This includes clinical interventions to prevent or treat cardiovascular disease, diabetes and mental health conditions (e.g. lifestyle advice and pharmacological treatment for hypertension)</td>
<td><strong>Key interventions to prevent or treat neglected diseases may include:</strong> (1) preventive chemotherapy via MDA; (2) vector control; (3) WASH; (4) diagnostic and treatment (e.g. surgery, wound care) of existing cases. Existing and upcoming technologies (vaccines, diagnostics, medication combinations, etc.) may be included – phase-in new technologies that may be priced rather than donated to analyse funding choices countries may face</td>
</tr>
<tr>
<td>Policy measures targeting NCD risk factors such as tobacco and alcohol use, salt consumption and physical inactivity (e.g. increasing tobacco taxes to reduce the affordability of cigarettes and other tobacco products)</td>
<td><strong>Interventions to facilitate health-system-service delivery</strong> of new or existing technologies may include: funding and strengthening regulatory approval institutions; developing HTA capacity; strengthening supply chain distribution and storage; and implementing track and trace systems. New or integrated platforms may be analysed for impact on service delivery, including potential alignment of neglected disease programmes within community health days, primary health care,</td>
</tr>
<tr>
<td>Health system capability is assumed but scale-up factors sometimes applied</td>
<td></td>
</tr>
</tbody>
</table>

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Guidance Note for the development of national investment cases for neglected diseases

20
### Investment Case Features

<table>
<thead>
<tr>
<th>NCD Investment Case</th>
<th>Neglected Diseases Technology Investment Case</th>
</tr>
</thead>
<tbody>
<tr>
<td>Focused investment cases have been conducted for tobacco control and mental health, and future ICs include an air quality investment case.</td>
<td>school feeding programmes, immunization campaigns, HIV programmes, etc. In addition, communication interventions (e.g. packaging of medicines, behaviour change) may be included to analyse impact on patient uptake of technologies.</td>
</tr>
</tbody>
</table>

### Measured outcomes

<table>
<thead>
<tr>
<th>Health</th>
<th>Health</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCD-attributable morbidity (health-state specific) and mortality.</td>
<td>NTD/TB/malaria – Infections averted, morbidity attributable to heavy infection (health-state specific) and mortality.</td>
</tr>
</tbody>
</table>

**Economic**

- Health care spending to prevent and treat NCDs.
- Productivity impacts due to absenteeism, presenteeism, labour exit due to disability, premature mortality.
- Intrinsic value of life.
- Per capita benefits and costs of interventions.
- Return on investment from scaling up packages of NCD interventions and individual interventions.

- Secondary health effects: mental health conditions, progression of other diseases (e.g. HIV and AIDS).

**Economic**

- Health care and out of pocket spending to prevent and treat neglected diseases.
- Productivity impacts (including informal or agricultural work and caregiving using credible alternative measures) due to absenteeism, labour exit due to disability, premature mortality.
- Intrinsic value of life.

<table>
<thead>
<tr>
<th>Education</th>
<th>Equity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days of school missed.</td>
<td>Potential breakdown of above outcomes by demographic groups.</td>
</tr>
</tbody>
</table>
- Ultimate level of educational attainment. |
- Impact on future earnings potential. |

**Equity**

- Cases avoided of catastrophic (i.e. impoverishing) health care expenditures.

### Costs

| Health system costs: medications, diagnostics, supplies, human resource time, and other direct and indirect costs of visits to primary health care facilities or hospital. | Health system or delivery system costs: vaccines, medicines, diagnostics, supplies, human resource time, and other direct or indirect costs embedded within the delivery platform. |
| Supply chain costs: added as a percent on-cost to the cost of medications, diagnostics and supplies. | Supply chain (logistics): transportation, distribution and storage of technologies. |
| Policy measures: cost to enact and enforce policies. | Policy and institutional costs that may facilitate supply chain strengthening (e.g. enacting enabling regulatory frameworks, funding HTA entities, resources for intra-government coordination). |
| Programme costs. | |
### Investment Case Features

**NCD Investment Case**

- Surveillance
- Aggregate and per capita cost of illness

**Neglected Diseases Technology Investment Case**

- Programme costs: staff dedicated to facilitating neglected-disease programmes, advocacy through media, or other mediums, meetings, training sessions, transportation, office supplies and other equipment
- Surveillance

**Considerations:**

1. Economies of scale and scope to delivery (integrated delivery may lower costs compared to status quo delivery platforms).
2. Diseconomies of scale: Last-mile costs should be considered for analyses of interventions to eliminate or eradicate neglected diseases, given that costs such as those for surveillance or programme delivery may increase dramatically approaching the end game.
3. It is recommended that donated technologies (e.g., medicines) and time (community health volunteers) be included and valued within the investment case, especially given that these costs may become more relevant to governments as shifts toward demand-side financing occur. These costs may be reported separately if they are not directly paid by governments.

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Good technical resources exist to fulfil many of the needed inputs for investment cases for neglected diseases. Some of these will come from other areas of global health but the *Uniting Efforts* community has many of the needed pieces and technical knowledge at hand. **Appendix 2** elaborates on the methods employed in conducting investment cases and points toward many of the extant resources to draw on.

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5. Lessons and Conclusions

A national investment case cannot solve all the challenges and barriers related to greater availability, accessibility and uptake of health technologies for neglected diseases. Producing a credible and useful national investment case requires many things. Without improved demand forecasting, an investment case cannot accurately estimate future product needs and costs of delivery. Without robust effectiveness data, reasonable incidence and prevalence estimates, programme information from which to determine costs, supplier and distributor willingness to share key information and devise system changes, and agents who can argue for change, a credible investment case is out of reach.

Most importantly, without an ethos of priority-setting that will imply eventual trade-offs, an investment case risks being just another plea for resources from a worthy cause. This guidance note sets the stage for development of national investment cases for neglected diseases by outlining what an investment case is – and what it is not; the ways that an investment case can be useful in the context of neglected diseases; and the types of considerations that need to inform development of an investment case.

Some of the lessons from a number of NCD and related investment cases may sound familiar to development practitioners but bear repeating and adding to in this context.

• **Investment cases should be country- and demand-driven.** A robust and credible investment case requires substantial inputs from government, ranging from hard-to-find data to honest discussions about what is feasible, including acceptable tradeoffs. A current example is how COVID-19 is affecting government priorities and whether resources are being diverted from neglected diseases or instead, whether COVID-19 augments the resources available to tackle infectious diseases and system strengthening for COVID-19 may enhance the value of investments in neglected diseases.

• **Local context is valid but local data is not always adequate.** A balance should be struck between using local quantitative data that may be incomplete or imperfect and global data that may be questioned by local stakeholders. Where global data is used for the quantitative analysis, the ICA can provide additional local perspective.

• **Seek buy-in from the highest possible political level without sacrificing action.** The investment case will be more valuable and impactful if it has support and is led by the appropriate government representative/s.

• **Involvement of key actors outside health ministries is crucial.** Producing a usable investment case requires leaders and respected actors from non-health ministries along with affected communities, civil society and private sector interests to provide key inputs and be prepared to act upon the conclusions of the investment case.

• **Simplicity leads to better communication and usability.** The results of an investment case should be easily explained and the methods should be readily replicable by the users in country. Simplicity of communication should not overlook the need to communicate directly to different audiences with targeted messages. In particular, the Ministry of Finance is the highest priority intended audience for many investment cases and the most relevant technical details should be accordingly conveyed.

• **Integrity of data and objectivity of results should be protected.** Whenever resource shifts are contemplated, stakeholders have an interest in the outcomes and must decide whether to protect the status quo or strengthen their advocacy for change. Within the constraints of sometimes weak evidence, the credibility of the investment case should be paramount and capable of withstanding scrutiny from any perspective.
For an investment case to bring about change that achieves the promise of better health for the available resources it must offer a specific call to action among all the stakeholders. *Uniting Efforts* stakeholders should consider this Guidance Note in follow up technical discussions that outline the top-line questions which may be answered by national neglected disease investment cases. The modalities, scope and parameters of a national investment case framework and methodology for neglected diseases can be tailored to these considerations. Major aspects of investment cases can be advanced virtually during the COVID-19 pandemic including supporting the development of methodologies and through the engagement with governments for the ICA component and presentations of the results to maximize impact, visibility and ownership across sectors.
References

20. HFJ (Heart Foundation of Jamaica), health ministry tackle obesity with new campaign, in Jamaica Gleaner. 2018.
Guidance Note for the development of national investment cases for neglected diseases

Appendix 1

a. Experts consulted

- **Isaac Chikwanha**, Senior Director, Investment Strategy, Access & Delivery, GHIT Fund (April 2020)
- **Christy Hanson**, Senior Program Officer, Infectious Diseases, Global Health Program, Bill & Melinda Gates Foundation (March 2020)
- **Paul Erasto Kazyoba**, Chief Research Scientist and Director of Research Coordination and Promotion, Tanzania National Institute For Medical Research (June 2020)
- **Sultani Hadley Matendecher**, Head of NTD unit, Ministry of Health, Kenya (April 2020)
- **Uzoma Nwankwo**, Federal Ministry of Health, Nigeria (April 2020)
  - Rebecca Flueckiger, Research Social Science Analyst, Monitoring and Evaluation, Global Health
  - Alexander Jones, Senior Research Health Policy Analyst, Neglected Tropical Diseases, Global Health
  - Scott Torres, Senior Manager, Health Policy, Global Health
- **Rob Terry**, Senior Strategic and Project Manager, TDR Special Programme for Research and Training in Tropical Diseases (April 2020)
- **Hugo Turner**, Head of Health Economics, NTD Epidemiology Research Group, Imperial College (July 2020)
- **Huang Xiao Xian**, Health Economist, WHO NTD Department (July 2020)

b. Resources shared by neglected diseases experts

- Ending the Neglect to Attain the Sustainable Development Goals: A WHO Roadmap for NTDs (draft)
- The Kenya National Breaking Transmission Strategy for Soil-transmitted helminthiasis, schistosomiasis, lymphatic filariasis and trachoma
- NTD Supply Chain Road Map for Sustainability – DRAFT MADE AVAILABLE BUT NOT FOR CIRCULATION
- Cost Effectiveness analysis of preventative chemotherapy – DRAFT MADE AVAILABLE BUT NOT FOR CIRCULATION
Appendix 2

a. Selected economic analytical methods used in investment cases

a.i. Modelling health outcomes

Assessing the current health burden of neglected diseases and the extent to which interventions can lower the burden requires robust country-adapted epidemiological models to quantify morbidity and mortality. Epidemiological models must be capable of capturing all direct and indirect health impacts of interventions and be flexible enough to reflect major changes in epidemiological patterns that could arise from the use of new technologies and delivery methods [77].

The NTD Modelling Consortium serves as a rich source of epidemiological analysis. It offers model summaries [78] and open-source code [79] for 12 diseases. The models capture NTD transmission dynamics, in-host life cycle and growth of the various pathogens, and the extent to which interventions can interrupt these processes. Some models (e.g. schistosomiasis [80]) have been used for cost-effectiveness analyses, though models are usually not structured for economic evaluations of health programmes. Building health economics in will “require a novel set of models, building on the [NTD Modelling Consortium work], but including the complications of health systems, diagnostics, surveillance systems, and delivery systems” [81 p. 3].

A comprehensive investment case will need to include not only short-term infection states, but also long-term chronic states caused by heavy infection. For instance, a schistosomiasis model should allow for analysis of the number of individuals who are infected and experiencing short-term disability states such as abdominal pain, diarrhoea, and blood in stools (see examples in Table 5) [82], but also assess how long-term exposure leads to chronic bladder or kidney conditions, physical underdevelopment, or death [83]. Modelling both short- and long-term disease sequelae would facilitate the calculation of intermediate and long-term outcomes – such as the number of days of school or work missed, disability-induced exit from the workforce, death – and the economic costs of those events. However, there is still debate over DALY estimates for some NTD sequelae. Examples include the extent to which neglected diseases foment mental health conditions and the impact of soil-transmitted helminths on cognitive impairment [77]. Consideration will need to be given to these types of uncertainty and inclusion or exclusion of certain impacts, especially where they may translate into significant economic impacts in the investment case.

Table 5. Short-term to medium-term schistosomiasis sequelae

<table>
<thead>
<tr>
<th>Sequela</th>
<th>Health state name</th>
<th>Health state lay description</th>
<th>Disability Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild anaemia due to schistosomiasis</td>
<td>Anaemia, mild</td>
<td>Feels slightly tired and weak at times, but this does not interfere with normal daily activities.</td>
<td>0.004</td>
</tr>
<tr>
<td>Mild schistosomiasis</td>
<td>Infectious disease, acute episode, mild</td>
<td>Has a low fever and mild discomfort, but no difficulty with daily activities.</td>
<td>0.006</td>
</tr>
</tbody>
</table>

1 Trachoma, leprosy, American trypanosomiasis (Chagas), human African trypanosomiasis (sleeping sickness), leishmaniasis, lymphatic filariasis, onchocerciasis, schistosomiasis, ascariasis, trichuriasis, hookworm infection and buruli ulcer.
<table>
<thead>
<tr>
<th>Sequela</th>
<th>Health state name</th>
<th>Health state lay description</th>
<th>Disability Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bladder pathology due to schistosomiasis</strong></td>
<td>Abdominopelvic problem, mild</td>
<td>Has some pain in the belly that causes nausea but does not interfere with daily activities.</td>
<td>0.011</td>
</tr>
<tr>
<td><strong>Moderate anaemia due to schistosomiasis</strong></td>
<td>Anaemia, moderate</td>
<td>Feels moderate fatigue, weakness and shortness of breath after exercise, making daily activities more difficult.</td>
<td>0.052</td>
</tr>
<tr>
<td><strong>Mild diarrhoea due to schistosomiasis</strong></td>
<td>Diarrhoea, mild</td>
<td>Has diarrhoea three or more times a day with occasional discomfort in the belly.</td>
<td>0.074</td>
</tr>
<tr>
<td><strong>Severe anaemia due to schistosomiasis</strong></td>
<td>Anaemia, severe</td>
<td>Feels very weak, tired and short of breath, and has problems with activities that require physical effort or deep concentration.</td>
<td>0.149</td>
</tr>
<tr>
<td><strong>Hematemesis due to schistosomiasis</strong></td>
<td>Gastric bleeding</td>
<td>Vomits blood and feels nauseous.</td>
<td>0.325</td>
</tr>
</tbody>
</table>

**Source:** IHME Global Burden of Disease Study 2017 (GBD 2017) Disability Weights [82]. (abbreviated for illustrative purposes)

### a.ii. Valuing averted health care expenditures

Preventative interventions (e.g. insecticide-treated bed nets, MDA) can stop disease before it starts. If more people stay healthy, there is less strain on health systems, and resulting savings in government and out-of-pocket health care expenditures.

Enumerating the out-of-pocket expenditures that patients avoid may provide an argument for equity, and potentially can be used to demonstrate the extent to which prevention and treatment can help low-income individuals to avoid catastrophic health expenditures that trap them in poverty. However, studies should be careful not to oversell potential savings. In some LMICs, low access to and affordability of treatment options may preclude people from ever seeking treatment for conditions. If people would not have received treatment in the first place, then there are fewer cost savings to scaling preventative interventions.

### Valuing non-health outcomes – productivity

In formal and informal labour markets, and within the household, individuals devote their knowledge, skills, and time to productive activities that generate value. Ill health can remove or lower individuals’ ability to participate in these activities, with resulting costs to families, communities and national economies. To enumerate these costs, analysts require estimates of two parameters: 1) the amount of productive time lost due to ill health; and 2) the monetary value of the time.

### a.iii. The amount of productive time lost due to ill health

National investment case for neglected diseases should assess the extent to which ill health causes losses in productive time. Poor health reduces productivity by permanently or temporarily removing individuals from formal and informal labour markets. When individuals die prematurely, the labour output that they would have produced in their remaining years is lost. In addition, individuals with ill health are less likely to participate in the workforce (e.g. due to disability), and more likely to miss days of work (absenteeism).

Premature death permanently removes individuals’ contributions, not only in the year in which they die, but also in every year that they would have productively contributed in the future. Thus, health and demographic
modelling should provide information to analysts about the age at which people die and the number of years of life lost. Analysts may convert these estimates into the number of years of productive life lost. For instance, in formal labour markets, a person might be expected to work up until a certain age on average, say age 65. When a person who would otherwise have been expected to live to old age dies at age 40, society loses 25 years of productive economic contributions from that person.

Ill-health, particularly disabling states, can change individuals’ ability to be economically productive, or contribute within households. Health modelling of mild, moderate, and severe disease sequelae – including disabling states such as blindness – can identify the number of people with conditions that may lower their ability to contribute in formal and informal markets, and over what time period. Fitzgerald and colleagues (2017) compiled evidence on the productivity impacts for select NTDs (Table 6). These estimates provide initial parameters for valuing morbidity while also encouraging analysts to seek locally-contextualized data on the morbidity impacts of neglected diseases.

Table 6: Loss of productivity due to NTD sequelae, reproduced from Fitzgerald, et al. (2017)

<table>
<thead>
<tr>
<th>Neglected tropical disease</th>
<th>Sequela</th>
<th>Annualized loss in productivity (%)b</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chagas disease</td>
<td>General (excluding heart failure)</td>
<td>2 to 5</td>
</tr>
<tr>
<td>Leprosy</td>
<td>Disfigurement</td>
<td>28</td>
</tr>
<tr>
<td>Lymphatic filariasis</td>
<td>Hydrocele</td>
<td>14 to 19</td>
</tr>
<tr>
<td></td>
<td>Lymphedema</td>
<td>2 to 23</td>
</tr>
<tr>
<td>Onchocerciasis</td>
<td>Visual impairment</td>
<td>14 to 38</td>
</tr>
<tr>
<td></td>
<td>Blindness</td>
<td>79 to 100</td>
</tr>
<tr>
<td>Schistosomiasis</td>
<td>General</td>
<td>1 to 23</td>
</tr>
<tr>
<td>Soil-transmitted helminthias</td>
<td>Anaemia</td>
<td>0.1 to 6.0</td>
</tr>
<tr>
<td>Trachoma</td>
<td>Visual impairment</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>Blindness</td>
<td>60 to 100</td>
</tr>
<tr>
<td>Visceral leishmaniasis</td>
<td>General (treated)</td>
<td>6 to 30</td>
</tr>
</tbody>
</table>

a Underlying sources: Lenk (2016) [68] and Ibe (2015) [84], b minimum and maximum from the literature

The monetary value of lost productive time

In the investment case, a monetary value will be placed on the amount of productive time lost due to neglected diseases. “In formal labour markets, earnings lost because of patients’ health status can be measured by means of a human capital approach,8 accounting for expected earnings in each time period in the patients’ lifetime…[where] the marginal value of a unit of time in the formal labour market is given by the wages plus fringe benefits” [85, p. 221]. Thus, a person who earns 50,000 in local currency units (LCU) and misses one-fifth of the working year would lose productive time valued at 10,000 LCU (50,000 * 0.2).

In practice, given that TB, malaria and NTDs disproportionately impact the world’s poorest populations, earnings of affected individuals may be small. For instance, individuals may earn as little as two dollars a day,
paling in comparison to, say, national average earnings. Analysts should seek to quantify the average earning among those affected by NTDs, and may wish to factor in projections in income growth over time to more fully account for productivity impacts. Even if small, productivity impacts still act to communicate that ill health has multiple reverberating impacts, including economic ones.

Equity issues may arise from only counting the productive losses of individuals who work in formal labour markets, especially in LMICs where informal labour can account for a significant share of economic activity. Measurements of the impact of neglected diseases on informal labour market outcomes are unlikely to exist. In addition, standardized methodological approaches to valuing the time of these workers are not well developed. Creative approaches may be needed. For instance, a recent World Bank analysis of data on formal and informal firms in 18 countries finds that in informal firms productivity per worker is about one-fourth of productivity per worker in formal firms, providing some insight into differences that exist in the value created within formal and informal markets [86].

Again, using lower-end values may generate equity issues. However, economic productivity impacts are only one part of the story. Analysts should seek to value the multifaceted impact of NTDs, and may choose to value other impacts of ill health that vary less by income level (e.g. see “Valuing non-health outcomes – social value” below). Moreover, they may call attention to the ways that lower productivity among individuals who are already economically challenged can exacerbate poverty. In addition, some neglected diseases particularly affect young children and the potential economic losses from ill health will accrue among future generations of workers. Below we suggest one possible way to include the value of future productivity from child health gains due to investments in neglected diseases (see Valuing non-health outcomes – education below).

a.iv. Valuing non-health outcomes - social value of a life year

There is intrinsic value to health and being alive – captured in the idea that individuals impart value to families and to communities that they are connected to. Analysts have sought to quantify this ‘social value’, and WHO analyses [10, 13] have commonly valued each healthy life year gained at 0.5 times GDP per capita in a country. Inclusion of social value within an analysis – as opposed to just productivity outcome – ensures a more equitable accounting of the value of life and health among all populations, regardless of income.

a.v. Valuing non-health outcomes - education

Valuing educational outcomes requires information on the extent to which neglected diseases cause children and adolescents to miss school or to not advance in school. Each investment case should seek to identify studies that have identified school absences attributable to neglected diseases in the country or area of interest. Educational impacts of neglected diseases have been estimated in multiple settings, but only for select diseases.

The returns to extra years of schooling have been estimated in developing country contexts, with Fink and colleagues reporting additional future income earnings of 10 percent in Latin America per year of extra educational attainment, 9.7 percent in sub-Saharan Africa, 6.1 percent in East Asia, and 6.2 percent in North Africa and the Middle East [87].

The benefits of higher wages do not accrue until these individuals enter the workforce later in life. A population model that tracks adolescents to adulthood can value expected increases in wages from treatment of certain neglected diseases in early childhood.
a.vi. Valuing non-health outcomes - equity

Equity is often a consideration in policy deliberation. Neglected diseases disproportionately impact vulnerable populations, including low-income earners and women. Valuing the extent to which policies or interventions may disproportionately act to improve the lives of vulnerable populations can provide additional impetus for action.

Extended cost-effectiveness analysis (ECEA) is a recent methodological development that evaluates equity outcomes. The ECEA approach stratifies outcomes by population sub-groups of interest (e.g., by income quintile) to examine how – or whether – one group is more impacted by an intervention than another. The ECEA typically examines how better health outcomes lead to less out-of-pocket spending (e.g. for transportation to seek care, health care expenditures), and how less out-of-pocket spending effects financial risk protection (e.g., the number of averted catastrophic health-care expenditures, cases of medically-induced poverty) [88].

Figure 7 shows investment case findings for the impact of a tobacco tax in Cambodia. Because people with lower incomes are more responsive to changes in price, and because people with lower incomes use tobacco at higher rates in Cambodia, the tax increase causes the largest drop in smoking prevalence in the low-income quintile groups. Consequently, many of the health benefits accrue to the low-income group. This means those individuals experience better health and reduce their medical expenditure which can account for more than 40 percent of annual income for the low-income group.

Figure 7. Catastrophic health care expenditures avoided due to tax increase, by income quintile

Verguet and colleagues (2016) outline the extensive data requirements of ECEA, which include data on the distribution of health (e.g., infection, and incidence, prevalence and mortality of disease) among sub-populations of interest; coverages and effect of interventions by sub-group; the probability of seeking care by sub-group, and out-of-pocket payments required to treat the examined health issues, and; the burden of expenditures on populations (e.g., data on disposable income, distribution of poverty) [88].
b. Conducting an institutional and context analysis (ICA) for an investment case

An ICA requires desk research and interviews with key informants to answer a series of questions about how social, economic, environmental and political factors inform the status quo. UNDP has published general guidance on conducting an institutional and context analysis [89], which has been adapted for specific contexts (e.g., noncommunicable diseases [90], the SDGs [91]). The basic UNDP ICA framework for NCDs [90] is relevant for neglected diseases, shown in Table 7.

<table>
<thead>
<tr>
<th>Step</th>
<th>Overarching question</th>
</tr>
</thead>
<tbody>
<tr>
<td>Define the scope of the problem and assess the opportunities/challenges for responses.</td>
<td>“What are the needs, opportunities, and challenges for neglected-disease-related interventions?”</td>
</tr>
<tr>
<td>Determine institutional and governance arrangements and capacities.</td>
<td>“Who are the relevant actors, how do they operate, and are they capable, effective and efficient?”</td>
</tr>
<tr>
<td>Assess available and potential resources.</td>
<td>“What current and potential mechanisms, strategies and opportunities exist for financing neglected-disease responses?”</td>
</tr>
<tr>
<td>Identify the political economy drivers.</td>
<td>“What are the political, economic and other priorities/incentives of the relevant actors – and how do these relate, broadly, to related interventions for neglected diseases?”</td>
</tr>
<tr>
<td>Propose priority actions and identify key supporters and key opposition.</td>
<td>“Which cost-effective interventions are most feasible given the political and economic context, and how are relevant actors likely to perceive them?”</td>
</tr>
<tr>
<td>Evaluate potential for change and identify enabling factors and strategies.</td>
<td>“How likely to be implemented are the priority actions and what factors/strategies can expand the political space for adoption, implementation and enforcement?”</td>
</tr>
</tbody>
</table>

While following this basic framework, an investment case will require careful attention to the unique context of TB, malaria and NTDs. Scoping the problem may begin with an assessment of barriers and bottlenecks within the access and delivery value chain for neglected diseases (Figure 4). Careful examination of the delivery value chain can identify priority actions to facilitate uptake of technologies for neglected diseases and evaluate their feasibility within existing political, social, and economic structures. Priority actions may exist anywhere along the access and delivery value chain. For instance, innovations such as TraceRx, an electronic track and trace drug supply management system currently being implemented in Nigeria [92], can track drug inventory in order to send the correct ‘demand’ signals to procurement agencies, reducing stockouts and drug wastage. Or, the feasibility of new service delivery modalities can be examined, with inquiry into whether – and how – existing neglected diseases programs can be synchronized with other health delivery platforms.

Assessments of available and potential resources must pay attention to the ways that market failure – and solutions to overcome it – have shaped development and delivery of medicines. While donated medicine is a mainstay of current NTD programming, shifts in corporate intentions have arisen in parallel with shifts in the donor ecosystem – both movements requiring changes in past assumptions and providing the opportunity to create new and revamped roles and relationships.

h Neglected Diseases has been substituted for NCDs.
Finally, an ICA for a national neglected disease investment case will grapple with a wide field of actors – with varying incentives and power – involved in development and delivery. Donors and non-state actors (e.g. pharmaceutical and medical device companies, donor organizations and non-governmental organizations) have traditionally driven much of the agenda. Intragovernmental relationships and power dynamics are at play between government ministries. In addition to the traditional ways that health governance intersects with finance, development and social sectors, the administration of some neglected diseases national programmes overlaps with the sectors of water and sanitation, agriculture and livestock, education and others. In addition, coordination – or lack thereof – between local, regional and national governance structures can drive outcomes [93]. At the local delivery level front-line providers, community drug distributors, teachers, programme managers, community leaders and community members may inform the acceptance and overall success of different delivery modalities [51]. Investigation of the political power, incentive structure and beliefs of these actors – as well as interactions between them – can identify drivers of the political economy and ensure impact in the design of strategies and interventions.