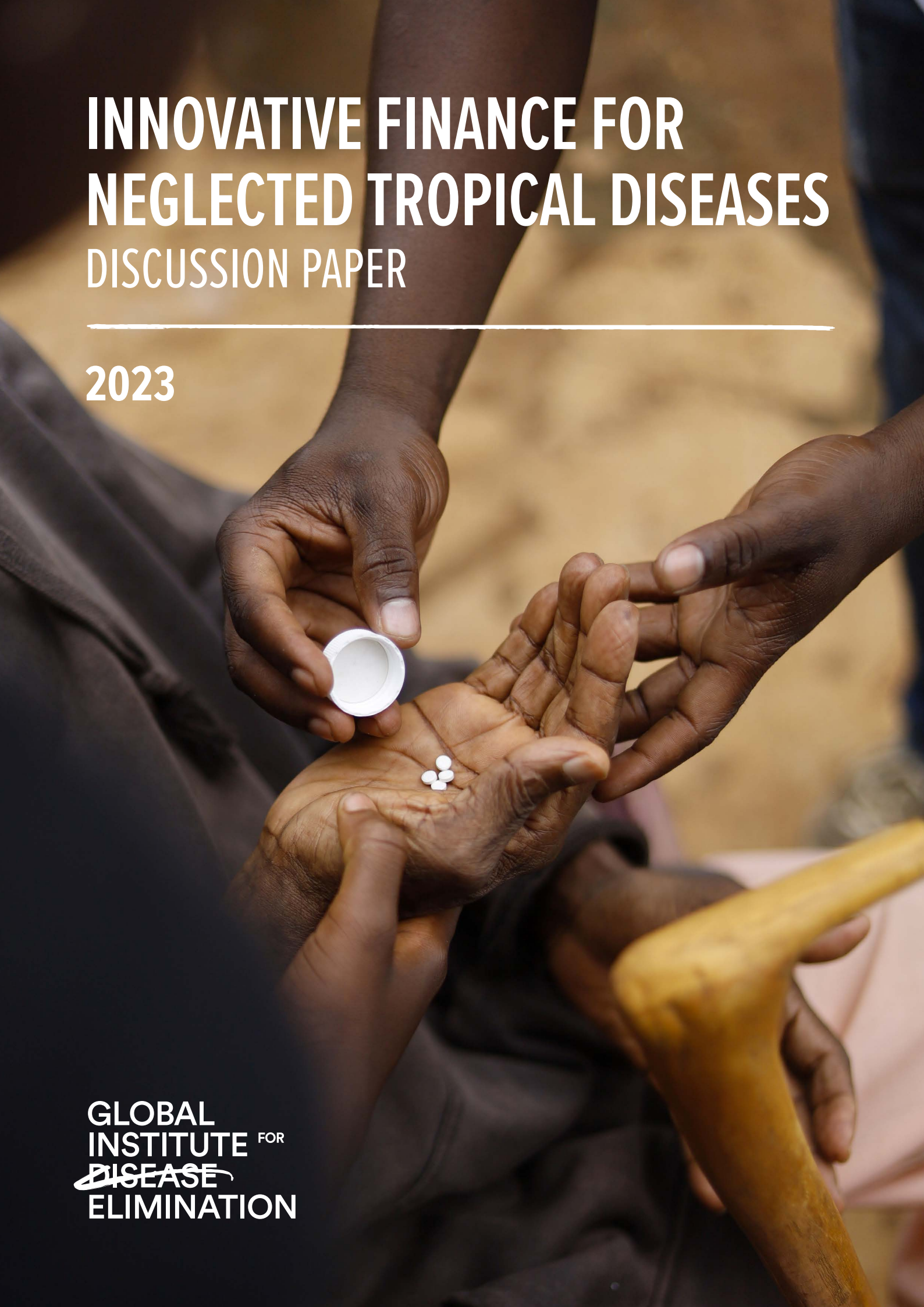
INNOVATIVE FINANCE FOR NEGLECTED TROPICAL DISEASES

DISCUSSION PAPER

2023



GLOBAL INSTITUTE FOR DISEASE ELIMINATION

EXECUTIVE SUMMARY

Despite affecting nearly two billion people—primarily across low- and middle-income countries—the availability and deployment of innovative new treatments for neglected tropical diseases (NTDs) are rare. For diagnostic tests, the situation is similarly concerning; of the 20 NTDs identified by the World Health Organization, tests do not exist for six NTDs, and for the remaining NTDs, the tests are either not fit-for-purpose or not accessible where they are needed.

Seizing the COVID-19 pandemic-induced opportunity to examine new ways of financing health initiatives and disease programs, GLIDE, with support from McKinsey Consulting, developed an innovative finance (IF) workstream to coordinate and lead a 6-month technical exercise with a small core group of 20 organizations, including representatives from traditional pharmaceutical companies, non-governmental organizations (NGOs), product development partnerships (PDPs), and civil society. The objectives of this exercise were to condense existing evidence, galvanize inter-sectoral discussions, and capture voices of leaders committed to finding IF solutions for NTDs. The results of this exercise are four prioritized finance mechanisms: i. debt swaps, ii. milestone-based funding for NTD diagnostics, iii. development impact bonds, and iv. pooled procurement (as a market shaping prospect)—that are proposed for further interrogation with a wider stakeholder community to understand the viability of application to specific disease(s), instrument(s), and country or regional contexts.

This paper presents each instrument and reflects the technical working groups' research and initial conceptualization of how they can be applied as finance mechanisms for NTDs. While this work reflects some consultative input from industry, endemic countries' Ministry of Health representatives, and NGOs, the aim of this preliminary work is to provide a starting point to move from concepts towards defining a solution. The paper intends to facilitate additional stakeholder participation and guide commitments to develop, test and implement a new instrument to reduce the morbidity and mortality of NTDs amongst affected communities.

This discussion paper aims to engage new and potential stakeholders committed to eliminating NTDS globally. GLIDE and its partners acknowledge that there will not be one instrument that can fill all the gaps. We have identified some promising areas for innovative finance, but there are many more and there is potential for IF instruments to be used in combination to even greater effect. Beyond this paper, GLIDE will facilitate several roundtables, in collaboration with partners, to resolve some of the questions through the contributions of endemic countries, impacted civil societies, NGOs, PDPs, and the private sector, as well as potential donor and investment entities.

More can and should be done to eliminate NTDs. More of the same is not enough: there is a meaningful potential for innovative finance solutions to provide transformative impact. To be able to eliminate NTDs, more investment and better tools are needed now at the last mile to find, test, and treat the remaining patients, often from more remote and hard-to-find or vulnerable patient groups.

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BACKGROUND

Medicines and diagnostic advances are amongst the most impressive achievements of science and economic development, allowing us to identify, categorise and treat many previously intractable and debilitating diseases. However, 85% of the world's population cannot access needed medicines—let alone the prospect of new and improved diagnostics and treatments.[1] Even when they are available and affordable, sustainable supply of NTD interventions remains an underpinning concern.

Despite affecting nearly two billion people—primarily across low- and middle-income countries (LMICs)—the availability and deployment of innovative new treatments for NTDs are rare. For diagnostic tests, the situation is similarly concerning; of the 20 NTDs identified by the World Health Organization (WHO), tests do not exist for six NTDs, and for the remaining NTDs, the tests are either not fit-for-purpose or not accessible where they are needed.

In 2021, worldwide funding for basic research and product development for medicines approached US$200 billion[2]—this went to looking for novel and effective treatments for diseases affecting people across the globe. Yet only 2% of that amount went to funding research and development (R&D) on neglected tropical diseases. In fact, the funding trend for NTDs dropped 4% in 2020 compared to 2019, reducing the already narrow share[3]. The lack of financial recompense for R&D expenses translates to stunted innovation and discourages research of novel solutions to prevent, diagnose and treat NTDs—this has resulted in a shocking disparity in access to effective treatments, with only 10 new drugs being developed in the last decade to combat diseases that affect 2.5 billion people. The research and development that does exist for NTDs is disjointed and has been characterized by poor return on investment, lack of demographic data and inadequate forecasting mechanisms, which have led to low levels of further investment. The focus on NTDs has been further diminished by the heavy burden the COVID-19 pandemic response placed on health service delivery.

In high income countries, the projected financial returns achieved during the period of patent protection warrant the investment risk and ensure continued investment in research and development for new products. In the absence of these returns, manufacturers deprioritize the development of unprofitable products, and the global health community struggles to find the required investment. Even for diseases where a positive return on investment can be generated, the additional work for approval and the complexities of dealing with a highly fragmented market in LMICs means that there is little incentive to innovate and serve these markets.

[1] Sachiko Ozawa, Raja Shankar, Christine Leopold, Samuel Orubu, Access to medicines through health systems in low- and middle-income countries, Health Policy and Planning, Volume 34, Issue Supplement_3, December 2019, Pages iii1–iii3, https://doi.org/10.1093/heapol/czz119

[2] Evaluate Pharma (2021) World Preview 2021, Outlook to 2026. London: Evaluate Ltd., p 23. Available at: https://info.evaluate.com/rs/607-YGS-364/images/WorldPreviewReport_Final_2021.pdf

[3] Policy Cures Research G-FINDER Report. Neglected Disease Research and Development: New Perspectives. https://policy-cures-website-assets.s3.ap-southeast-2.amazonaws.com/wp-content/uploads/2022/01/27175130/G-FINDER-2021_ND_Executive-Summary.pdf

Uniquely for NTDs, donation of medicines remains the key public health strategy, with twelve out of the 20 neglected tropical diseases benefitting from a medicine donation program. Still, donation programs rely on the generosity of a few industry partners and these programs are limited and finite.

Despite this important philanthropy, there remain serious issues, including:

- Access to donated medicines is limited by the scale of the donation program, rather than disease burden and patient need;
- An incumbent donation program can be perceived as a disincentive for the development of new or alternative therapies;
- Reliance on pharmaceutical company donation presents a risk to treatment availability in the case that a program ends;
- The potential reduction in appetite of countries or donors willingness to pay for a new product to replace one that is already given for free, even if the new product is superior, is suppressed;
- There are gaps in treatment of certain population segments due to insufficient treatment availability;
- Parallel health financing and supply mechanisms created for donation supported disease programs are not integrated with mainstream country mechanisms.

The existing financing model for NTDs reduces country ownership and buy-in, disincentivizes investments and innovations, and requires a potentially endless (and unrealistic) expectation on some pharmaceutical industry stakeholders. We further describe the stakeholder specific pressures that underscore the challenge of NTD financing in Box 1.

To combat these issues, supply-side financing of research, product development, quality assurance and distribution are required, in addition to continued government investments and industry donations. Tractable diseases remain underserved, shortages of essential drugs are becoming increasingly frequent globally, a lack of testing drives ineffective and inefficient (mass) drug administration, and health systems are over-burdened. The status quo is inadequate and financial innovation to develop new treatments and diagnostics and to supply existing commodities is needed.

BOX 1.
STAKEHOLDER'S PRESSURES IN THE CURRENT NTD FUNDING ECOSYSTEM

THE PERSON AFFECTED:

NTDs disproportionately affect impoverished and marginalized communities. Many NTDs cause disfigurement which can lead to social stigma, reduced mobility, and decreased quality of life. Many people who are at risk of NTDS do not have access to quality diagnostics or preventative treatment. Additionally for the few treatments that are available, not all of them are included in drug donation programs. These treatments are generally unaffordable and unsuitable for low-income settings, especially for subpopulations such as children and pregnant women.

ENDEMIC COUNTRIES:

While countries endemic with NTDs have increased levels of domestic funding in the last decade, a significant number of resources are from external entities (e.g., high-income countries, pharmaceutical drug donation programs, multilateral organizations). Additionally, little scientific research originates from disease-endemic countries which can hinder quick assimilation of new findings and technology and lead to misalignment of community needs and contextual realities. Further, inadequate funding to endemic countries impeded disease burden measurement and broader programmatic planning.

THE PHARMACEUTICAL DRUG DONATION PROGRAMS:

In the last 30 years, pharmaceutical companies have established programs to donate 17 different medicines for the prevention and treatment of NTDs. This includes the manufacturing of billions of tablets and solutions as well as the subsidization of supply chain efforts. While some companies have made commitments to continue these donation programs until their target NTD is eliminated, in the current constrained economic environment, these commitments may become strained or unreliable.

PRODUCT DEVELOPMENT ENTITIES AND MANUFACTURERS:

The funding shortfalls for NTD R&D has left a gap in the development of tools needed to prevent and control these diseases that impact 20% of the most neglected people in the least economically developed countries. The NTD landscape also rarely attracts private pharmaceutical research investments and funding from other private sector entities. For diagnostics, the R&D picture is even more limited with only five industry partners accounting for 65% of funding in the last decade. This reality has led to poor and inequitable access to effective treatment and diagnostics.

PURPOSE OF THIS PAPER

While there are several activities for understanding the risk and opportunities around financing solutions for NTDs—most notably the Uniting Efforts for Innovation, Access and Delivery global dialogue series that started in 2019[4] and the Results for Development work on Sustainable Financing & Supply of NTD Medicines in 2021—the post-COVID-19 global discourse on and initiatives for strengthening health systems and reaching the last mile has revived momentum in developing financing solutions across the health space.

For NTDs, there is a need for a far more dedicated effort to develop new systems to fund research and development, and to reduce the reliance on philanthropy to fund the supply of existing medicines in order to take an important step towards health equity. As described above, the current system provides a patchwork of solutions and does not offer a sustainable systemic alternative. If stakeholders across the NTD space can learn from several global financing initiatives that have catalyzed external financing in target areas, e.g., the *Outcomes Fund for Fevers (OFF)* launched in 2022 by the *Health Finance Coalition*[5], then there is an opportunity to address gaps and mobilize funds where they are most needed.

Seizing the COVID-19 pandemic-induced opportunities to examine financial instruments, GLIDE developed an Innovative finance for NTDs (IF-NTD) workstream to coordinate and lead a 6-month technical exercise with a small core group of 20 organizations, including representatives from traditional pharmaceutical companies, non-governmental organizations (NGOs), product development partnerships (PDPs), and civil society (see Annex A for list of members). The objectives of this exercise were to condense existing evidence, galvanize inter-sectoral discussions, and capture voices of leaders committed to finding IF solutions for NTDs. As it was essential to ensure that this work was built on a strong foundation of expertise, GLIDE enlisted McKinsey and Partners for research and analysis activities. The results of this exercise are four prioritized finance mechanisms, i. debt swaps, ii. milestone-based prizes for NTD diagnostics, iii. development impact bonds, and iv. pooled procurement (as a market shaping prospect). These are proposed for further interrogation with a wider stakeholder community to understand the viability of application to specific disease(s), instrument(s), and country or regional contexts.

This paper presents each instrument and reflects the technical working groups' research and initial conceptualization of how they can be applied as finance mechanisms for NTDs. While this work reflects some consultative input from industry, endemic countries ministry of health representatives, and NGOs, the aim of this preliminary work is to provide a starting point and to move beyond discussion of concepts. The paper intends to facilitate additional stakeholder participation and guide commitments to develop, test and implement a new instrument to reduce the morbidity and mortality of neglected tropical diseases amongst affected communities.

[4] https://www.unitingeffortsforhealth.org

[5] https://healthfinancecoalition.org/#about

WHAT ARE INNOVATIVE FINANCE MECHANISMS FOR NTDS?

Although national NTD programs in endemic countries have committed significant investments and demonstrated leadership, NTDs remain largely underfunded and are highly dependent on external donor funding. The shift from traditional Official Development Assistance (ODA)-driven resourcing towards more innovative finance has helped to mobilize significant additional avenues of funding in the global health landscape.

Employing several different instruments—debt swaps, milestone-based funding to incentivize R&D, specialized bonds that blend capital from public and private investors, and mechanisms built around pooled procurement platforms to better leverage donor and philanthropic funding—the global health community has effectively unlocked resources and achieved enormous benefits for people suffering from HIV/AIDS, tuberculosis, malaria, and polio. Similarly, innovative finance approaches could benefit NTDs by sourcing capital to complement existing funding or deploying capital with better allocation of risk.

Despite this progress, however, securing resources within the NTD space remains a challenge. Total funding for NTDs to WHO in 2020 totaled $323 million USD reflecting a declining trend of funding since 2019. Funding in the NTD space continues to depend largely on "traditional" financing sources including bilateral funding, philanthropic grants and in-kind donations.[6] Drug donations are the most significant in-kind contribution, with the financial value of drug donations surpassing the total NTD funding by three to four times per year.

Approximately two-thirds of all NTD funding originates from international donor sources. The US and UK governments have traditionally accounted for approximately 80 percent of bilateral donations.[7] However, funding has become increasingly difficult to predict. The impact of COVID-19 and global political instability are significantly reshaping overseas development assistance in terms of quantity, as well as where and how it is allocated. Financing, through private channels and from international development banks, could support scaling up domestic spending, especially as some NTDs will only need a short-term campaign that can lead towards eradication, from which significant economic long-term returns can be expected.

The resources that are available are skewed towards the upstream areas of the value chain where capital costs are high, e.g., around 50 percent of international funding for NTDs is targeted for research and development. There is less focus on the downstream value chain areas, such as mechanisms to improve access and delivery of new tools—where the potential for return on investment may be higher.[8] Additionally, preliminary insights show that NTD funding is more likely to be focused on a few specific diseases (e.g., polio, kinetoplastids, high-burden diseases).[9]

[6] 40% and 35% of all international funding, respectively

[7] Desk research by McKinsey & Company

[8] Desk research by McKinsey & Company

[9] Desk research by McKinsey & Company

SIGNIFICANT POTENTIAL BENEFITS OF INNOVATIVE FINANCE

Innovative finance mechanisms are being discussed to achieve two outcomes: to improve access to existing diagnostics and medicines that are constrained by limitations on the scope and/or duration of donations, and to drive new medicines and diagnostics through funding that better reflects the risks and public health impacts of innovation.

Specifically, the innovative finance mechanisms have the potential to boost the NTD ecosystem through several means. They could:

- Provide additional avenues of funding as complementary sources of capital to traditional development finance by bringing on board a set of non-traditional funders, addressing the perspective that financing participation is for the few;
- Unblock research and development by de-risking investments through spreading risks across different types of financing instruments or funders with many times lower-than-market or zero return expectations;
- Enhance the efficiency of financial flows by reducing transaction costs and delivery times and/or costs, consolidating investment from multitude of actors;
- Make financial flows more effective and results-oriented, by explicitly linking funding flows to measurable performance on the ground;
- Allow independent assessment of (financial) results and impact without the potential dilution in the context of a wider high-risk-high-return investment portfolio.

Broadly speaking, the term 'Innovative finance' encompasses a range of mechanisms with differing investment return expectations, from achieving impact as the core determinant of success with no expectation of cost recovery to anticipating that there will be a financial return, over and above cost recovery. Given the competitive post-pandemic resource mobilization landscape, one compelling advantage is that IF instruments can enable public, private, and philanthropic funders to transact across an increasingly diverse capital landscape. See Figure 1.

STAKEHOLDER ECOSYSTEM ALONG THE CAPITAL LANDSCAPE

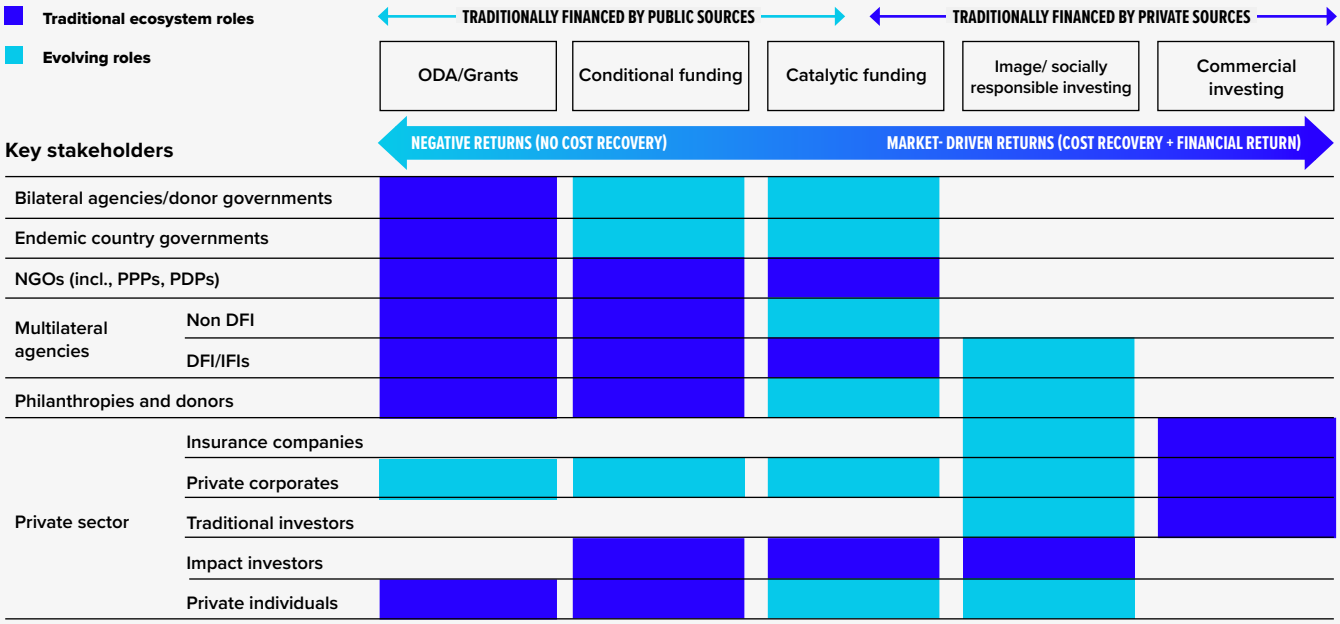


Figure 1: Stakeholder ecosystem along the capital landscape

Innovative finance funders have different risk appetites from traditional donors and aim to hedge different types of risks, including market- and context-specific risks and general financial risks. These risks can target specific or multiple value chain areas for NTDs and can be unlocked with a tailored set of financing instruments. See Figure 2.

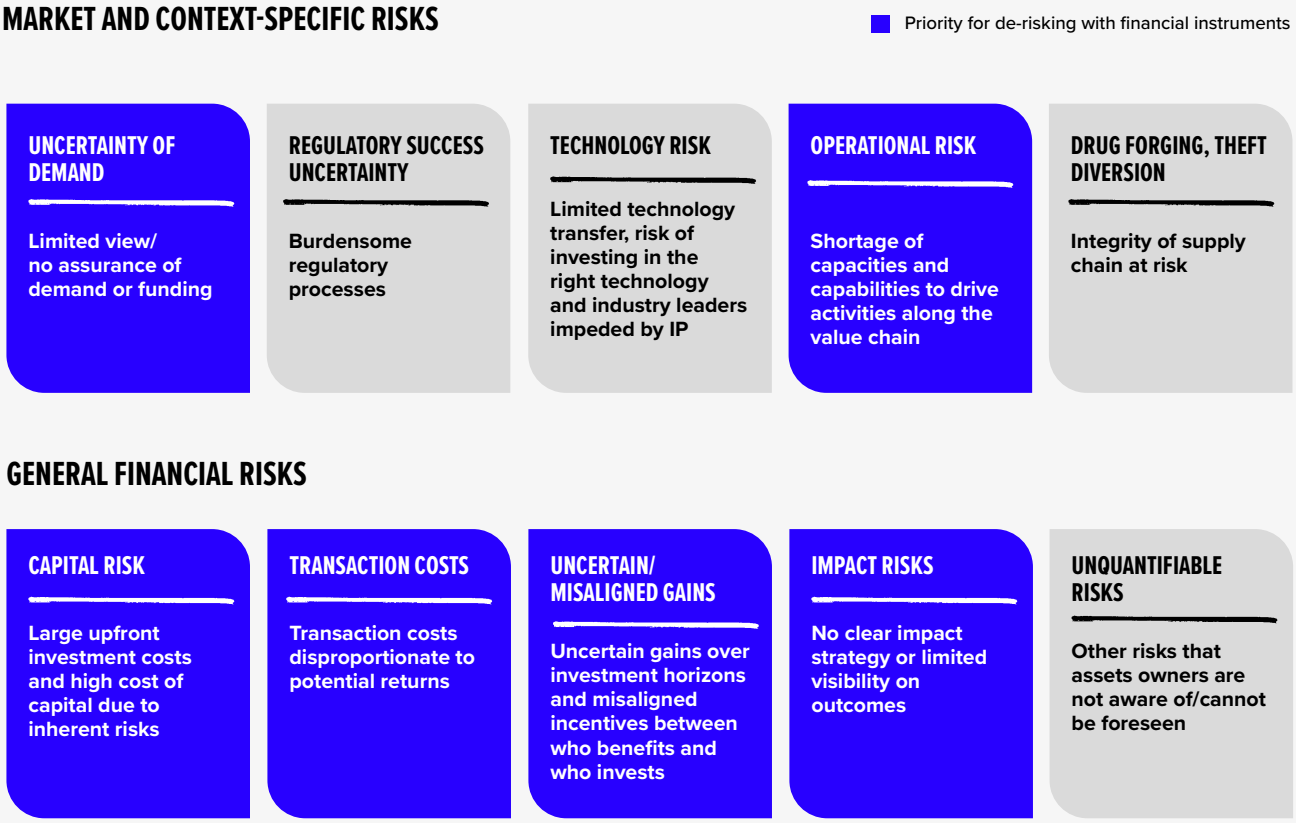


Figure 2: Market and context-specific risks

While these mechanisms have been effective in mobilizing innovative finance in the wider global health landscape, not all of them are directly transferable to the NTD space and several factors need to be considered:

- What value chain component is the innovative funding mechanism best placed to target? Are the instruments well-suited to cater to the specificities of the NTD space?
- What risks does this funding mechanism address and for whom (e.g., high capital costs for R&D, regulatory risk, demand uncertainty)?
- What core funding problem needs solving? Is the mechanism best suited to enable more effective financing (e.g., improved incentives) or could it attract a larger pool of financing as well (e.g., from existing or new sources)?
- How would this link to the existing ecosystem? Who are the key stakeholders and what are their objectives? How would the instrument mobilize new funding and how does that link with existing funding flows?
- Which NTDs are targeted and are there synergies with other NTDs or diseases? What is the level of funding needed? Would the funding flows be truly additive / sustainable / predictable?

PRIORITIZING INNOVATIVE FINANCE SOLUTIONS

Considering these dimensions, innovative finance shows good potential to unlock solutions and fill gaps across the value chain. In a hybrid workshop held in Berlin in October 2022, the IF-NTD Core group aligned on a set of priority gaps along the NTD value chain to focus on, with consensus that ensuring sustainable access to existing products and strengthening multi-sectoral integration are the "must-win" priorities.

Potential mechanisms to facilitate this—including pooled procurement platforms, volume guarantees, and demand pooling and other instruments—were identified by the group as having the most compelling potential for IF-NTD solutions.

Given the diversity and complexity of the NTD space and limited funding resources, it is important to analyze the optimal scope and applicability of mechanism(s) to specific diseases and geographies. Therefore, the objective was to prioritize instruments that have the most appealing impact and/or ease of implementation profile. The IF-NTD Core Group undertook a deep-dive analysis of priority instruments to understand the potential scope of interventions: desk research and iterative discussions among the collaborators fed into a workshop to develop a high-level directional prioritization of potential IF solutions to address key NTD gaps. For each gap, a range of innovative finance mechanisms could be tailored to suit specific needs and geographies. IF mechanisms themselves are flexible in terms of target and could be developed for specific research and development or implementation goals.

As a starting point, the IF-NTD Core Group identified priority gaps and explored potential innovative finance instruments. See Figure 3.

To be considered innovative, the financing mechanisms needed to be compliant with the following principles:

- **Catalytic:** mobilize significant funding for the NTD ecosystem;
- **Additivity:** be net additive and cannot replace existing flows of funding;
- **Complementarity:** must not substantially increase the complexity of the existing financing ecosystem;
- **Sustainability:** contribute to the long-term financial sustainability of the ecosystem.

PRIORITY GAPS IDENTIFIED & ALIGNED BY THE CORE GROUP	PRIORITY THAT COULD BE ADDRESSED WITH IF	POTENTIAL IF INSTRUMENTS TO ADDRESS GAP (deep-dive to follow)
1. **DIAGNOSTICS** Increase funding and focus on R&D & capacity for diagnostics	• Upfront catalytic funding with or without milestone payments - focus: early stage Dx R&D	• Tax credits • End or milestone-based prizes • Pooled Procurement
2. **EFFECTIVE INTERVENTION TECHNOLOGY RESEARCH** Strengthen funding & incentives for R&D of non-Dx interventions	• Catalytic support to push products through the late development stages	• Tax credits • De-linking/subscription models • Volume guarantees • Offtake agreements (AMC or APCs) • Priority review vouchers
3. **ACCESS AND LOGISTICS** Ensure sustainable access to existing products	• Mechanisms to lower prices/transaction costs of procurement of drugs/Vxs/diagnostic and to decrease the cost of treatment at the 'last mile'	• Pooled procurement (with potential co-financing) • Volume guarantees • Insurance models • Transportation vouchers
4. **ADVOCACY AND FUNDING** Strengthen domestic funding and evidence-based advocacy	• Increased/incentivized domestic funding, specific for NTDs • Catalytic support to scale interventions in-country • Mechanisms to strengthen health systems and infrastructure	• Debt buydown/debt swaps/loan conversion • Development impact bonds • Matching funds • Voluntary contributions/crowdfunding/ remittances/corporate donations
5. **COLLABORATION & MULTISECTORAL ACTION** Strengthen collaboration & multisectoral action/integration	*Limited applicability for IF mechanisms to target alone, however, potential for cross-sectoral/ collaborative interventions targeting gaps 1-4, e.g., Development impact bond for health and educational outcomes*	

Figure 3: Potential IF instruments to address NTD gaps

The instruments were prioritized based on their impact versus ease of implementation profiles and mapped into quadrants (see Figure 4). Four promising instruments were selected for a deep-dive analysis: development impact bonds, pooled procurement, debt swaps and milestone-based prizes.

HIGH-LEVEL DIRECTIONAL PRIORITIZATION OF POTENTIAL INNOVATIVE SOLUTIONS TO ADDRESS KEY NTD GAPS

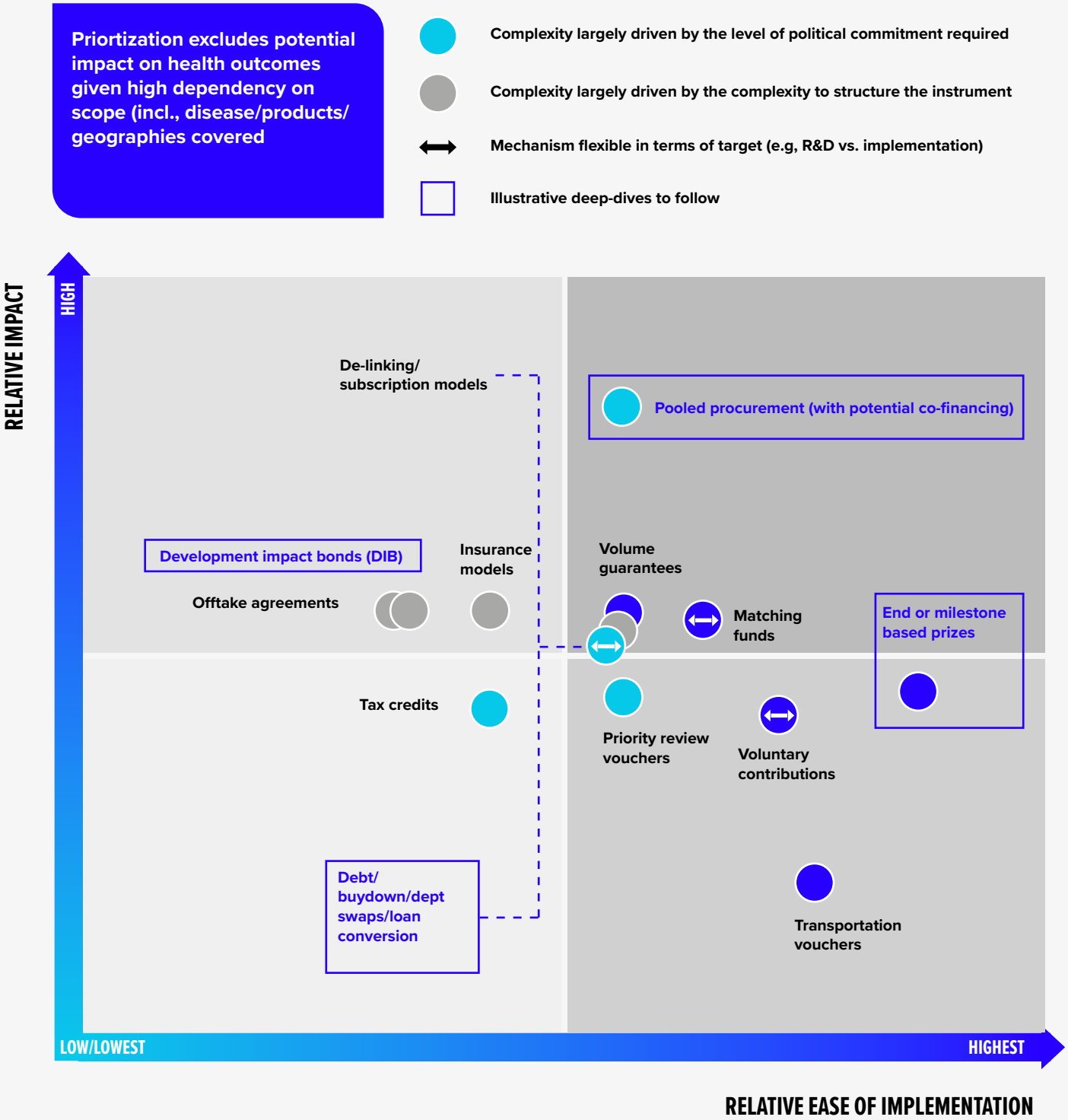
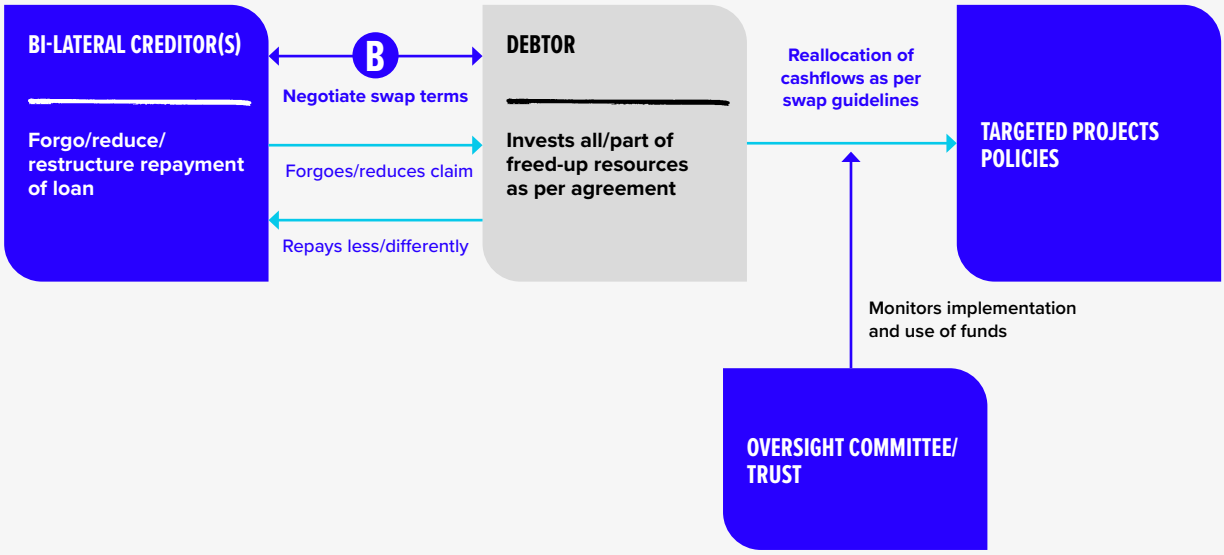


Figure 4: High-level directional prioritization of potential innovative solutions to address key NTD gaps

DEEP DIVES – CAN THESE PROPOSED INNOVATIVE FINANCE MECHANISMS BE APPLIED TO NTDS?

ARCHITECTURE

A BILATERAL SWAP



A BILATERAL SWAP WITH THIRD-PARTY IMPLEMENTOR

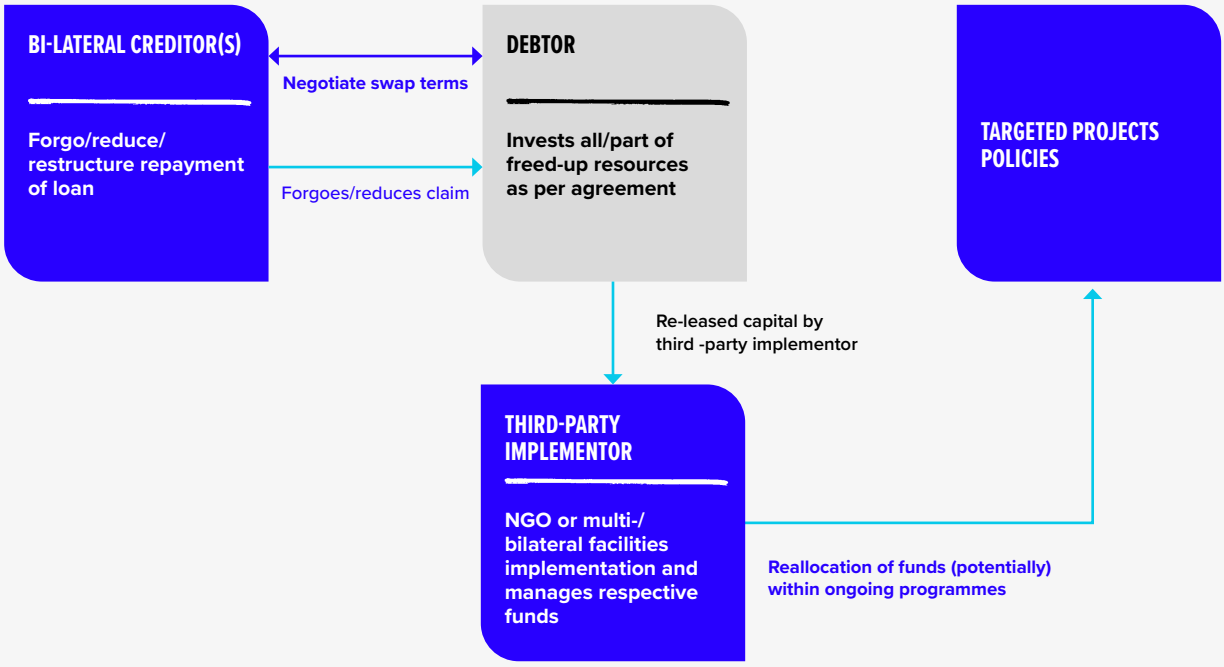


Figure 5: Development Impact Bond funding architecture

DEBT SWAPS

Overview

Debt swaps refer to a transaction where a country's debt is replaced by a new instrument or financial commitment which both allows some financial relief for the debtor and enables a reallocation of cash flows towards specific objectives. Debt swaps redirect capital that would have been utilized to pay off an original commitment towards grants, bonds, or funds for pre-agreed investments.

There are two broad debt swap types: i) A bilateral debt swap, which occurs directly between debtor and creditors, and ii) A third-party debt swap, which involves purchasing debt from an initial creditor and reselling it to a debtor through a donor. Key architectural considerations are depicted in Figure 5.

Several design considerations inform the negotiation of a debt swap:

- A clear target for re-allocated capital should be agreed upfront and aligned with creditor/debtor priorities.
- Governance structures need to be agreed and involvement of key stakeholders and their roles be well articulated. In addition to debtor and creditor(s), stakeholders could include third-party intermediaries, oversight committee, etc.
- The debt swap structure must adequately incentivize desired outcomes e.g., total funds and disbursement frequency, funding flexibility. Consideration can be given to including additional mechanisms to increase NTD funding or to incentivize targeted outcomes, for example philanthropic matching funds based on achieved outcomes.

Debt swaps are highly dependent upon the political commitment and willingness of creditors and debtors. Hence, the geographical and NTD scope of a potential "Debt2NTD" swap would largely be driven by the identification of suitable and politically committed creditor(s) and debtor(s). Negotiations would determine the most appropriate NTD-/value-chain component focus for the re- allocated capital. For example, cashflows re-allocated through the debt swap could be used to increase domestic budgets for a specific NTD or multiple NTDs, including program implementation, product procurement, M&E, logistics, or NTD-specific health system strengthening.

Beyond an exclusively NTD focus, a "Debt2Health" swap with a broader healthcare strengthening remit that included NTDs could be considered. NTD-specific outcomes could be incentivized in this context, through layering additional mechanisms including results-based philanthropic funding based on NTD-specific outcomes. Debt swaps can incentivize and increase domestic funding in NTDs, and address key risks faced in the NTD ecosystem, including those listed in Table 1.

Risks Addressed

Table 1: Debt Swap mechanism - Risks addressed

FINANCE RISK ADDRESSED	IF MECHANISM - MITIGATING CHARACTERISTIC
OPERATIONAL RISKS:	Increase in domestic financing to strengthen in-country capacities and capabilities to drive activities along the NTD value chain.
UNCERTAIN / MISALIGNED GAINS:	Increase in domestic funding/domestic ownership aligns incentives between who benefits and who invests.
ADDITIONAL/OTHER	Depending on the scope of the debt swap, additional risks can be addressed e.g., impact risk if capital re-allocated towards M&E/ surveillance.

The feasibility of a debt swap is highly dependent on the commitment and willingness of the debtor and creditors, and requires strong oversight to ensure reallocation of cashflows as per swap guidelines. Key design considerations include assessing the potential involvement of a third party implementor, ensuring the commitment of and alignment across stakeholders, and structuring the debt swap to incentivize outcomes. The challenges of introducing new debt swaps for NTDs are expected to be even greater in today's evolving global health landscape: given increased needs across the global health stemming from the COVID-19 pandemic, the appetite for introducing debt swaps for NTDs may be reduced.

MILESTONE-BASED FUNDING

ARCHITECTURE

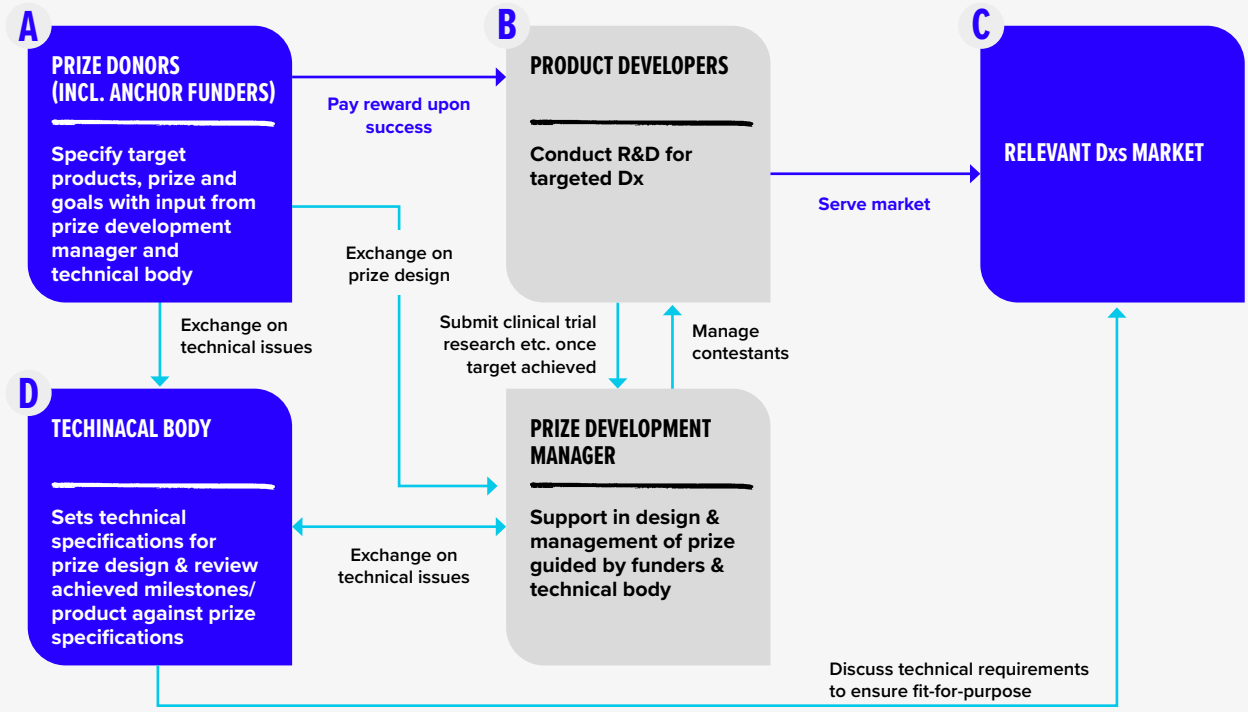


Figure 6: Milestone-based funding architecture

Overview

Milestone-based funding (MBF)—which also be referred to as milestone-based payments or milestone-based prizes—awards cash rewards for the achievement of specific objectives or milestones to incentivize the development of new technology, treatment, or tools.

MBF essentially is results-based financing, which is structured to incentivize an Award Holder to conduct early-stage R&D by providing the initial (or seed) funding at the beginning of the process and awarding subsequent tranches of funding once a milestone is achieved. Typically, MBFs do not provide 'prizes' on success, MBF acts as a payment for the R&D being conducted. Whether the Award Holder (i.e., organization or entity conducting the R&D) receives more funding is dependent on them achieving milestone criteria.

MBFs can be funded by a wide range of donors, including governments and philanthropic organizations. They can be combined with other mechanisms and contractual requirements to promote access, affordability, increase the pool and diversity of funding, and further strengthen incentives for researchers and developers. Competitions can include both milestone and end-prize components (e.g., awards at several stages including a prize for the final product). Key architectural considerations are depicted in Figure 6.

MBF is best formulated when the scope is targeted and where there is a specific need and potential funder interest. This could include:

1. Adapting the priority review voucher for regulatory expedited review of NTD diagnostics;
2. Patent boxes;
3. Pre-purchase agreements;
4. Point of Care test for NTDs where currently none are available, such as Leprosy;
5. New Point of Care test for NTDs where current options are not most fit-for purpose and there is a high disease burden and demand: e.g., Visceral Leishmaniasis, Lymphatic Filariasis, Onchocerciasis or Rabies;
6. Bi-/multiplex Point of Care test for NTDs with bi-/multiplex diagnosis needs and potential to attract additional non-NTD funders: e.g., Lymphatic filariasis and Loiasis, Onchocerciasis and Loiasis, Yaws and Syphilis, and lymphatic filariasis and malaria;
7. (New) distribution channels are available in the market - such as pharmacies.

The additional factors to further narrow down the target of a prize include awareness around diseases, as where awareness is very low, other interventions could be more impactful than developing a new diagnostic or whether ongoing R&D could close an existing gap.

A number of design considerations inform the scope of the award. For example, the product development milestones must be specifically detailed and technically achievable and the award can be linked to reaching a milestone towards an achievement. It is important to note that there is no risk for the Award Holder, as they receive their first milestone tranche in advance.

The following questions should be considered to fit the MBF award to the specific product needs and context:

- How to guarantee the continued availability of the award over a long potential development period, which can be a decade or more for drugs and vaccines?
- How will longer-term access to the award product be assured? How will future cost, IP transfer, penetration issues be addressed?
- Will potential manufacturers be provided with additional incentives?

There are also considerations to ensure implementation and use of the end product. For example, if the MBF is originating from outside an endemic country and has a nationally-directed objective, it is important that the prize is designed in a way that aligns with national priorities or designed in consultation with the appropriate country authorities.

Milestone-based funding may attract more lower-capital firms (e.g., biotechs, start-ups) given lower risks and costs. Alternatively, depending on the level of resourcing, MBF may not be attractive enough for larger firms where there is a relatively small or low-priced market.

As noted above, investments in early-stage research and development through MBF would work well for fit-for- purpose diagnostics, which can be further incentivized through addressing key risks listed in Table 2.

Risks Addressed

Table 2: Milestone-based funding - Risks addressed

FINANCE RISK ADDRESSED	IF MECHANISM - MITIGATING CHARACTERISTIC
IMPACT RISKS:	Targeted, efficient, impactful use of donor funds pays for each phase of development in advance as milestones are reached.
UNCERTAIN / MISALIGNED GAINS:	R&D in line with funder objectives and incentivized through increasing rewards (linked to success) and de-linking from market/prices.
OTHER RISKS:	Depending on MBF features, additional risks e.g., demand uncertainty or capital risk (including limited domestic financing) can also be addressed.

Beyond the financial risks, another key challenge is whether to fund a single project versus a portfolio, as well as a consideration of how far the available funding will go, given the challenges with stage gaps and with products being designed for different stages without a clear justification of which should be prioritized.

In summary, the success of MBF will depend on well-defined specifications that reflect the interests of stakeholders and a sufficient level of available funding to incentivize product developers. If interested donors are identified, there is a clear opportunity to launch milestone-based funding to target high-burden NTDs that lack fit-for-purpose diagnostics. Specific diseases that this type of IF mechanism could be most impactful and feasible for include Leprosy, Visceral Leishmaniasis, Lymphatic filariasis, Onchocerciasis, Rabies, Loiasis and Syphilis.

DEVELOPMENT IMPACT BONDS (DIBs)

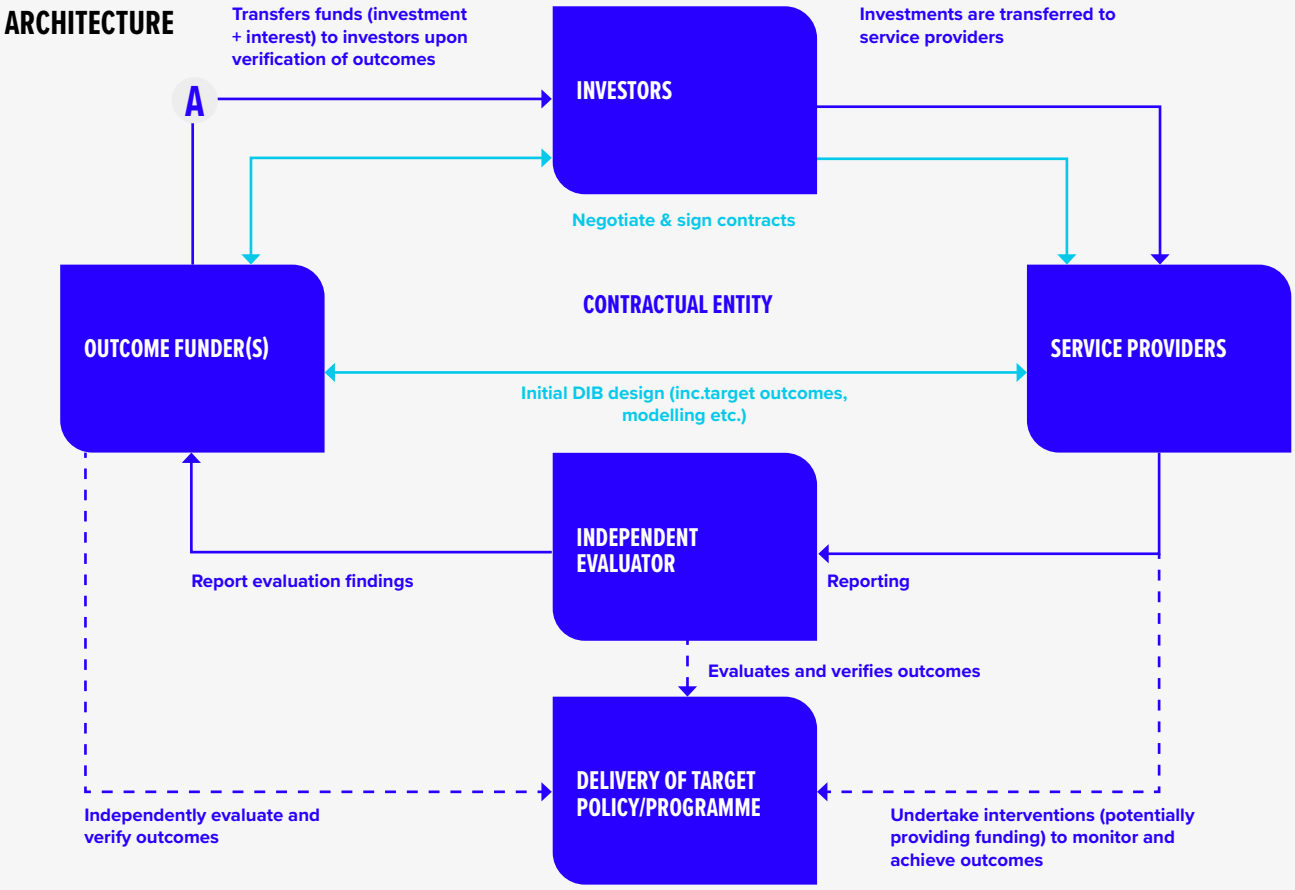


Figure 7: Development Impact Bond funding architecture

Overview

Development Impact Bonds (DIBs) use private investments from banks or philanthropies to provide upfront risk capital to service providers for development programs.

Funding is only repaid—at a potential return rate below the market rate—by a third-party (institutional donors for example) once clearly defined and measured development outcomes are achieved. The overall risk is shared between investors, outcome funders and service providers (See Table 3). Key architectural considerations are depicted in Figure 7.

DIBs could either be used for broader healthcare strengthening (e.g., with extra outcome payments for NTD-specific outcomes) or NTD-specific interventions. Programs that build on synergies between diseases/sectors have the potential to attract non-traditional NTD investors.

DIBs targeting NTD-specific interventions or programs are best suited for use where they set out to scale-up existing, effective, fit-for-purpose tools or programs, given they need public engagement and mobilization of financial resources to support effective operational delivery to be successful. They need a clear definition of scope, including geography, desired outcomes, timeline and required program/policies. Within that scope, clear measurable and defined outcomes and a clear, well-defined population cohort must be included to ensure feasibility of consistent monitoring of outcomes that can be defined to trigger bond payments.

Another clear target for DIBs is for programs that need to fund programmatic change to allow scale-up and impact, for instance, to fund the change process from broad, expensive mass drug administration approaches aimed at disease control—at the risk of creating significant antimicrobial resistance—to more targeted test & treat approaches to drive elimination efforts.

Negotiations to align on payment triggers, levels of return, etc. between investors, outcome funders and service providers can be extensive and burdensome given potential conflicting perspectives and priorities on funding and contract structures. The selection of service providers should consider alignment of the organization and its respective programs with outcome funder objectives.

Well-functioning organizational structure with effective communication between independent evaluator, service provider, outcome funder and investors ensure strong governance, no misuse of funds or tampering of outcome metrics and alignment on desired outcome. Surveillance and monitoring and evaluation are core to DIB, given outcome payments are contingent on ability to evaluate whether pre-agreed outcomes have been achieved—hence, coordinated effort is required to ensure robust performance management system. Equally, the financial plan should clearly reflect the program funding and payment structure including the amount of max outcome funding, levels of return, timing, and thresholds for payment triggers.

Risks Addressed

Table 3: Development Impact bonds - Risks addressed

FINANCE RISK ADDRESSED	IF MECHANISM - MITIGATING CHARACTERISTICS
OPERATIONAL AND IMPACT RISKS:	DIBs transfer part of operational & impact risk to investors with higher risk appetite (private investors vs. governments/ donors) and improve operational and outcomes through providing incentives and support structures.
UNCERTAIN / MISALIGNED GAINS:	DIBs secure necessary upfront financing through attracting private investments to sustainably deliver interventions at scale and introduce incentives for investors to support the performance of projects.
LONG-TERM TIMELINE:	DIBs take 1-3 years to design and set up incl. statistical modelling to estimate expected outcomes and costs, stakeholder engagement, contracting, establishment of surveillance systems, baseline surveys, piloting reporting, strengthening policy framework and 3-5 years for implementation. However, a longer implementation phase with a tiered-payments approach could be considered to ensure sustained impact.

The level of funding required for the DIB will depend on the scope of the program, including target geography, population, NTDs and agreed outcomes. However, the level of funding required is unlikely to exceed $100 million dollars, given the need for a targeted scope to deliver against. Upfront and outcome funders are required for the design of the mechanism, including the definition of desired outcomes.

POOLED PROCUREMENT

ILLUSTRATIVE ARCHITECTURE AND STAKEHOLDERS

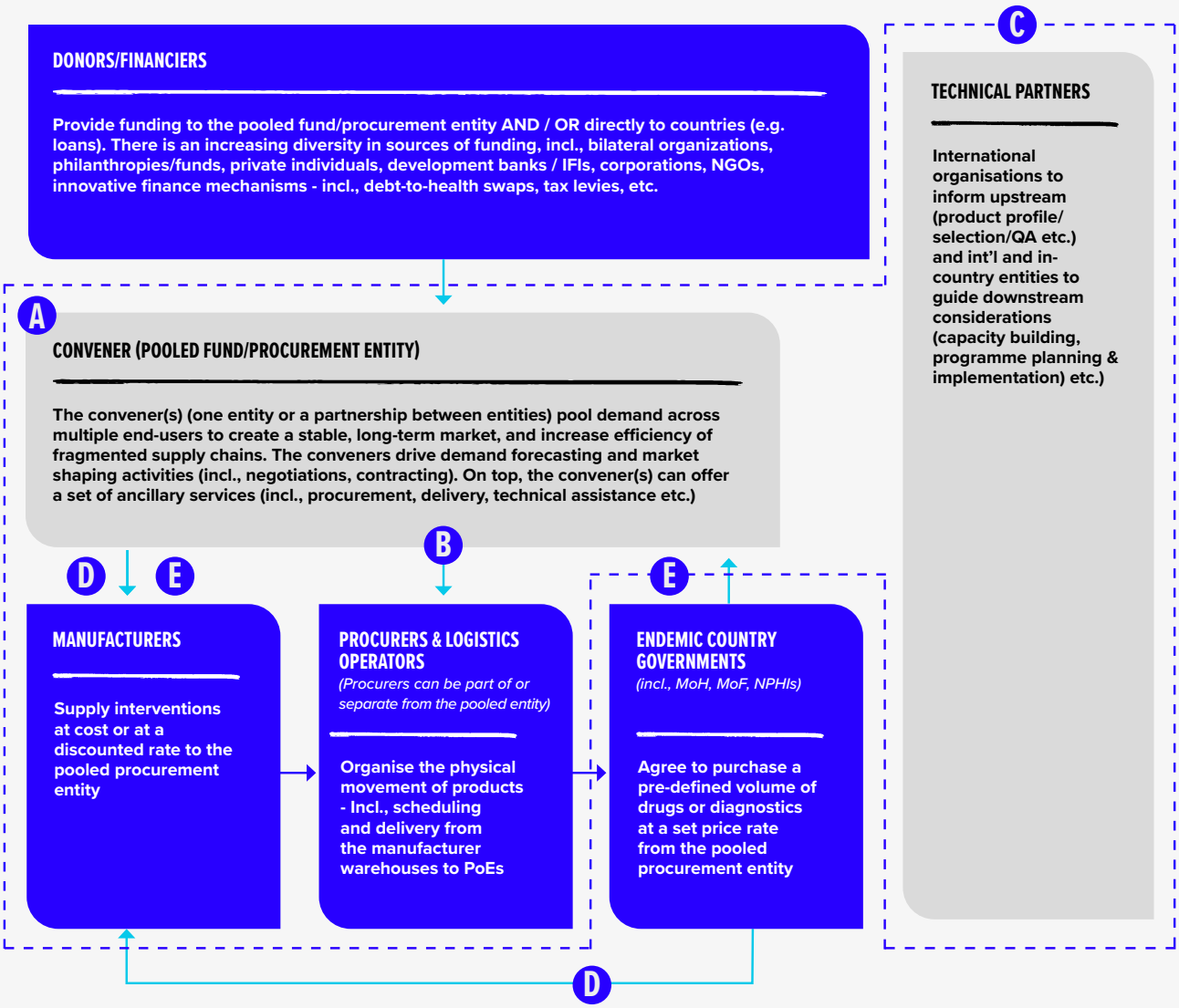


Figure 8: Pooled procurement funding architecture

Overview

Pooled procurement refers to the bulk purchase of interventions from producers at higher volume and thus lower cost and high volume to provide these interventions at a lower rate. While not a financing instrument per se, the potential of pooled procurement for NTDs centers around the industry mechanisms that surround procurement of health commodities.

Pooled procurement conveners pool demand across multiple end-users to create a stable, long-term market, thereby increasing the efficiency of fragmented supply chains. Pooled procurement can mitigate risk and aggregate demand, which can create meaningful market incentives for innovation and reduce the costs of delivery. In the context of this paper, the IF-NTD Core Group views pooled procurement platforms for NTDs opportunistically—both as a market-shaping mechanism integrating commodity volume and price requirements, increasing private sector and PDP incentives, and as an incentive to NTD stakeholders to pool NTD financing more effectively. Pooled procurement could be well suited to address access risks and challenges, see Table 4.

Risks Addressed

Table 4: Pooled procurement - Risks addressed

FINANCE RISK ADDRESSED	POOLED PROCUREMENT - MITIGATING CHARACTERISTICS
DEMAND UNCERTAINTY	Pooled procurement can defragment demand and incorporates a longer-term view.
OPERATIONAL RISKS:	Capacities and capabilities of pooled procurement partners can reduce operational risks, including risk allocation that currently is allocated to the in-country distributor, which increases their costs of capital, therefore increasing ultimate market prices.
TRANSACTION COSTS:	Central negotiations and collaboration on delivery can achieve economies of scale and scope and reduce transaction costs.
UNCERTAIN / MISALIGNED GAINS:	Clarity and certain demand provide incentives for manufacturers to maintain supply capacities.
TRANSPARENCY	A mechanism that can provide funding and capture prices at every stage of the supply chain (from manufacturer to importer of record, distributor, and re-seller) can inform stakeholders and empower them for better negotiations.

These advantages have led to pooled procurement being widely used for global health, with the Stop TB Global Drug Facility, UNICEF, Gavi and The Global Fund all offering examples of well-functioning pooled procurement mechanisms. Examples of regional pooled procurement instruments include the Pan American Health Organization (PAHO) Revolving Fund, the Asia Pacific Vaccine Access Facility (APVAX) and the Africa Vaccine Access Trust (AVAT). Recent large-scale pooled procurement for COVID-19 tools (C19RM, COVAX) showed the potential for rapid development, wide and large-scale global supply, and the ability to drive affordability of health products. In the NTD space, the Children's Investment Fund Foundation (CIFF)-funded ARISE Program[10] used pooled procurement to deliver over 20 million preventive treatments for Lymphatic Filariasis and Schistosomiasis in one year, on an 'emergency' basis, following the sudden end of the UK Government-funded Ascend Program in 2021.

Pooled procurement mechanisms can set up new structures or can potentially build on existing pooled mechanisms. The pooled fund can cover end-to-end services (demand-pooling to delivery) or focus on specific parts of the value chain (such as basic information sharing, demand pooling, negotiations, contracting, delivery etc.). Pooling of funds can be embedded in the core pooled procurement entity responsible for supplier negotiations (e.g., Gavi model) or can be split out in a separate trust (e.g., AVAT model). Often, the beneficiary countries able to use these mechanisms (and obtain preferential prices) are limited to LMICs, but access can be expanded, and may offer an incentive for high-income countries that want to access products very occasionally. Ensuring that the mechanism is also used for procurement from domestic budgets is critical, as some countries require competitive bidding for health commodities and the pooled systems don't always participate in domestic tenders.

There are multiple options for the flow of funding to the manufacturers: via the pooled entity—either directly or via trust—or directly from countries. Payments can include:

1. payment for specific product / service (based on commercial negotiations);
2. payment by patient (set price for the treatment for one patient);
3. payment by clinical outcomes or;
4. payment by value (e.g., beyond clinical outcomes, such as economic value, qualitative value).

[10] https://www.crownagents.com/project/arise-accelerating-resilient-innovative-sustainable-elimination-of-ntds/

The funding flows and payment methods must encompass adequate seed funding and any transactional or outcomes-based payments.

The incentive structure must encourage domestic ownership of the instrument, whether through co-financing or, at least, demand guarantees, to ensure sustainable demand. The interventions (Rx/diagnostics) are either paid fully by the beneficiaries or are co-financed, with the participation of one or a consortium of partners. Other elements, such as demand guarantees, can also play an important part in generating sustainability. Co-financing can be either a flat percentage of the product price or—as in the Gavi model—provided at tiered co-financing levels, based on the specific country's domestic financing capacity/GNI levels.

The potential target scope for an IF-NTD pooled procurement platform must be narrowed by geographies, populations, or disease scope. At first glance, the most promising targets include products that are:

- Under-supported or potentially losing donation support soon;
- Currently not used or available with access challenges for NTDs, including cost factors;
- Tackling high burden or high-prevalence NTDs, especially within a specific region where pooled procurement could benefit from efficiencies and existing collaboration structures.

Time-to-impact is dependent on the potential to leverage existing mechanisms and building appropriate political commitment for any new pooled procurement instrument. Normally, it could be expected to take one-to-two years to design a pooled procurement entity (including stakeholder engagement, negotiations / contracting, etc.), and an additional year to ramp up operations (operationalizing supply chains, start the supply of products). Impact generation starts roughly at year three. See Figure 8 for an illustrative architecture for IF-NTD pooled procurement.

NTDs with sub-optimal support and a burden of disease and prevalence could be potential targets for pooled procurement. Depending on geographical coverage, pooled procurement could potentially facilitate 1-310 million units per annum. Though it is important to note that the prevalence is likely underestimated for many NTDs as testing and diagnostics needs are inadequate and for some deadly diseases, incidence often isn't reported except on death certificates.

In summary, a pooled procurement platform could address supply chain issues partially but not fully. It would require an initial strong commitment and political will for stakeholders at the global and national levels—which may require a heavy investment of time in the setup phase. At a regional level, pooled procurement may be a useful instrument for NTD treatments and diagnostics. A next step could be to explore the opportunity for endemic countries to include NTD commodities on the African medical supply platform that was developed for COVID-19 countermeasures.

BOX 2. POOLED PROCUREMENT FOR NTDS: THE CASE FOR DIAGNOSTICS

While pooled procurement for diagnostics is used for TB and malaria, this instrument hasn't been applied commonly or systematically for NTDs. A few procurement mechanisms cover diagnostics; those that cover NTD-related diagnostics in their product catalogue, including UNICEF (dengue) and Africa Medical Supplies platform (for dengue and chikungunya).

There are also some dedicated diagnostics procurement platforms, such as the WHO Pooled Procurement for Lymphatic Filariasis. WHO also helps coordinate the global procurement of diagnostics for use in the Global Program to Eliminate Lymphatic Filariasis. Through the WHO, diagnostics are subsidized for buyers (e.g., end-user governments) to monitor the impact of mass drug administration programs with the goal of being able to determine progress against the elimination targets.

The IF-NTD Core Group analyzed which market barriers could best be resolved with pooled procurement for NTDs, they include:

- Fragmented, unpredictable demand: Diagnostics currently deployed for NTDs, but could benefit from scale, aggregated demand, and market transparency (e.g., diagnostics under donations but limited quantities, diagnostics not under donations but countries need additional tests for case confirmation, cases where countries are close to elimination and lower demand could not otherwise benefit from lower prices, etc.
- Lack of availability, affordability, and awareness for procurement: Fit-for-purpose diagnostics on the market, countries may not have access due to cost or other limiting factors or multiplex-type of diagnostics that can be highly synergistic across diseases beyond NTDs
- Insufficient funding for late-stage development: Alternatively, diagnostics that are in late stages of development that NTDs could benefit from advance offtake agreements, which could be potentially initiated while the pooled procurement platform is being set-up / operationalized.
- Global need: To further refine scope (if needed), similar criteria could be used for diagnostics as for drugs (presented earlier), including burden of disease, prevalence of disease etc. on a local / regional / global level.

Based on this analysis, and especially where point-of-care tests are available but are not being used at scale, the following diseases were identified as strong candidates for pooled procurement:

- Foodborne Trematodiases
- Echinococcosis
- Rabies
- Chromoblastomycosis and other deep mycoses
- Cutaneous Leishmaniasis
- Human African Trypanosomiasis gambiense
- Chagas

CONCLUSION

Despite progress toward disease elimination, more can and should be done to eliminate NTDs. More of the same is not enough: there is a meaningful potential for innovative finance solutions to provide transformative impact.

Innovation is possible: this field is ripe for new approaches, new financing mechanisms, and new partnerships. The NTD space remains reliant on traditional financing—but the global health landscape has profoundly changed over the past few years, and both existing and new stakeholders may be open to new solutions to long-standing problems. COVID-19 may have narrowed the financing arena, but that has led to new thinking on financing research and development products across disease areas. NTDs can benefit from this thinking.

There is a catalytic opportunity for many NTDs that have become a victim of their own success, i.e., reduced burden of NTDs has also reduced their visibility and political popularity. To be able to eliminate NTDs, more investment is needed now at the last mile, and better tools to find, test and treat the remaining patients, often from more remote and hard-to-find or vulnerable patient groups, are critical.

We have identified some promising areas for innovative finance, but there are many more. There is potential for IF instruments to be used in combination to even greater effect.

This includes renewed considerations around advance market commitments and facilitating increased de-risking of private sector investments, as well as an understanding of how new promising efforts to localize manufacturing and supply chains, particularly in Africa, present an opportunity to develop new financing mechanisms that integrate NTDs. What is needed is additional focus on cross-sectoral efforts to understand which mechanisms can work in specific countries and regions with specific diseases. Partnering with the Uniting Efforts initiative led by Global Health Innovation Technology Fund (GHIT) and United Nations Development Program (UNDP), endemic-country voices, including civil society and patients, and realities need to be at the center of these conversations. Potential funders' interests and ability must be shared and considered to shape a realizable solution.

This discussion paper aims to engage new and potential stakeholders committed to eliminating NTDS globally. GLIDE and its partners acknowledge that there will not be a single instrument that can address all the gaps to eliminate NTDs.

Beyond this paper, GLIDE will facilitate several roundtables, in collaboration with partners, to resolve some of the questions through the contributions of endemic countries, impacted civil societies, NGOs and PDP, industry and private sector, and all potential donor and investment entities. Together, we can build toward a sustainable and significant solution towards systemic change for improved NTD treatments and diagnostics.

ANNEX A:
LIST OF CORE GROUP MEMBERS AND ORGANIZATIONS

*Note that some members participated in their personal capacity

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